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Analysis and validation of a Parkinson's disease register as a recruitment tool for clinical studies

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ABSTRACT – Promotion of research is a key strategy of the National Health Service (NHS). Currently, many patients are not afforded the opportunity to participate in clinical studies. A register of research-interested patients has the potential to maximise inclusivity. We have established a register of research-interested patients with Parkinson's disease within the South West of England, with pragmatic inclusion criteria and multiple recruitment routes. We undertook an analysis of the register, investigation of its utility as a recruitment tool and a survey of recruiters. There were 529 active participants; 30% were self-referred and 70% were recruited by a healthcare practitioner. Response rate to annual questionnaires was 86.5%. Staff time required for pack preparation, recruitment and data entry was 15 min per new recruit and 5 min per follow-up questionnaire. In total, 85% of recruiters viewed the register positively. A single mailing to participants resulted in a recruitment rate that significantly exceeded that achieved by traditional recruitment methods.

KEY WORDS: Parkinson's disease register, registry, recruitment tool

Introduction

Research-active organisations experience better patient outcomes[1] as well as other benefits,[2] compared with centres which are not research active. The promotion and conduct of research are core National Health Service (NHS) functions.[3] However, many patients are not afforded the opportunity to participate in clinical studies. Limitations to the involvement of patients with Parkinson's disease (PD) in clinical studies are disease-specific and reflect the inherent difficulties in conducting clinical studies in older people.[4] Traditional recruitment relies on face-to-face contact between patient and recruiter and generally occurs in a secondary care setting, community-based cohorts being more difficult to recruit. Therefore, studies involving such patients are limited. In addition, the demands of a busy clinical service might limit the participation of interested healthcare practitioners (HCPs). As a result, trial data might be generated from a non-representative patient population. One means of overcoming these challenges is to establish a register of research-interested patients. As well as facilitating recruitment, registers can inform clinical trial design.[5] Several PD registers have previously been established[6–12] and used to provide information on epidemiology, clinical features and therapeutics.

In this article, we describe our experience of establishing the Parkinson's Register of the Dementias and Neurodegenerative Diseases Research Network (PRO-DeNDRoN), an inclusive register of research-interested patients with PD within the South West of England. The inclusion criteria and recruitment routes are broad, the information collected being the minimum required to facilitate study recruitment. Further determination of individual eligibility for specific studies is then performed by investigators as part of the screening process. Here, we analyse the register three years after it was initiated, with the primary aim of demonstrating the pitfalls and benefits of establishing the register, as well as its utility as a recruitment tool. We also demonstrate that the model used enables the register to fulfil its aims in a manner that is pragmatic and resource efficient.

Methods

Overview

Register development and management is overseen by the PRO-DeNDRoN coordinating team. A steering committee independently oversees the running of the project, monitors recruitment rate and reviews studies applying to use the register. The committee includes representatives of each of the main recruitment sites as well as a patient and carer representative. Ethical approval for the register was obtained in August 2007, with a substantial amendment being approved in August 2008 following an adjustment to the consent form. All register participants were required to re-consent to remain on the register.

Database design

A bespoke database for the register is hosted on a Structured Query Language (SQL) server within the University of Plymouth (UoP) and is backed up daily. Access is password protected and restricted to the database development team. Front-end access is web based to enable online access at different levels. Data are entered into the database from patient-completed questionnaires by the study administrator. Data input and utilisation of the database informs its continued development.

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Participating sites and recruitment

The project was initiated in September 2007 in the peninsula of Devon and Cornwall in the South West of England and was extended in November 2009 to cover the whole of the South West DeNDRoN region. The recruitment strategy includes self-referral by either telephone or returning a reply slip from a flyer, recruitment in clinic by an HCP or research nurse, or recruitment at a local PD meeting. Personal details of new referrals are kept for 90 days, following which they are removed from the database if the consent form has not been returned.

The inclusion criteria are as follows:

- must be more than 18 years of age
- must reside within the South West DeNDRoN region
- must have had a clinical diagnosis of PD
- must be capable of giving fully informed consent.

There are no exclusion criteria.

