What "big population data" tells us about neurological disorders comorbidity

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ABSTRACT

Objective: To use a large population dataset to examine neurological disorder comorbidity. Seventeen main classes of Diagnosed International Classification of Disease (ICD) disorder codes were grouped and compared to ICD-9 Nerurological disorder codes.
Methods: Calgary, Alberta, health zone diagnosis, sex and age data from 1994-2009 physician billings (n = 763,449) were grouped and tallied on the basis of the presence or absence of any neurological disorder across the 17 remaining ICD main disorder classes and represented as odds ratios (ORs with 95% confidence intervals).
Results: Within the ICD categories the 17 classes were ranked by ORs: Ill-defined conditions (OR 7.42), musculoskeletal and connective tissue system disorders (OR 4.22), and psychiatric disorders (OR 3.81) were the ranked the highest main classes, respectively. Thirteen additonal main classes had ORs greaeter than 2.00.
Conclusions: There was a strong relationship between neurological disorders and the ICD main classes. The results of this broad stroke analysis point to the requirement for analysis of the both the temporal relationships (e.g., before vs. after) between neurological disorders and comorbid disorderss as well as more fine-grained description of the specifice intra-class disorders underlying the reported odds ratios.

Key Words: Comorbidity, Neurological disorders, Epidemiology

1. INTRODUCTION

The strategic use of "big data" has been identified as a gateway to improving understanding how to best treat patients who the generate the health care system data.[1] However, the construction of this gateway is acknowledged as being in its infancy with multiple barriers to be overcome to ensure an unbiased integral scientific approach.[1–4] The present paper represents an illustration of how big data might begin to inform clinical practice through describing the complex matrix of comorbidity related to specified disorders.

Research from Health Canada,[5] the United Kingdom[6] and the World Health Organization[7] has examined the point prevalence of neurological disorders finding 4.8/1,000 individuals affected.[8]

Neurological disorders are a main class of International Classification of Diseases (ICD) disorder distinct from other main ICD classes. Neurological disorders range from bacterial and viral infections to acquired insults and genetic disabil-

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ities. Neurological disorders are often long-term debilitating diseases from which there is increasing impairment and functional decline. Neurological disorders often emerge in the company of other independent or related disorders. A literature review of neurological disorders focusing on comorbidity revealed papers that were based on population studies.[9–14] Only three of these studies emerge that held the potential to compare directly with the present study,[10, 12, 15] as most featured an examination of neurological disorders as a consequence or in association with only one or two other disorders.[14, 16–48] In addition to the annual and cumulative prevalence, this paper is perhaps the first population-based description of neurological disorders comorbidity. The results have been published in abstract form.[49]

2. METHODS

The randomly selected unique identifiers of 764,449 individuals (46% male) were related to 90,611,984 direct physician billings for treatment (1994-2009) and amonymized. Visit dates were associated with ICD diagnosis, sex and age at index visit. All disorders were groupd according to the main ICD classes. The main ICD classes represent distinct sets of disorders. Within the ICD classification system there are approximately 13,000 subdiagnoses and 1,000 main diagnoses in 18 main classes. Neurological disorders (ICD-9 codes 320-359) represented the dependent variable and other 17 main ICD classes repesented the independent variables (e.g., psychiatric disorders: ICD codes 290-319, neoplasms: ICD codes 140-239, etc.). Individuals could be represented in multiple main ICD classes, forming the basis of examining comorbidity (e.g., the association of disorders within individuals) across the study period.

The annual population rates for neurological disorders were estimated based on the number of unique individuals diagnosed per year with the annual civic census from 1994-2009 denominating these resulting values.

The dependent variable, presence or absence (+/-) of any neurological disorder was tallied within and between the categories (+/-) of the major class ICD diagnostic groupings (independents variables) given the presence or absence of any neurological disorder, expressed as the odds ratio [OR = (AD/BC)] of the remaining classes of ICD disorders (independent variables) compared to those without neurological disorder. Overlapping and non-overlapping 95% confidence intervals (95%CI) were used to assess significant statistical differences ($p < .05$; $z = 1.96$) between ORs. Using this approach neurological disorder comorbidity within the independent ICD categories was examined.

3. RESULTS

The 16-year cumulative rate of neurological disorders in the population was 108/1,000 for females and 58/1,000 for males. The annual rate between 1994 and 2009 was stable for males (8/1,000) and females (15/1,000).

