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Distinction between Episodic Mood Disorder and Attention Deficit Disorder with Hyperactivity based on their Association with the Main Classes of International Classification of Disease in a Child and Adolescent Population

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Abstract

Background: Few studies comprehensively examine specific mental disorders in terms of associated bio-medical comorbidities with focus on the pattern of similitude and distinction. The present study compares the profile of independent classes of physical disorder for Episodic Mood Disorder (EMD), Attention-Deficit Disorder with Hyperactivity (ADHD) and all Other Mental Disorders (OMD).

Methods: Physician billing data for 235893 individuals up to 18 years old spanning sixteen fiscal years (1994-2009) in Calgary, Alberta, was compiled, permitting the examination of Odds Ratios (ORs) comparing the main classes International Classification of Diseases (ICD) within each of four groups of psychiatric disorders: EMD, ADHD, both EMD/ADHD and OMD.

Results: Each group profile was distinct: The EMD group presented Odds Ratios (OR) greater than ADHD and all other mental disorder across most ICD classes. For both sexes, ADHD and EMD differed significantly in profile across 11 independent ICD disorder classes, with an additional three classes being specific to females and one specific to males. The ADHD group ORs tended to be lower than the EMD group and the OMD group.

Conclusion: This study represents the premiere pediatric population-based report on the patterns of main class ICD disorders associated with EMD and ADHD and OMD. In opposition with most research focusing on EMD and ADHD, the different clinical profile pattern of ICD disorders for EMD and ADHD disorders suggest an independent etiology. Profiling comorbidity represents a novel approach to understanding disease and etiology.

Keywords: Attention deficit hyperactivity disorder; Episodic mood disorder; Comorbidity; Population; Epidemiology; International classification of diseases

Abbreviations

ADHD: Attention Deficit Hyperactivity Disorder; CI: Confidence Intervals; EMD: Episodic Mood Disorder; ICD: International Classification of Diseases; OMD: Other Mental Disorders; OR: Odds Ratio

Introduction

There is overlap of the descriptive criteria underpinning the definition and diagnosis of different mental disorders. Furthermore, much research has focused on common etiology or shared liability or comorbidity of Attention Deficit Hyperactivity Disorder (ADHD), Episodic Mood Disorder (EMD) and other mental disorders in pediatric populations [1-3]. This report supports the contention that ADHD and EMD are distinct entities based on their respective physical disorder profiles.

Background

There has been debate regarding the associations and etiology of EMD and ADHD [4-12]. Research has distinguished between subtypes of chronic and episodic irritability in youngsters, however has not associated chronic and episodic irritability with particular mental disorders [13]. Others have associated early-onset chronic irritability, a feature of EMD, with ADHD [14,15]. Furthermore, studies have identified EMD to be associated with a range of child psychiatric disorders [16-18]. Overlapping symptoms can account for some observed comorbidity in studies [19], however, the application of diagnostic criteria in clinical settings may be influenced by the clinician background and orientation. For example, clinicians are influenced by the debate regarding the phenomenology of EMD, as this relates to diagnostic criteria as applied in children, in addition to its relationship to other childhood mental disorders [20]. While

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Table 1: Cell counts used to calculate Odds Ratios.