Interested patients are provided with an information sheet, consent form, baseline questionnaire and freepost envelope to return the documentation to the coordinating centre. Patients consent to their details being kept on the database, their medical records being consulted when necessary, being contacted in the future regarding studies for which they might be eligible, and for their anonymised data to be shared with local authorities for the purpose of service development. The questionnaire asks for details regarding demographics, disease duration, diagnosis and therapies (pharmacological and non-pharmacological). The register is updated on an annual basis using a postal questionnaire. Patients and referring clinicians receive an annual newsletter giving details of clinical research activity in the region.

Register utilisation by researchers

The procedure for allowing researchers access to the register comprises a feasibility screen, steering committee approval and letters of invitation being sent to eligible patients by the PRO-DeNDRoN team, with reply slips to be sent to the researchers. Researchers are sent anonymised data informing them of which patients have been sent letters. Researchers confirm who has been assessed and/or recruited to their study, thereby preventing patients from being recruited to too many or conflicting studies. This information also facilitates monitoring of recruitment levels and assessment of register utility.

Register utility

We conducted an initial study of utilisation of the register in association with the Cure Parkinson's Trust (CPT). The register has also been used to recruit to two further studies: a sample collection study and a questionnaire-based study.

Survey of register recruiters

We conducted a web-based survey of HCPs who might have recruited to the register to ask for their feedback, specifically regarding ease of recruitment, any concerns that they or their patients might have and their impression of register utility.

Results

Demographics of recruits

At the time of register analysis (October 2010), there were 529 active participants (589 recruits, 60 withdrawn). There were 327 (61.8%) men and 202 (38.2%) women. Mean age at time of consent was 69.9 yr and, at time of register analysis, 71.4 yr. Mean disease duration at the time of recruitment was 7.4±6 yr from symptom onset, 6.5±5.7 yr from first consultation with a general practitioner and 5.7±5.4 yr from diagnosis.

Routes of referral and recruitment

Recruitment packs were distributed either directly to patients following self-referral (n=262, of which 177 (67.5%) were returned) or HCPs for distribution (n=1,246, of which 412 (33%) were returned). It is not possible to determine how many packs were distributed by HCPs and not returned. In 90 instances, the consent form was not fully completed and had to be returned to the patient; in total, 75 forms were eventually returned fully completed. Approximately half of the incomplete forms were lacking a patient signature. In 22% of cases, the last box ('I consent to take part in the study') on the consent form was not initialled. The overall response rate to annual questionnaires was 86.5%, although this reduced with time (Table 1).

Diagnosis of recruited patients

A diagnosis of PD was assumed in initial recruits (n=214); a question investigating this in more detail was added to amended versions of the baseline questionnaire (Table 2). Of the 529 recruits who provided diagnostic information, 92% had a baseline diagnosis of PD (or were assumed to have PD), 4.2% had possible or probable PD, and 2.1% had Parkinsonism or Parkinson Plus syndrome. The proportions in those who provided this information in their 24-month questionnaire (n=127) were 83%, 2.4% and 5.5% respectively; 20 (15.7%) had a changed diagnosis from month 12 (Table 3), and 23 (18.1%) from baseline.

Non-pharmacological therapies

The details of non-drug therapies, both formal and informal, being accessed by patients are detailed in Table 4. The most common was physiotherapy (20% at baseline, 19% at month 12 and 17.2% at month 24).

Table 1. Response rate to questionnaires.

	Total sent	Total returned	Response rate (%)
Total number of questionnaires sent	1,152	991	86.5
Baseline	589	585	99.3
Month 12	330	260	78.8
Month 24	233	146	62.7

Table 2. Diagnosis at baseline and follow-up.

Diagnosis	Baseline (%)	Month 12 (%)	Month 24 (%)
Null[a]	214 (40)		105 (83)
Parkinson's disease (PD)	275 (52)	182 (88.3)	3
Possible or probable PD	22	4	78.8
Parkinsonism or Parkinson's plus syndrome	11	7	7
Not sure	4	7	4
Other	3	6	8
No response	56	54	19
Total	**585**	**260**	**146**

[a]Null indicates the change in questionnaire, presumed to equal PD.

Table 3. Details of change in diagnosis between months 12 and 24.

