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and Northern California Ascertainment

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14. ABSTRACT The primary goal of this project is to conduct a pilot study for the legally mandated population-based Parkinson's disease (PD) registry in the state of California. This study is one of two linked research programs with the goals of establishing and using California PD registry data. The Parkinson's Institute was funded to serve as the coordinating center for the pilot project (including maintaining a secure data enclave), conduct ascertainment work in Santa Clara County and explore utilization of registry data. To date, approximately 8,000 parkinsonism cases have been identified in Santa Clara County via legally mandated reporting sources, including physicians and health care facilities. With the majority of case-finding work accomplished, project effort is being directed to investigate possible associations between PD and toxicant exposure using state databases, to define disease prevalence and care patterns among registrants, and to assess the value of the registry to stakeholders.					
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A. Introduction

This project consists of a pilot study conducted in partnership with the California Department of Public Health (CDPH) and the University of California-Los Angeles School of Public Health (UCLA) to implement a legally mandated statewide population-based Parkinson's disease (PD) registry in California to serve health surveillance and research aims. As the coordinating center for the surveillance activities, the Parkinson's Institute has achieved multiple milestones, including the development of data collection tools, staff training materials, a secure database, and policies and procedures for registry operations. Case ascertainment activities by the PI and UCLA have been underway in the four target counties in northern and southern California for more than two years with approximately 10,000 PD cases identified to date. As the database grows, we are applying systematic de-duplication procedures to ensure unique entries, validating registry content (i.e. confirmation of diagnosis and other qualifying criteria) and evaluating the quality and completeness of registry data using census, Medicare and death certificate data. Other analyses considered include assessing differences in PD prevalence and patterns of care across different groups, exploring associations between toxicant exposure and PD patterns utilizing state hazardous substances databases, determining the value of the registry to key stakeholder groups, and evaluating the cost of registry operation.

B. Body

The goals of this project are to conduct a feasibility study for the legally mandated California statewide population-based PD registry and utilize pilot registry data to explore trends in PD prevalence, patterns of care, possible relationship to the distribution of environmental toxicants, stakeholder priorities and cost efficiency of operations. This project is linked with a USAMRMC-funded project based at UCLA (Award Number W81XWH-07-1-0005, Principal Investigator: Beate Ritz), under which case ascertainment in Southern California and exploratory analyses are being performed.

The initial phase of this project focused on the establishment of a secure, high quality registry database, and launch of health surveillance activities, including active case ascertainment and clinical abstraction. This initial project phase encountered significant administrative and regulatory delays. As a result, we have requested and been granted a project extension (copy of request and approval attached) in order to be able to carry out the next phase of the project, which involves ongoing organization and compilation of data and initiating analyses.

C. Key Accomplishments

1. Deputization status from the CDPH as designated agents for creation of a state registry: Zero-dollar contracts between CDPH and PI were developed, and signed in October, 2007.
2. Approval from Institutional Review Boards: Human subjects research waivers for the initial surveillance-oriented work were obtained from the Army Medical Research and Materiel Command Office of Research Protections Human Research Protection Office, the State of California Committee for the Protection of Human Subjects (CPHS), the Kaiser Permanente Northern California Institutional Review Board and the UCLA Office for Protection of Research Subjects. CPHS has also authorized work to link registry data

