MEDINFO 2017: Precision Healthcare through Informatics
A.V. Gundlapalli et al. (Eds.)

doi:10.3233/978-1-61499-830-3-536

Establishment of New National Rare Disease (Nambyo) Registry and Registry Guidelines in Japan

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Abstract

A New legal structure for rare disease (nambyo) has been established in Japan this year,after 42 years of measures of nambyo. We have been accumulating registry for nambyo from 2003, however, as it was based on paper registration, quality was not enough.

Our new registry system will be based under ISO13606 which is a new medical international standard. Authorized doctors can put in data On Line by the new system, which has data cleaning filter for accurate data entry. Patients will be supported their medical expense by authorization by this system, so the registry will be efficient.

Keywords:

Rare Diseases; Registries; Demography

Introduction

In 1972, the Ministry of Health and Welfare enacted the "General Outlines for taking Measures to deal with Intractable Disease [NAMBYO]" which was the first one ever established in the world. The extent of Nambyo was proposed as : a) Unknown etiology b) Un-established therapy c) Frequent after-effects d) Chronic course e) Heavy burdens in terms of economical, psychological and physical issues.

At this stage, there was no concept of rareness in the extent of Nambyo. More than 25 years was needed until rareness was added to the extent.

A revised definition of Nambyo in 1995 was: a) Etiology is unknown. b) Frequency is low (less than 50,000). c) Therapy is not established. d) Economical, psychological and physical burdens. e) Diagnostic criteria should be established.

Frequency in Japan (< 4/10,000 : below 50K) is similar to that in EU(< 5/10,000) or in US(< 7/10,000: below 200K)

Selection of Nambyo

One hundred and thirty diseases were selected as Nambyo for special research. Two hundred and fourteen diseases were further selected as candidates of the second group of Nambyo for research support. Of 130 diseases, 56 diseases were targets for being treated with special favor in terms of medical expenses (see Table 1).

Budgets for researches (for 364 diseases) are 10 billion yen, and budgets for medical expenses (for 56 diseases) are 35 billion yen. Number of recipients of medical expenses are approximately 700,000 patients and increased by 30,000/year.

Nambyo was reviewed and a new legal structure was established in June 2014. This included: medical system, subsidized health care costs, promotion of research, consultation and support, human services, work and employment support, international cooperation, and awareness.

At this time, supporting diseases were expanded from 56 to about 300, which will be defined by the committee and authorized by the government. This will double the patient numbers. New law will be effective from January 1, 2015. There are 330 from April 2017.

However, the most important issue to date is that the current registry system is done in paper form and not well organized.

As a result, we established a new registration system, which doctors input the data themselves which is then sent to an online national database.

This will be the first national online database for rare disease, and will support the patient care and research for rare diseases.

Methods

Systematic design of the registration system was done by analyzing the current paper-based registry system. Research in international standardization of terminology and modeling architecture was also completed. Prototype system was constructed with Mitsubishi Space Software, NISplus, and R102 company.

Results

Problems of Nambyo

Comprehensive measures for Nambyo are important, however demographics of the 56 diseases are changing. As shown in Figure 1, some diseases, such as Ulceratuve Colitis, Parkinson's Disease and SLE were included from the beginning, but they alread exceed the the patient size (50,000).

Also, as this registry is based on the application for the medical expence reimbersement, doctors tend to write more severe notes for better approval by the government.

New Registry System

A diagram for new registry system is shown in Figure 2. Any doctor can complete the form in the current system, however, only certified doctors for Nambyo can write (input) the form. This will make the report more accurate. Data will be inputted in to the system, and cheking will filter inacurate data entries. At this point, the doctors can be notified when they have the patient data (in current system, it required long time as government staff askes the doctor after the application).

Also, it was prefectural govement's task to input the paper allication to the database system, and not required for the patient reimbersement. As a result, some prefecture did not get imputted in to the national registry. Doctor's data entry is

nessesary to make the application for the prefectural government, to ensure all patinet information should be in the system comprehensively.

International Standardization

International collaboration is very important in rare diseases, as the patient size is limited for each disease. There are many standard coding systems, however each one varies per country. We have serached for many registries and many international discussions about which terminology to use, and which clinical modeling should be used.

As rare diseases are premature in clinical research, many diseases are not well discribed in the terminology. Even in ICD-10, most of the rare diseases in Orphanet (http://orpha.net/), the most well known rare disease directory) are not coded. This is also the case for Japanese standard nomenculture, SNOMED, and HL7.

We are still waiting for this international standardization, but currently following Orphanet as disease names, CIMI for clinical information Modeling, and ISO13606 for archytype.