Month 12 diagnosis	Month 24 diagnosis	Total
Parkinson's disease (PD)	Other	3
	Parkinsonism or Parkinson Plus syndrome	4
	Not sure	1
	Possible or probable PD	1
Parkinsonism or Parkinson Plus syndrome	Other	1
	PD	2
	Not sure	1
Other	Parkinsonism or Parkinson Plus Syndrome	1
	PD	1
Possible or probable PD	Not sure	1
	PD	1
Not sure	PD	2
	Possible or probable PD	1

Table 4. Details of non-drug therapeutic resources utilised by patients.

	Baseline	Month 12	Month 24
Number of participant responses recorded	**546 of 585**	**228 of 260**	**128 of 146**
Total responses listed	**611**	**246**	**146**
None/Not answered	383	162	88
Total number of treatments listed	**228**	**84**	**58**
Physiotherapy	109	43	22
Speech and language therapy	48	14	12
Occupational therapy	15	6	3
Massage	3	4	2
Acupuncture	2	0	1
Reflexology	4	1	1
Other:	47	16	17
Exercise	18	5	7
Pilates and/or yoga	4	1	
Tai Chi	1		
Deep brain stimulation	4	1	1
Podiatrist	1	1	1
Other medication assistance	2		
Counselling	1	2	1
Education	1		
PD nurse specialist	3	1	
Botulinum toxin clinic	1		1
Chiropractor and/or osteopath	4	1	
Memory clinic and/or support group	2		
Lip strengthener	1		
Bone density scan	1		
Alexander Technique	2		1
Craft	1		
Hearing aid		1	
Reiki		1	
Dietician			2
House alterations			2
Other assistance		2	1

Table 5. Duration on register and reason for withdrawal.

Reason for withdrawal	Number	Time on register (mo) mean ± SD	Age at withdrawal (yr) mean ± SD
Total	**60**		**76.6±9.2**
Re-consent	22	17.6±3.7	
Deceased	19	18.1±7.8	81.7±4.7
Moved away	2	18.5±7.8	
Unknown	11	11.9±8.1	
Other:	6	6.3±7.4	
Duplicates	2		
Deterioration	3		
Only has Parkinson's disease in legs	1		

Withdrawals from the register

In total, 40 men and 20 women had withdrawn from the register, representing approximately 10% of the recruits of each sex. The average duration on the register and the reason for withdrawal are given in Table 5. In total, 68% of withdrawals were because of either death of the patient or failure to re-consent. This was reflected in the annual withdrawal rate, which was higher in 2009 (10%), probably precipitated by the change in consent form, compared with 2008 (3.3%) and the first 10 months of 2010 (1.9%).

Register utilisation

In our initial feasibility assessment, 256 participants were approached with a single mailing to take part in the CPT pilot, seeking patients who had a follow-up appointment with their PD practitioner within the following eight weeks. In total, 33% did not respond, 45 (17.6%) stated that they did not wish to take part and 127 (49.6%) expressed a desire to participate. Of these 127, 45 completed the pilot within the required timeframe and a further 10 shortly thereafter. By comparison, another UK centre used traditional face-to-face recruitment in clinic over a four-week period. Approximately 30 patients were approached, of whom six completed the pilot.

The register was subsequently used for recruitment to a sample collection study in Cornwall. Traditional recruitment methods had resulted in five patients being recruited in the six months before using the register. In total, 113 patients on the register were approached by a single mailing to take part in the study in March 2011; 91 responded positively (80.5%), 61 of whom had been recruited by October 2011 (54% of those approached). A questionnaire-based study also utilised the register for recruitment in April 2011, when the number of people on the register was greater than that at the time of analysis. In total, 627 patients were approached by a single mailing, of whom 358 (57%) expressed interest in the study, with 295 finally being recruited (47% of those approached).

Survey of PD practitioners

A web-based survey was emailed to 59 PD practitioners, comprising geriatricians and neurologists, research nurses and PD specialist nurses. The overall response rate was 51% (n=30). In total, 63% of responders reported recruiting to, or arranging recruitment to the register. Of the 11 responders who had not recruited to the register, 45% cited lack of appropriate paperwork, 36% lack of time in clinic, 18% forgetting about the register in the clinic setting and 36% being unaware of the register.