Group	ICD Main Class	a	b	c	d
Males					
All Other	infectious-parasitic diseases	59202	41690	9227	9598
	neoplasms	60630	42303	7799	8985
	endocrine etc	62051	42425	6378	8863
	blood-blood-forming organs	65315	47892	3114	3396
	nervous system	64269	43714	4160	7574
	sense organs	22683	11287	45746	40001
	circulatory system	63370	43481	5059	7807
	respiratory system	9955	3096	58474	48192
	digestive system	46627	26592	21802	24696
	genitourinary system	54373	34786	14056	16502
	complications of pregnancy childbirth	67723	50490	706	798
	skin subcutaneous tissue	25599	11570	42830	39718
	musculoskeletal system connective tissue	37394	18140	31035	33148
	congenital anomalies	64078	46416	4351	4872
	perinatal conditions	63107	47258	5322	4030
	symptoms signs ill-defined conditions	14686	3974	53743	47314
	injury poisoning	16938	5081	51491	46207
	V Codes	23441	8606	44988	42682
EMD	infectious-parasitic diseases	99576	1316	18529	296
	neoplasms	101658	1275	16447	337
	endocrine etc	103277	1199	14828	413
	blood-blood-forming organs	111713	1494	6392	118
	mental disorders	68429	1610	49676	1610
	nervous system	106755	1228	11350	384
	sense organs	33512	458	84593	1154
	circulatory system	105651	1200	12454	412
	respiratory system	12932	119	105173	1493
	digestive system	72511	708	45594	904
	genitourinary system	88106	1053	29999	559
	complications of pregnancy childbirth	116627	1586	1478	26
	skin subcutaneous tissue	36844	325	81261	1287
	musculoskeletal system connective tissue	55111	423	62994	1189
	congenital anomalies	108992	1502	9113	110
	perinatal conditions	108786	1579	9319	33
	symptoms signs ill-defined conditions	18576	84	99529	1528
	injury poisoning	21928	91	96177	1521
	V Codes	31760	287	86345	1325
ADHD	infectious-parasitic diseases	88998	11894	15657	3168
	neoplasms	90147	12786	14508	2276
	endocrine etc	91843	12633	12812	2429
	blood-blood-forming organs	99104	14103	5551	959
	mental disorders	68429	15023	36226	15062
	nervous system	94994	12989	9661	2073

	sense organs	31381	2589	73274	12473
	circulatory system	93685	13166	10970	1896
	respiratory system	12191	860	92464	14202
	digestive system	65336	7883	39319	7179
	genitourinary system	79084	10075	25571	4987
	complications of pregnancy childbirth	103406	14807	1249	255
	skin subcutaneous tissue	33610	3559	71045	11503
	musculoskeletal system connective tissue	49452	6082	55203	8980
	congenital anomalies	97093	13401	7562	1661
	perinatal conditions	96884	13481	7771	1581
	symptoms signs ill-defined conditions	17489	1171	87166	13891
	injury poisoning	20484	1535	84171	13527
	V Codes	29999	2048	74656	13014
BOTH	infectious-parasitic diseases	100892	515	18825	159
	neoplasms	102933	519	16784	155
	endocrine etc	104476	482	15241	192
	blood-blood-forming organs	113207	630	6510	44
	nervous system	107983	498	11734	176
	sense organs	33970	129	85747	545
	circulatory system	106851	500	12866	174
	respiratory system	13051	28	106666	646
	digestive system	73219	280	46498	394
	genitourinary system	89159	415	30558	259
	complications of pregnancy childbirth	118213	658	1504	16
	skin subcutaneous tissue	37169	105	82548	569
	musculoskeletal system connective tissue	55534	187	64183	487
	congenital anomalies	110494	613	9223	61
	perinatal conditions	110365	645	9352	29
	symptoms signs ill-defined conditions	18660	25	101057	649
	injury poisoning	22019	29	97698	645
	V Codes	32047	59	87670	615
Females					
All Other	infectious-parasitic diseases	45488	42559	9945	18184
	neoplasms	47654	44371	7779	16372
	endocrine etc	49030	44244	6403	16499
	blood-blood-forming organs	51688	52110	3745	8633
	nervous system	50799	46762	4634	13981
	sense organs	17225	11872	38208	48871
	circulatory system	51261	48802	4172	11941
	respiratory system	7592	2293	47841	58450
	digestive system	37540	27400	17893	33343
	genitourinary system	29220	10961	26213	49782
	complications of pregnancy childbirth	49492	38024	5941	22719
	skin subcutaneous tissue	19312	9964	36121	50779
	musculoskeletal system connective tissue	30550	16425	24883	44318
	congenital anomalies	52441	56046	2992	4697