As for the minimum dataset for the registry, we have compared it with Global Rare Disease Registry (GRDR http://rarediseases.info.nih.gov/) at NIH/NCATS, and EUCERD/Epirare (http://eucured.eu)

Grouping Datasets as Modules

Current registry form is defined by each disease,and no there was no concept of systematic cross disease analysis. There were difference in units or abbrebations between diseases. As we are disigning a new registry system, we wanted to standardize the data set, and also wanted to be systematic as we have to add about 250 new diseases.

Figure 3 currently shows 14 Neurological Nambyo grouped into 4 groups and extracts common data sets for each groups. From this analysis, we were able to define a dataset as set module so we can design a new registry by just combining the modules.

We also made the dataset module management software, to make the registry for new diseases a systematic process.

Web-Based Entry System

Our new registry looks like Figure 4. Sections are categrized by tabs which have a) Basic information Diagnosis; b) Onset and Prognosis; c) Clinical evidence; d) Laboratory findings; e) Severity; f) Differential diagnosis; and g)Therapy and care.

There are filtes and mandatory defined datasets. Tabs will be red if mandatory data is not sufficient or data is out of range.

Offline Regitration Tool

There are some hospitals where internet access is restricted. Some local governments also have restrictions in internet use. To support data entry in these conditions, offline data entry application were developed. Data entry is similar with the on-line system however, data will be stored locally with encription, and will be uploaded with other methods. Printing application forms for local government can be perfored using this application.

This will also enhance the security issue using internet, as data upload is much more safer than online data entry.

Discussion

We are planning to perform a pilot study using this system at some hospitals along with local government installation.

Total numbers of registry entries will be about 1,500,000 every year. This will be one of the largest registry for rare disease in patient numbers.

This will be the first National Registry System by remote data entry with standardized coding. We are hoping to include other registries in the near future.

Conclusion

A New legal structure for rare disease (Nambyo) has been established in Japan this year,after 42 years of measures of Nambyo. We have been accumulating registry for Nambyo since 2003, however, as it was based on paper registration, quality was not strong enough.

Our new registry system will be based under ISO13606, which is a new medical international standard. Authorized doctors can input data online by the new system, which has a data cleaning filter for accurate data entry. From the discussion about integrating the data from registry for each diseases, we established a guideline in Japan. This guideline is now in the process of finalization and authorization.

01 Behcet disease
02 multiple sclerosis
03 myasthenia gravis 0
4 systemic lupus erythematosus (SLE)
05 subacute myelo-optico-neuropathy (SMON)
06 aplastic anemia
07 sarcoidosis
08 amyotrophic lateral sclerosis (ALS)
09 scleroderma , dermatomyositis, or polymyositis
10 idiopathic thrombocytopenic purpura
11 (1) polyarteritis nodosa (2) microscopic polyangiitis
12 ulcerative colitis
13 Takayasu arteritis
14 thromboangiitis obliterans, Buerger disease
15 pemphigus
16 spinocerebellar degeneration
17 Crohn disease
18 fulminant hepatitis
19 malignant rheumatoid arthritis (rheumatoid vasculitis)
20 Parkinson disease and related diseases -progressive supranuclear palsy -corticobasal degeneration -
Parkinson disease
21 amyloidosis
22 ossification of posterior longitudinal ligament (OPLL)
23 Huntington disease
24 moyamoya disease
25 Wegener granulomatosis
26 dilated cardiomyopathy, congestive cardiomyopathy
27 multiple system atrophy - striatonigral degeneration (SND) -olivopontocerebellar atrophy (OPCA) -Shy-Drager syndrome
28 epidermolysis bullosa
29 pustular psoriasis
30 disseminated spinal canal stenosis
31 primary biliary cirrhosis
32 severe acute pancreatitis
33 idiopathic necrosis of the femoral head
34 mixed connective-tissue disease
35 primary immunodeficiency syndrome
36 idiopathic interstitial pneumonia
37 retinitis pigmentosa
38 prion diseases -Creutzfeldt-Jakob disease (CJD) - Gerstmann-Straussler-Sheinker syndrome -fatal familial insomnia
39 primary pulmonary hypertension
40 neurofibromatosis type 1, neurofibromatosis type 2
41 subacute sclerosing panencephalitis (SSPE)
42 Budd-Chiari syndrome
43 idiopathic chronic pulmonary thromboembolism with pulmonary hypertension
44 lysosomal-storage diseases - Fabry disease -other lysosomal storage diseases
45 adrenoleukodystrophy (ALD)
46 Familial Hypercholesterolemia (Homozygous type)
47 spinal muscular atrophy (SMA)
48 spinal and bulbar muscular atrophy (SBMA)
49 Chronic Inflammatory Demyelinating Polyneuropathy
50 Hypertrophic cardiomyopathy
51 Restrictive cardiomyopathy
52 Mitochondrial disease
53 lymphangioleiomyomatosis
54 Severe erythema multiforme (Acute Phase)
55 Ossification of the ligamentum flavum
56 Diencephalo-hypophysial dysfunction -Syndrome of abnormal secretion of prolactin -Syndrome of abnormal secretion of gonadotropin -Syndrome of abnormal secretion of antidiuretic hormone - Syndrome of abnormal secretion of Thyroid stimulating hormone - Cushing disease - Acromegaly -Hypopituitarism