Recruitment mainly occurred in clinic with the primary method of recruitment being for the patient to be given a recruitment pack (70%). Other methods included passing the patient's details to the research nurse (55%) or the PRO-DeNDRoN team (20%). The time taken to recruit patients was reported as 0–5 min by 75% and 5–10 min by 25% of recruiters. One-third of respondents had experienced patients refusing to take part in the register, for reasons including lack of interest in research, unwillingness to complete questionnaires, concerns about data access (one patient) and struggling to come to terms with their diagnosis. Three respondents had received feedback from patients about the register, namely that they appreciated the opportunity to take part in research.

Of the respondents, 85% felt that the register was a useful means of facilitating research and providing data for planning of service provision. However, concern was expressed over access to data, as well as the extent to which patients would be approached to take part in studies for which their treating physician would deem them unsuitable. Suggestions for improvement included development of a website for patients to register their interest and ensuring involvement of local practitioners in recruitment to potential studies.

Discussion

Research as a core NHS activity is receiving increasing recognition within the UK.[2] Centrally funded infrastructure has been developed to assist with delivering research opportunities to all patients within the NHS. Despite this, many patients with PD are not afforded the opportunity to take part in clinical studies. We have established a register of research-interested patients with PD in a resource-efficient manner and have demonstrated that it can successfully be used as a recruitment tool. Most practitioners require less than 5 min to discuss the project with potential participants. Total staff time required for pack preparation, recruitment and data entry is 15 min for each new recruit and 5 min for each follow-up questionnaire. Our experience of register utilisation has demonstrated that a single mailing to participants can result in a final recruitment rate that significantly exceeds that achieved by traditional face-to-face recruitment.

A common concern with regard to registers is the need to balance patient privacy with investigator access to patients.[13] Such concerns have been highlighted by both patients and clinicians participating in our register. To minimise these concerns, it is explicit that no patient details are shared with

researchers, unless the patients themselves return the reply slip to the investigator.

Difficulties of recruiting to the register

Recruitment rate following self-referral was 67.5%. It was not possible to determine active recruitment figures from our data. However, in some centres, there was insufficient time in clinic for recruitment by HCPs. In others, physicians wished to act as 'gatekeepers' for research involving their patients. This phenomenon is well demonstrated in trials involving older people,[14] despite evidence that patients themselves are willing to participate in clinical studies.[15] Nevertheless, it has equally been demonstrated that endorsement of a study by the patient's own physician can be a powerful recruitment tool.[16] By adjusting paperwork to reflect local ownership of the register, and including representatives from each of the sites on the steering committee, we were able to overcome these misgivings.

Difficulties with retention

We found a reduction in response rate to the annual questionnaires over the 3 years. The problem of attrition in long-term studies involving older people is well documented, factors including being in poorer health and cognitive impairment.[17] Web-based access to details of their own patients on the register could provide clinicians with an opportunity to send a reminder if a questionnaire has not been returned.

Diagnosis

A clinical diagnosis of PD carries with it a degree of uncertainty, with studies estimating correct diagnosis in 83% of cases in a community setting,[18] 82% of cases in secondary care[19] and 91% in a specialist movement disorder clinic.[20] A previous community-based PD registry was able to confirm the diagnosis in 78% of registrants.[11] We found a self-reported rate of PD diagnosis in respondents of 92% at baseline, 88% at month 12 and 83% at month 24, probably reflecting the overdiagnosis of clinically uncertain cases at presentation.[21] Despite 30% of participants self-referring to the register, all patients were being seen in secondary care, either by a neurologist (40%) or a geriatrician with a specialist interest in movement disorders (60%). Therefore, our diagnosis figures are consistent with those previously reported for secondary care. Although these figures could be regarded as limiting, the diagnostic inaccuracies are offset by the potential for inclusivity. Studies utilising the register will have their own screening procedures to ensure eligibility. There is also the facility to scrutinise patients' medical records to verify diagnostic information.

Register benefits

We are able to extract data that might be of value in planning future research initiatives and service developments. For example, the delay between symptom onset and diagnosis might represent an opportunity for education of patients and GPs. The identification of alternative resources being utilised by patients can facilitate studies focussing on particular interventions and inform planning of local service provision. Finally, the register provides a means of increasing overall research awareness among patients and HCPs.

Planned register improvements

We have identified several areas of potential improvement, including the visual layout of the consent form to increase accuracy of completion, development of web-based access for expression of interest and expansion of our recruitment strategy to include primary care and patients with cognitive impairment.

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