- with Medicare data from the Center for Medicare and Medicaid Services (CMS), in order to evaluate the efficiency of the registry ascertainment methods utilizing capture-recapture analytic methods. A joint TPI-UCLA application to conduct exploratory analyses (evaluating diagnostic validity, linkage to toxicant databases, defining patterns of PD care) has been approved by CPHS.
3. Notification of case reporting sources and professional organizations of registry implementation, as required by the California Parkinson's Disease Registry Act: A formal notification letter was developed in conjunction with CDPH, and mailed on January 2008 to the state Medical Board and the Board of Pharmacy, professional organizations representing potential case reporting sources (pharmacists, physicians and health care facilities) and public health officers in the project target counties. Inquiries from reporting sources/organizations about the registry have been addressed via email, telephone and in public and scientific gatherings.
 4. Conduct outreach to stakeholders: A public stakeholders' meeting was convened in March, 2006. A free-standing website (www.capdregistry.org) and email box were created and launched in March, 2008. Requests for information about the registry from patients, colleagues and the public have consistently been answered within several days of receipt. A public fact sheet and informational brochure were developed and have been utilized in mailings, at patient-oriented events and are also posted on the website.
 5. Convene a Stakeholders' Advisory Committee: Under the direction of its leaders, Mr. Greg Wasson, Ms. Anne Wasson and Mr. Mark Siegel, a committee is acting to create a forum and network in which registry stakeholders can be informed of project activities, provide valuable input to the project and strategize about future funding and expansion opportunities for the registry. In addition, two new members, Dr. James Wong and Dr. Ronald Kobayashi have joined the committee. In the past year, a Stakeholder's Committee Teleconference meeting was conducted on March 9, 2010. Email communication was used otherwise to review project strategies and project output.
 6. Define case ascertainment strategies: Investigators at the PI and UCLA initiated case ascertainment activities by approaching physician offices (neurology practices in particular), medical groups and large health care facilities, to enhance the willingness of these high-yield sources to cooperate with the reporting requirements.
 7. Creation of tools and instruments for data collection: A data collection form and Microsoft Access database was developed and pilot-tested by staff (both physicians and non-physicians) at the PI. The form includes fields for obtaining information on basic demographics, key clinical parameters and characterization of data collection feasibility.
 8. Establishment of a secure registry database: A secure, non-networked data repository was established in a dedicated room with access limited to trained project personnel.
 9. Develop policies and procedures for ensuring data confidentiality, quality and appropriate use: Policies and procedures have been developed, together with staff training materials. TPI and UCLA project employees have attended group training sessions in September and October, 2008 and again in June and July of 2009. With the launch of field data collection in October, 2008, weekly conference calls have been held to keep all field staff updated on progress and the latest standard operating procedures on safe data collection/transmission and storage. In addition, all registry staff members are required to complete Information Security training in a yearly basis.

10. Hiring and training staff: Registry staff members have been hired and trained in communication with potential reporting sources, project security procedures, data collection and clinical abstraction. In addition, weekly conference calls between TPI and UCLA staff members and principal investigators have continued to keep all registry staff updated on progress and the latest standard operating procedures for field work and data safety.
11. Active case ascertainment and data collection in designated counties: The cumulative data collection accomplishments from October 2008 through Feb 2013 are shown in the Table 1 in Reportable Outcomes section. The table shows the total number of patients reported to us as well as the total number of unique cases identified after systematic de-duplication procedures have been applied. All reported cases have basic identifying data and some demographic information available. Detailed clinical information has been collected directly from medical records on a random subsample of cases for diagnosis validation purposes.
12. Development of systematic de-duplication procedures: Because cases are being ascertained from multiple reporting sources, some cases are reported more than once. Utilizing the CDC's LinkPlus software platform, procedures have been developed to compare all new incoming data against existing registry data to identify duplicate cases in the database. This ensures a more accurate estimate of the cases within the designated reporting areas.
13. Activation of voluntary patient self registration: A mechanism for self registration has been established. Interested patients can print a registration form directly from the registry website (<http://www.capdregistry.org/NewPatient.html>).
14. Application for external validation data: Assessment of registry validity and ascertainment efficiency can be accomplished through linkage with external datasets listing Parkinson's disease cases. Applications have been filed for Medicare data with the University of Minnesota Research Data Assistance Center/CMS, and with the California Vital Statistics Advisory Committee/CPHS for death certificate data. Both applications have been approved and datasets have been received, however receipt of Medicare data from CMS was significantly delayed due to administrative barriers on the part of CMS. The Medicare dataset was obtained in February 2011.