Table 1 – List of 56 diseases of Nambyo which Patients are Supported for Their Medical Expence

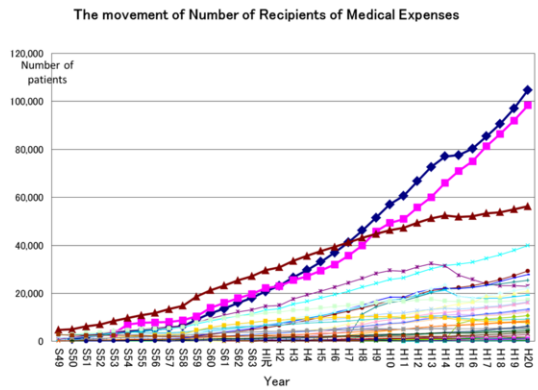

Figure 1 – Number of Patients from 1974 to 2008

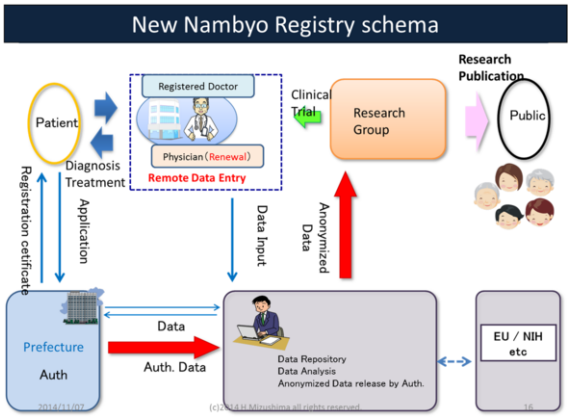

Figure 2 – New Nambyo Registry Schematic Diagram

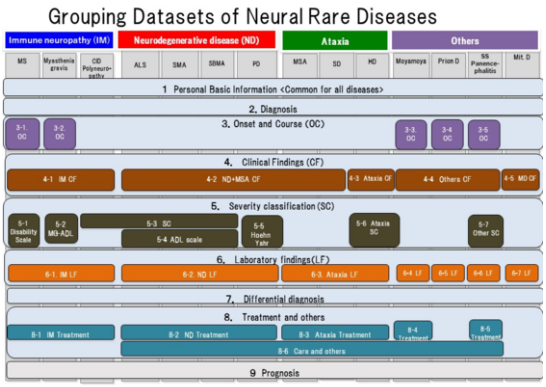

Figure 3 – Grouping of Datasets for Neurological Diseases

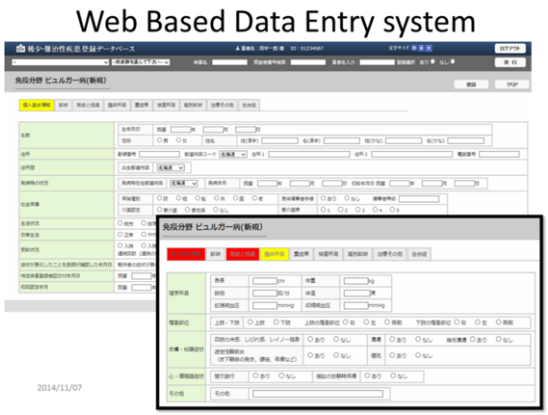

Figure 4 – Web based Data Entry System

References

[1] H.Mizushima, M.Tanabe, Y.Sato, Y.Kanatani; New legal structure and National Registry system for Rare disease (Nambyo) in JAPAN. IRDiRC conference 2014 Abstract book (2014).

[2] OrphaNet. The portal for rare diseases and orphan drugs. Retrieved from http://www.orpha.net/

[3] National Institute of Health. Genetic and rare disease information center. GARD. Retrieved from http://rarediseases.info.nih.gov/

[4] European Union Community of Experts on Rare Disease. EUCERD. Retrieved from http://www.eucerd.eu

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