	perinatal conditions	51459	54879	3974	5864
	symptoms signs ill-defined conditions	10588	2427	44845	58316
	injury poisoning	17765	6645	37668	54098
	V Codes	12929	2572	42504	58171
EMD	infectious-parasitic diseases	86549	1498	27286	843
	neoplasms	90470	1555	23365	786
	endocrine etc	91931	1343	21904	998
	blood-blood-forming organs	101936	1862	11899	479
	mental disorders	55433	2339	58402	2339
	nervous system	96090	1471	17745	870
	sense organs	28688	409	85147	1932
	circulatory system	98431	1632	15404	709
	respiratory system	9827	58	104008	2283
	digestive system	64201	739	49634	1602
	genitourinary system	39999	182	73836	2159
	complications of pregnancy childbirth	86372	1144	27463	1197
	skin subcutaneous tissue	29012	264	84823	2077
	musculoskeletal system connective tissue	46570	405	67265	1936
	congenital anomalies	106333	2154	7502	187
	perinatal conditions	104254	2084	9581	257
	symptoms signs ill-defined conditions	12969	46	100866	2295
	injury poisoning	24274	136	89561	2205
	V Codes	15450	51	98385	2290
ADHD	infectious-parasitic diseases	84148	3899	26224	1905
	neoplasms	87438	4587	22934	1217
	endocrine etc	88915	4359	21457	1445
	blood-blood-forming organs	98667	5131	11705	673
	mental disorders	55433	5795	54939	5804
	nervous system	92963	4598	17409	1206
	sense organs	28339	758	82033	5046
	circulatory system	95146	4917	15226	887
	respiratory system	9658	227	100714	5577
	digestive system	62317	2623	48055	3181
	genitourinary system	38589	1592	71783	4212
	complications of pregnancy childbirth	83121	4395	27251	1409
	skin subcutaneous tissue	28271	1005	82101	4799
	musculoskeletal system connective tissue	45073	1902	65299	3902
	congenital anomalies	103241	5246	7131	558
	perinatal conditions	101156	5182	9216	622
	symptoms signs ill-defined conditions	12761	254	97611	5550
	injury poisoning	23800	610	86572	5194
	V Codes	15189	312	95183	5492
BOTH	infectious-parasitic diseases	88047	229	28129	171
	neoplasms	92025	295	24151	105
	endocrine etc	93274	223	22902	177
	blood-blood-forming organs	103798	324	12378	76

	nervous system	97561	257	18615	143
	sense organs	29097	41	87079	359
	circulatory system	100063	293	16113	107
	respiratory system	9885	9	106291	391
	digestive system	64940	104	51236	296
	genitourinary system	40181	39	75995	361
	complications of pregnancy childbirth	87516	239	28660	161
	skin subcutaneous tissue	29276	45	86900	355
	musculoskeletal system connective tissue	46975	83	69201	317
	congenital anomalies	108487	356	7689	44
	perinatal conditions	106338	365	9838	35
	symptoms signs ill-defined conditions	13015	6	103161	394
	injury poisoning	24410	15	91766	385
	V Codes	15501	7	100675	393

the improvement of diagnostic precision helps to resolve difficulties in establishing the independence of specific child disorders, another approach to understanding these differences may derive from an examination of the physical disorder profiles associated with specific childhood disorders, such as EMD and ADHD. The present study reports on the annual prevalence of EMD and ADHD, in addition to the similarities and differences in comparing the profiles of major class International Classification of Diseases (ICD) of those with EMD and ADHD in relationship to those with both EMD/ADHD and all Other Mental Disorders (OMD).

Methods

Using a population sampling frame, the unique identifiers of 238303 individuals (51% male) up to 18 years of age were selected from the regional health service registry in the Calgary health zone (Calgary, Alberta, Canada) and merged with all direct physician billings (n =10802484) from 1993-2010 for treatment of any presenting concern, resulting in 16 years of fiscal data (1994-2009). Each billing record pertains to services rendered to patients on specified dates resulting in the assignment of an ICD diagnostic code. This study employed an anonymous data set that included International Classification of Diseases (ICD) diagnoses, visit date, age at index visit, and sex.