Table 1 provides the counts in each cell constructing the odds ratio calculation for males and females, respectively. The counts represent the unique individuals within each cell required to calculate the odds ratio [A those with neither disorder (-/-), B (-/+) and C (+/-) those with one and not the other and D those with both (+/+)].

Table 2 shows the OR values within the ICD categories given the presence or absence of any neurological disorder. The highest ranked OR was for symptoms, signs, and ill-defined conditions followed by musculoskeletal system and connective tissue disorders, then mental disorders. The ORs for males were slightly lower than the ORs for females. With the exception of perinatal conditions in males, values equal to or greater than 2.00, indicating significant comorbidity, were observed across most main ICD classes.

4. DISCUSSION

The present study summarized the 16-year cumulative prevalence and overall changes in annual rates of neurological disorders, which are logically greater than the point prevalence reported by the World Health Organization[9] and comparable to the range of prevalences reported for specific neurological disorders reported in the United Kingdom.[7] The results of the Canadian study[5] were not directly comparable to the present study, as these were survey-based. Our data represented utilization within a health care system based on universal access to health care, similar to that of the United Kingdom. Our results may not be directly comparable to survey-based epidemiogical estimates or coutries with different types of health care systems.

The two most comparable population-based studies examined the relationship between neurological disorders and comorbid disorders, and each focused, respectively, on general neurological disorders and mental disorder[50] and symptomatic atherosclerotic and cancer.[35] Another study focused on general neurological disorders, mental disorder and substance disorders.[12] The study that examined 301 diseases in 188 countries,[10] while achieving its research objectives in a sophisticated way, did not provide integrated information from a single population. As a result, the present study provides a unique perspective on the issues of neurological disorder comorbidity within a single population, wherein anonymized unique identifiers for each patient linked all ICD diagnoses of record and permitted detailed examination of

the association of physician-assigned disorders within the population's individuals.

The majority of studies focused on general or specific neurological disorders (Parkinson, epilepsy, multiple sclerosis, essential tremor, etc.) and one other comorbid disorder (cardiovascular, Tourettes, depression, etc.)[11, 23–32, 34, 36, 41–44, 48, 51–53] The remaining studies included from the literature review focused on neurological disorders and multiple comorbid disorders.[13–15, 21, 37, 46, 54] Similar, as in comparison to the population-based studies, and not possible in examining many of the studies, the ability to examine all of the neurological disorder comorbidities

within a population holds the potential to rank order the relative importance of specific comorbid disorder relationships. Being able to accomplish the comparison, as illustrated in Table 2, in terms of the comorbidity of neurological disorders and the main ICD classes of disorder, permits more precise policy and planning related to the relative magnitude and prevalence of the comorbidities. This is perhaps the first study of its kind in the published literature.

The main limitation of the paper is the precision of a diagnosis assigned to a given patient. Threats to diagnostic validity, however, are universal and likely have a unique distributions more or less equal within main classes of ICD disorder.

Table 1. Counts in respective cells contructing Odds Ratio formula

	ICD Main Class	A (--)	B (-+)	C (+-)	D (++)
	infectious-parasitic diseases	244,127	75,258	62,333	32,585
	neoplasms	199,277	51,036	107,183	56,807
	endocrine etc.	200,818	46,114	105,642	61,729
	blood-blood-forming organs	261,846	79,892	44,614	27,951
	mental disorders	125,827	16,954	180,633	90,889
	sense organs	101,951	17,034	204,509	90,809
	circulatory system	195,738	42,224	110,722	65,619
	respiratory system	50,978	6,557	255,482	101,286
Females	digestive system	166,723	32,813	139,737	75,030
	genitourinary system	78,731	10,892	227,729	96,951
	complications of pregnancy childbirth	226,978	76,562	79,482	31,281
	skin subcutaneous tissue	92,914	14,867	213,546	92,976
	musculoskeletal system connective tissue	98,489	10,408	207,971	97,435
	congenital anomalies	290,394	98,856	16,066	8,987
	perinatal conditions	285,704	99,483	20,756	8,360
	symptoms signs ill-defined conditions	32,890	1,637	273,570	106,206
	injury poisoning	79,615	9,429	226,845	98,414
	infectious-parasitic diseases	251,326	45,669	40,071	12,080
	neoplasms	220,340	33,400	71,057	24,349
	endocrine etc.	207,492	27,877	83,905	29,872
	blood-blood-forming organs	269,974	47,592	21,423	10,157
	mental disorders	151,860	13,775	139,537	43,974
	sense organs	108,709	11,728	182,688	46,021
	circulatory system	201,797	23,994	89,600	33,755
	respiratory system	60,545	5,549	230,852	52,200
Males	digestive system	166,142	19,290	125,255	38,459
	genitourinary system	200,197	28,186	91,200	29,563
	complications of pregnancy childbirth	287,746	56,280	3,651	1,469
	skin subcutaneous tissue	106,582	11,398	184,815	46,351
	musculoskeletal system connective tissue	105,916	7,728	185,481	50,021
	congenital anomalies	277,700	53,566	13,697	4,183
	perinatal conditions	280,674	55,789	10,723	1,960
	symptoms signs ill-defined conditions	45,946	1,685	245,451	56,064
	injury poisoning	64,426	4,842	226,971	52,907