There are 170,322 entries (service records) in the datasets received, representing 4,274 individuals. On average, each individual had 40 entries. Among the 4,274 individuals, 49.3% are male and 50.7% are female. 77.8% are non Hispanic White, 9.8% are Asian, 6.2% are Hispanic, 2% are black, and 4.2% are others. 80% reported single diagnosis of Parkinson's disease, 8% reported single diagnosis of Parkinsonism, and another 12% reported multiple diagnoses of Parkinson's disease and Parkinsonism. Table 2 below lists the cases by county.
15. Assessment of Surveillance efficiency: We have initiated collaborative planning with Dr. Lorene Nelson (Stanford University) for the capture-recapture analytic work to evaluate registry data collection efficiency, and have completed the analysis plan. The final 2007 ascertainment data have been received from Dr Ritz at UCLA and data queries have been resolved as of end of year 2012.

16. Preparation of analytic datasets: Preparation of the analytic datasets which include the dataset for the capture-recapture analytic work and the dataset for prevalence reporting work is in progress. Major achievements are summarized as below.
- Review and rectification of discrepant diagnosis information reported by providers for cases within and across data sources. 1422 cases with approximately 17,000 service records have been reviewed to rectify discrepant diagnoses reported to the registry project.
 - Review and rectification of discrepant diagnosis information reported by Medicare data. 316 cases with 15,270 service records have been reviewed to rectify discrepant diagnoses reported in Medicare data.
 - Compiling and verification of vital status and residency in the 4 counties for the reported cases.

D. Reportable Outcomes

Table 1, Number of Reported Cases from Providers					
	Northern California Ascertainment (TPI)	Southern California Ascertainment (UCLA)			
County	Santa Clara	Fresno	Kern	Tulare	Total
Total Population (Census)	1,764,499	909,153	800,458	426,276	3,900,386
Population >65 (Census)	192,330	90,006	72,041	40,922	395,299
Physicians Reporting	18	15	16	8	57
Medical Groups and Facilities Reporting	7	12	9	7	35
Total Patients Reported	5526	3083	3600	2308	14517
Total Unique Patients Reported**	4406	2234	2374	1475	10489
Constitution of each county	42.0	21.3	22.6	14.1	100%

*Data records w/ queries under investigation

**Unique cases after duplicates reported from multiple sources have been removed

Table 2, Number of Reported Cases From Medicare Data					
County	Santa Clara	Fresno	Kern	Tulare	Total
Total Patient Reported	1710	1227	775	562	4,274
Constitution of each county	40.0	28.7	18.1	13.2	100%
% of patients with diagnosis of PD within the county	94.9%	84.0%	96.1%	93.1%	79.5%
% of patients who visited neurologists in the year 2007	24.9%	14.3%	17.7%	14.0%	19.3%

E. Conclusions

Since our last annual progress report, most milestones in the project's primary specific aims, including developing methods for active ascertainment and registration of cases with PD and parkinsonism have been successfully achieved. Establishment of the registry now enables us to transition our effort to organize the data and address the exploratory aims of the project which will utilize the registry data. Important next steps for the project include the following:

1. Final preparation of analytic datasets as described above.
2. Ongoing ascertainment of incident cases and clinical abstraction.
3. Diagnosis validation comparing source-reported cases with detailed clinical information abstracted from medical records.
4. Data analysis:
 - a. Compile and summarize demographic characteristics of reported cases.
 - b. Carry out capture-recapture validation analysis to assess the efficiency of data collection approaches using census, Medicare and California death certificate data.
 - c. Implement projects analyzing patterns of PD prevalence and care, and explore the feasibility of assessing possible associations between toxicant exposure and PD.
5. Conduct ongoing meetings with project staff at TPI and UCLA and convene Working Group and Stakeholder's Committee meetings, as necessary.

F. References

None.