The annual population rates of the diagnostic groupings were based on the number of unique individuals diagnosed by a physician with ADHD or EMD, or both, or any other mental disorders in any given year, denominated by the civic census of those up to 18 years of age from 1994-2009. The 16-year prevalence was based on the total number of unique individuals diagnosed denominated by a standardized base population (e.g., 2001).

The data was collapsed into four basic groups representing the dependent variables: Presence or absence of EMD (+/-EMD) or ADHD (+/-ADHD), or both EMD and ADHD (+/- BOTH) or any other mental disorder (+/-OMD). EMD did not include schizophrenia, or single or recurrent Major Depression, but included Manic Depressive Disorder, Bipolar Affective Disorder, and Affective Psychosis NOS). These three dependent variables were expressed as the odds ratios of the remaining classes of ICD disorders including V codes (independent variables) as compared to the base category, those without mental disorder. Differences were based on a comparison of overlapping and non-overlapping 95% confidence intervals. For rates, significant statistical differences between proportions in any given year were estimated by comparison of the 95% confidence intervals using the standard formula, wherein non-overlapping 95% confidence intervals represent significant differences ($p < 0.05$, with z set to 1.96). The sexes were examined separately.

In each case (Table 1), column a represents those without any psychiatric diagnosis or the independent main ICD class disorder, column b represents the frequency of those with the independent man ICD class disorder and without the dependent mental disorder (OMD, EMD, ADHD, both ADHD/EMD), column c represents those without the independent man ICD class disorder and with the dependent mental disorder (OMD, EMD, ADHD, both ADHD/EMD), column d represents those with both the independent man ICD class disorder and the dependent mental disorder (OMD, EMD, ADHD, both ADHD/EMD). Calculation of the odds ratio was based on the formula OR = [(ad)/(bc)].

Results

The sample included 116176 females and 119717 males with a total of 10802484 visits with physician-assigned diagnoses for 3490912 unique patient-diagnoses (50% male). On average individuals had 15 diagnoses (median 13; 90th percentile 21; range 1-89). Thirty-two percent had at least one mental disorder over 16 fiscal years from 1993-2009 [21]. For females, the prevalence rates were 1.2% for EMD 4.5% ADHD and 0.25% for Both EMD/ADHD. For males, the prevalence rates were 0.92% for EMD 12%, ADHD and 0.38% for Both EMD/ADHD.

The EMD diagnoses represented 2866 individuals (44% male) of mean age 15.6 years. EMD diagnoses were made primarily by psychiatrists (58%), followed by general practitioners (30%) and other specialties (12%). The EMD first diagnosis date was assigned by general practitioners 248 days on average before the EMD first diagnosis date assigned by psychiatrists and 397 days in the median.

The mean age was 10.7 years (22486 individuals, 73% male) among those having a diagnosis of ADHD. ADHD diagnoses were made

Table 2: Annual rates per 100,000 of EMD and ADHD for males and females combined in the population.

	Females			Males		
Year	EMD	ADHD	Both EMD/ADHD	EMD	ADHD	Both EMD/ADHD
16 yr	1210	4530	253	920	11938	384
1994	42	234	6	34	604	10
1995	81	341	9	40	947	9
1996	93	423	7	51	930	15
1997	76	330	6	48	914	16
1998	75	342	7	39	828	12
1999	65	323	14	56	800	18
2000	80	284	14	52	694	20
2001	76	274	16	65	697	21
2002	75	257	10	60	682	31
2003	51	230	9	39	690	15
2004	81	273	24	70	725	30
2005	87	299	23	64	745	26
2006	93	249	23	73	696	34
2007	84	243	25	67	671	34
2008	92	210	28	80	627	40
2009	64	213	21	66	589	34

primarily by pediatricians (45%), followed by general practitioners (43%) and by psychiatrists (11%) and the remaining 1% by other specialties. The ADHD first diagnosis date was assigned by general practitioners 98 days on average before the ADHD first diagnosis date assigned by psychiatrists and 132 days in the median.