Table 2. Odds Ratios with 95% Confidence Intervals (CI) for Females and Males

	ICD Main Class	Odds Ratio	Lower 95%CI	Upper 95%CI
Females	infectious-parasitic diseases	1.7	1.67	1.72
	neoplasms	2.07	2.04	2.1
	endocrine etc.	2.54	2.51	2.58
	blood-blood-forming organs	2.05	2.02	2.09
	mental disorders	3.73	3.67	3.8
	sense organs	2.66	2.61	2.71
	circulatory system	2.75	2.71	2.79
	respiratory system	3.08	3	3.17
	digestive system	2.73	2.69	2.77
	genitourinary system	3.08	3.01	3.14
	complications of pregnancy childbirth	1.17	1.15	1.18
	skin subcutaneous tissue	2.72	2.67	2.77
	musculoskeletal system connective tissue	4.43	4.34	4.53
	congenital anomalies	1.64	1.6	1.69
	perinatal conditions	1.16	1.13	1.19
	symptoms signs ill-defined conditions	7.8	7.42	8.2
	injury poisoning	3.66	3.58	3.75
Males	infectious-parasitic diseases	1.66	1.62	1.7
	Neoplasms	2.26	2.22	2.3
	endocrine etc.	2.65	2.6	2.7
	blood-blood-forming organs	2.69	2.62	2.76
	mental disorders	3.47	3.4	3.55
	sense organs	2.34	2.29	2.39
	circulatory system	3.17	3.11	3.23
	respiratory system	2.47	2.4	2.54
	digestive system	2.64	2.6	2.69
	genitourinary system	2.3	2.26	2.34
	complications of pregnancy childbirth	2.06	1.93	2.19
	skin subcutaneous tissue	2.35	2.29	2.4
	musculoskeletal system connective tissue	3.7	3.6	3.79
	congenital anomalies	1.58	1.53	1.64
	perinatal conditions	0.92	0.88	0.97
	symptoms signs ill-defined conditions	6.23	5.93	6.54
	injury poisoning	3.1	3.01	3.2

Traditionally, examination of comorbidity has largely focused on the relationship between only a few comorbid disorders related to a primary disorder of interest. With the advent of large integrated data repositories, it is possible to understand comorbidity in a much more comprehensive manner. For example, an examination of comorbidity has given rise to a novel population health index and provided evidence in support of the adverse childhood experience study (`acestudy.org`).[55] Additionally, examination of the temporal dependence of the occurrence of comorbid disorders that arise within individuals has provided insight into disease mechanism.[56] The present work makes a small contribution to the field of neurology. Notwithstanding the substantial information in the broad strokes of examining the odds ratios between the dependent category (neurological disorders) and each independent main class of ICD disorder, within specific main classes of disorder reside hundreds of disorders, which may carry more or less weight in establishing the relationships underpinning what in this paper is a thumbnail sketch of such relationships. Furthermore, for every individual with a neurological disorder, there is a temporal order in which patterns of diseases arise, patterns that may help elucidate a more formal understanding of the etiology and prognosis of sets of disorders within given groups of individuals.

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CONTRIBUTORS STATEMENT

Sara Anwar conceptualized the study, interpreted the analyses, reviewed and revised manuscript, and specifically approved the final manuscript as submitted.

Dr. Cawthorpe designed the overall study, carried out the initial analyses, drafted the initial manuscript, reviewed and revised the manuscript and approved the final manuscript as submitted.

CONFLICTS OF INTEREST DISCLOSURE

No conflict of interest to declare.

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