The mean age was 14.8 years for 865 individuals (61% male) among those having a diagnosis of ADHD and EMD. Where both diagnoses co-occurred, diagnoses were made primarily by pediatricians (1.3%), followed by general practitioners (25%) and by psychiatrists (63%) and the remaining 10.7% by other specialties.

Table 2 shows the annual rates per 100,000 of EMD and ADHD for those up to the age of 18 years. The rate of ADHD is less consistent from year to year and two to four times higher than the rate of EMD in the population in various years.The population rate for episodic mood disorder and ADHD are relatively stable (Table 2). Compared to males, the 16-year prevalence rate of EMD is higher for females (132%) and for each year. The 16-year prevalence rate of ADHD is less for females (38%) and for each year, as is the rate for both EMD/ADHD (66%).

Table 3 shows the odds ratios and 95% confidence intervals by sex and main ICD class for each dependent group category is rank ordered from the highest to the lowest odds ratio bison for the category with the highest value which in each case was the column containing the group with both ADHD/EMD.

For males with both ADHD/EMD, the main ICD class disorders injury poisoning, symptoms signs ill-defined conditions, V Codes, nervous system, circulatory system and respiratory system ranked highest. For females with both ADHD/EMD, V Codes, symptoms signs ill-defined conditions, injury poisoning, genitourinary system, respiratory system, digestive system, endocrine etc, sense organs, nervous system, skin subcutaneous tissue and musculoskeletal system connective tissue were the highest ranking main ICD class disorders.

Tables 4 summarizes the significant differences in the OR distributions for males and females comparing groups based on direction (TRUE/FALSE) and significance (with "+" representing non-overlapping 95%CIs and "-" representing non-significance). The constellations of ORs denoted as TRUE or FALSE satisfying the condition in the column header, being in each case with the independent class of ICD disorder being greater than or less than another dependent category of OR category. For both male and females, ADHD is significantly different from EMD across the following ICD main disorder classes: blood and blood-forming organs, circulatory system, and digestive system, endocrine, genitourinary system, musculoskeletal system connective tissue, neoplasms, nervous system, respiratory system, skin subcutaneous tissue, symptoms signs ill-defined conditions. For females, ADHD is significantly different from EMD across the following ICD main disorder classes: sense organs, perinatal conditions, congenital anomalies. For males, ADHD is significantly different from EMD across the ICD main disorder class injury and poisoning.

Discussion

The relationship between mental and physical disorders in children and adults and overall prevalence rates in this population are well-described [21-23]. Compared to males, the female rates for EMD were higher and lower for ADHD and for both EMD/ADHD, respectively. The sex difference in the rates of these disorders indicates an independent etiology for EMD and ADHD and supports the concept of these disorders being distinct diagnostic entities. That the rates for those with both EMD/ADHD were lower and intermediate in comparison of the sexes does not provide evidence of the combination being a distinct diagnostic entity.

Table 3: Odds ratios for males and females [with 95% CIs] for each condition.

	Group			
ICD Main Class	Any Other MD	EMD	ADHD	BOTH EMD/ADHD
Males				
injury poisoning	2.99 [2.89 3.09]	3.81 [3.08 4.71]	2.14 [2.03 2.27]	5.01 [3.45 7.27]
symptoms signs ill-defined conditions	3.25 [3.13 3.38]	3.4 [2.72 4.23]	2.38 [2.24 2.53]	4.79 [3.21 7.15]
V Codes	2.58 [2.51 2.66]	1.7 [1.49 1.93]	2.55 [2.43 2.68]	3.81 [2.92 4.98]
nervous system	2.68 [2.57 2.79]	2.94 [2.62 3.3]	1.57 [1.49 1.65]	3.25 [2.74 3.87]
circulatory system	2.25 [2.17 2.33]	2.91 [2.6 3.26]	1.23 [1.17 1.3]	2.89 [2.43 3.44]
respiratory system	2.65 [2.54 2.76]	1.54 [1.28 1.86]	2.18 [2.03 2.34]	2.82 [1.93 4.12]
endocrine etc	2.03 [1.96 2.1]	2.4 [2.14 2.69]	1.38 [1.31 1.44]	2.73 [2.31 3.23]
skin subcutaneous tissue	2.05 [2 2.11]	1.8 [1.59 2.03]	1.53 [1.47 1.59]	2.44 [1.98 3.01]
musculoskeletal system connective tissue	2.2 [2.15 2.25]	2.46 [2.2 2.75]	1.32 [1.28 1.37]	2.25 [1.9 2.67]
digestive system	1.99 [1.94 2.03]	2.03 [1.84 2.24]	1.51 [1.46 1.57]	2.22 [1.9 2.58]
complications of pregnancy childbirth	1.52 [1.37 1.68]	1.29 [0.88 1.91]	1.43 [1.24 1.63]	1.91 [1.16 3.15]
neoplasms	1.65 [1.6 1.71]	1.63 [1.45 1.84]	1.11 [1.05 1.16]	1.83 [1.53 2.19]
genitourinary system	1.84 [1.79 1.88]	1.56 [1.41 1.73]	1.53 [1.48 1.59]	1.82 [1.56 2.13]
sense organs	1.76 [1.71 1.8]	1 [0.9 1.11]	2.06 [1.97 2.16]	1.67 [1.38 2.03]
infectious-parasitic diseases	1.48 [1.43 1.52]	1.21 [1.06 1.37]	1.51 [1.45 1.58]	1.65 [1.38 1.98]
blood-blood-forming organs	1.49 [1.41 1.56]	1.38 [1.14 1.67]	1.21 [1.13 1.3]	1.21 [0.89 1.65]
congenital anomalies	1.55 [1.48 1.61]	0.88 [0.72 1.06]	1.59 [1.5 1.68]	1.19 [0.92 1.55]
perinatal conditions	1.01 [0.97 1.06]	0.24 [0.17 0.34]	1.46 [1.38 1.55]	0.53 [0.37 0.77]
Female				
V Codes	6.88 [6.58 7.19]	7.05 [5.34 9.31]	2.81 [2.5 3.15]	8.64 [4.09 18.26]
symptoms signs ill-defined conditions	5.67 [5.42 5.94]	6.41 [4.79 8.59]	2.86 [2.52 3.24]	8.28 [3.7 18.56]
injury poisoning	3.84 [3.72 3.96]	4.39 [3.69 5.23]	2.34 [2.15 2.55]	6.83 [4.08 11.44]
genitourinary system	5.06 [4.93 5.2]	6.43 [5.52 7.48]	1.42 [1.34 1.51]	4.89 [3.52 6.81]
respiratory system	4.05 [3.85 4.25]	3.72 [2.86 4.83]	2.36 [2.06 2.69]	4.04 [2.09 7.83]
digestive system	2.55 [2.49 2.61]	2.8 [2.57 3.06]	1.57 [1.49 1.66]	3.61 [2.88 4.51]
endocrine etc	2.86 [2.77 2.95]	3.12 [2.87 3.39]	1.37 [1.29 1.46]	3.23 [2.65 3.94]
sense organs	1.86 [1.81 1.91]	1.59 [1.43 1.77]	2.3 [2.13 2.49]	2.93 [2.12 4.04]
nervous system	3.28 [3.16 3.4]	3.2 [2.94 3.49]	1.4 [1.31 1.5]	2.92 [2.38 3.58]
skin subcutaneous tissue	2.72 [2.65 2.8]	2.69 [2.37 3.06]	1.64 [1.53 1.76]	2.66 [1.95 3.63]
musculoskeletal system connective tissue	3.31 [3.23 3.39]	3.31 [2.97 3.69]	1.42 [1.34 1.5]	2.59 [2.04 3.3]
infectious-parasitic diseases	1.95 [1.9 2.01]	1.78 [1.64 1.94]	1.57 [1.48 1.66]	2.34 [1.92 2.85]
circulatory system	3.01 [2.9 3.12]	2.78 [2.54 3.04]	1.13 [1.05 1.21]	2.27 [1.82 2.83]
complications of pregnancy childbirth	4.98 [4.82 5.14]	3.29 [3.03 3.57]	0.98 [0.92 1.04]	2.06 [1.68 2.51]
blood-blood-forming organs	2.29 [2.2 2.38]	2.2 [1.99 2.44]	1.11 [1.02 1.2]	1.97 [1.53 2.53]
congenital anomalies	1.47 [1.4 1.54]	1.23 [1.06 1.43]	1.54 [1.41 1.69]	1.74 [1.27 2.39]
neoplasms	2.26 [2.19 2.33]	1.96 [1.79 2.14]	1.01 [0.95 1.08]	1.36 [1.08 1.7]
perinatal conditions	1.38 [1.33 1.44]	1.34 [1.18 1.53]	1.32 [1.21 1.44]	1.04 [0.73 1.47]

Table 4: Summary of Significant differences for females and males.

	Condition of gorup comparsion (+ = p < .05. - = ns)					
ICD Main Class	ADHD<Any OTHER	ADHD<EMD	ADHD<BOTH	EMD>Any OTHER	EMD>BOTH	BOTH>Any OTHER
Male						
sense organs	FALSE-	FALSE-	FALSE-	FALSE-	FALSE-	FALSE-
congenital anomalies	FALSE-	FALSE-	FALSE-	FALSE-	FALSE-	FALSE-
perinatal conditions	FALSE-	FALSE-	FALSE-	FALSE-	FALSE-	FALSE-
infectious-parasitic diseases	FALSE-	FALSE-	TRUE-	FALSE-	FALSE-	TRUE-
complications of pregnancy childbirth	TRUE-	FALSE-	TRUE-	FALSE-	FALSE-	TRUE-
V Codes	TRUE-	FALSE-	TRUE+	FALSE-	FALSE-	TRUE+
respiratory system	TRUE+	FALSE-	TRUE-	FALSE-	FALSE-	TRUE-
blood-blood-forming organs	TRUE+	TRUE-	FALSE-	FALSE-	TRUE-	FALSE-
genitourinary system	TRUE+	TRUE-	TRUE-	FALSE-	FALSE-	FALSE-
skin subcutaneous tissue	TRUE+	TRUE-	TRUE+	FALSE-	FALSE-	TRUE-
neoplasms	TRUE+	TRUE+	TRUE+	FALSE-	FALSE-	TRUE-
nervous system	TRUE+	TRUE+	TRUE+	TRUE-	FALSE-	TRUE-
digestive system	TRUE+	TRUE+	TRUE+	TRUE-	FALSE-	TRUE-
musculoskeletal system connective tissue	TRUE+	TRUE+	TRUE+	TRUE-	TRUE-	TRUE-
symptoms signs ill-defined conditions	TRUE+	TRUE+	TRUE+	TRUE-	FALSE-	TRUE-
injury poisoning	TRUE+	TRUE+	TRUE+	TRUE-	FALSE-	TRUE+
endocrine etc	TRUE+	TRUE+	TRUE+	TRUE+	FALSE-	TRUE+
circulatory system	TRUE+	TRUE+	TRUE+	TRUE+	TRUE-	TRUE+
Female						
injury poisoning	FALSE-	FALSE-	TRUE+	FALSE-	FALSE-	TRUE+
V Codes	FALSE-	FALSE-	TRUE+	FALSE-	FALSE-	TRUE+
infectious-parasitic diseases	TRUE-	TRUE-	TRUE-	FALSE-	FALSE-	TRUE-
complications of pregnancy childbirth	TRUE-	TRUE+	FALSE-	TRUE+	TRUE+	FALSE-
respiratory system	TRUE+	FALSE-	TRUE-	FALSE-	FALSE-	TRUE-
circulatory system	TRUE+	FALSE-	TRUE+	FALSE-	FALSE-	FALSE-
neoplasms	TRUE+	TRUE-	TRUE-	FALSE-	FALSE-	FALSE-
congenital anomalies	TRUE+	TRUE-	TRUE-	FALSE-	TRUE-	FALSE-
perinatal conditions	TRUE+	TRUE+	FALSE-	TRUE+	TRUE+	FALSE-
nervous system	TRUE+	TRUE+	TRUE-	TRUE+	TRUE+	FALSE-
endocrine etc	TRUE+	TRUE+	TRUE+	FALSE-	FALSE-	FALSE-
sense organs	TRUE+	TRUE+	TRUE+	FALSE-	FALSE-	FALSE-
digestive system	TRUE+	TRUE+	TRUE+	TRUE-	FALSE-	TRUE-
skin subcutaneous tissue	TRUE+	TRUE+	TRUE+	FALSE-	FALSE-	TRUE-
musculoskeletal system connective tissue	TRUE+	TRUE+	TRUE+	FALSE-	FALSE-	TRUE-
genitourinary system	TRUE+	TRUE+	TRUE+	TRUE+	FALSE-	TRUE+
symptoms signs ill-defined conditions	TRUE+	TRUE+	TRUE+	TRUE+	FALSE-	TRUE+
blood-blood-forming organs	TRUE+	TRUE+	TRUE+	TRUE+	TRUE+	FALSE-

In particular, children with mental disorders suffer physical disorders twice as frequently as those who do not [22], however, the profiles for those with EMD and ADHD were different from all other mental disorders, and distinct from one another. The profile of physical disorders distinguished EMD and ADHD. Furthermore, in terms of the independent ICD physical disorder classes, the Odds Ratio (OR) for EMD was greater than most of both the ADHD and the OMD groups. This primary finding indicated a distinct clinical pattern, suggesting a different independent etiology for EMD and ADHD. If the two entities had a similar pathophysiology, one would expect to find much more similitude between the aggregates of diseases than observed for each disorder. In opposition, the OR showed a wide disparity between the two diagnostic categories suggesting that they are distinct disorders. The further support of this distinction is found in the different annual and cumulative prevalence rates of ADHD and EMD. For ADHD and EMD to have a common etiology, one would expect more similar prevalence rates, in addition to similar physical disorder profiles.

A primary limitation of the study is the diagnostic precision or the reliability and validity of physician diagnosis. Diagnostic precision necessarily affects results at some level in terms of false positive and negative rates. Diagnoses within each category suffer more or less equally from this problem to the extent that a random distribution of more or less accurate diagnoses based on physician expertise would arise in the data.

Further, the main ICD class diagnostic groupings combine diagnoses providing a general approach to illustrate the relationship between the dependent variables. As a result, more specific diagnosis-related associations may well be masked. Detailed analysis of all unique diagnoses may eventually be warranted to provide more information about etiology, especially in relation to the temporal order of diagnoses.

Another issue worthy of consideration, beyond the scope of this current paper, is a full description of the epidemiology and physical disorder profiles of those who have both EMD and ADHD. It may be that there is yet another etiological dimension within the continuum of mental disorders that may be conceptualized and examined as a discrete entity. More research is required to examine whether or not this is the case or if the combination of ADHD and EMD represents, in terms of physical disorder profiles, the intensity of having two discrete concurrent disorders. The present paper does not provide evidence in support of the contention that the combination of ADHD and EMD represents a novel diagnostic entity.

Notwithstanding the limitations, understanding the relationships between comorbid disorders in a population, as presented in this paper, is a novel approach to comparative disease study. The presented results illustrate the potential to understand the complex nature of clinical profiles associated with a given disease state in that it reveals key aspects potentially related to etiological and prognostic comorbidity. Future work will focus on clinical pathways.

Main Formula: Odds Ratio: OR = [(ad)/(bc)].

P values based on comparison of 95% confidence intervals, where $p < 0.05$ is based on non-overlapping 95% confidence intervals.

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