

Disclaimer

The following report(s) provides findings from an FDA-initiated query using its Mini-Sentinel pilot. While Mini-Sentinel queries may be undertaken to assess potential medical product safety risks, they may also be initiated for various other reasons. Some examples include determining a rate or count of an identified health outcome of interest, examining medical product use, exploring the feasibility of future, more detailed analyses within Mini-Sentinel, and seeking to better understand the capabilities of the Mini-Sentinel pilot.

Data obtained through Mini-Sentinel are intended to complement other types of evidence such as preclinical studies, clinical trials, postmarket studies, and adverse event reports, all of which are used by FDA to inform regulatory decisions regarding medical product safety. The information contained in this report is provided as part of FDA's commitment to place knowledge acquired from the Mini-Sentinel pilot in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in Mini-Sentinel queries will continue to be communicated through existing channels.

FDA wants to emphasize that the fact that FDA has initiated a query involving a medical product and is reporting findings related to that query does not mean that FDA is suggesting health care practitioners should change their prescribing practices for the medical product or that patients taking the medical product should stop using it. Patients who have questions about the use of an identified medical product should contact their health care practitioners.

The following report contains a description of the request, request specifications, and results from the modular program run(s).

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Overview

Request Description MSOC initiated a query using Modular Program #3 (MP3) to investigate anti-depressant use (SSRIs, SNRIs, and tricyclics) and risk of bleeding events (intracerebral and gastrointestinal hemorrhage) among members with a pre-existing condition of depression, and members with no pre-existing condition requirements. The query was run against the Mini-Sentinel Distributed Database for the time period 1/1/2009 to 12/31/2011 (query period). The package was distributed to 18 Data Partners on February 12, 2012.

Results provide counts of new SSRI, SNRI, and tricyclics users, treatment episodes, dispensings, total days supplied, days at risk, events, eligible members, and member-days. Total days supplied are from the MSCDM outpatient pharmacy table for records identified using valid NDC codes (for any form, e.g., tablet, vial, topical). A user is considered a new user if they 1) are unexposed to the anti-depressant class of interest in the 183 days before index (exposure washout period); and 2) have not had an event of interest in the 183 days before index (event washout period).

Request ID msy4_mpr17_v1

Specifications Program parameter inputs and scenarios

Glossary List of Terms found in this Report and their Definitions

Table1 Table displaying the Number of New Users, New Episodes, Dispensings, Total Days Supplied, Days at Risk, New Events, Eligible Members, Member-Days, New Users per 1,000 Eligible Members, Days Supplied per User, Dispensings per User, Days Supplied per Dispensing, and New Events per 100,00 Days at Risk by Drug Class, Outcome, and Pre-Existing Condition Criteria - January 1, 2009 to December 31, 2011.

Figure1 Three figures displaying the information in Table 1.

Table2 Table displaying the Number of New Users, New Episodes, Dispensings, Total Days Supplied, Days at Risk, New Events, Eligible Members, Member-Days, New Users per 1,000 Eligible Members, Days Supplied per User, Dispensings per User, Days Supplied per Dispensing, and New Events per 100,00 Days at Risk by Drug Class, Outcome, Pre-Existing Condition Criteria, and Age Group - January 1, 2009 to December 31, 2011.

Table3 Table displaying the Number of New Users, New Episodes, Dispensings, Total Days Supplied, Days at Risk, New Events, Eligible Members, Member-Days, New Users per 1,000 Eligible Members, Days Supplied per User, Dispensings per User, Days Supplied per Dispensing, and New Events per 100,00 Days at Risk by Drug Class, Outcome, Pre-Existing Condition Criteria, and Sex - January 1, 2009 to December 31, 2011.

Table4 Table displaying the Number of New Users, New Episodes, Dispensings, Total Days Supplied, Days at Risk, New Events, Eligible Members, Member-Days, New Users per 1,000 Eligible Members, Days Supplied per User, Dispensings per User, Days Supplied per Dispensing, and New Events per 100,00 Days at Risk by Drug Class, Outcome, Pre-Existing Condition Criteria, and Year - January 1, 2009 to December 31, 2011.

Notes: Please contact the Mini-Sentinel Operations Center (MSOC_Requests@harvardpilgrim.org) for questions and to provide comments/suggestions for future enhancements to this document.

Glossary of Terms in Modular Program 3*

Blackout Period - number of days at the beginning of a treatment episode that events are to be ignored. If an event occurs during the blackout period, the episode is excluded.

Care Setting - type of medical encounter or facility where the exposure, event, or condition code was recorded. Possible care settings include: Inpatient Hospital Stay (IP), Non-Acute Institutional Stay (IS), Emergency Department (ED), Ambulatory Visit (AV), and Other Ambulatory Visit (OA).

Days at Risk - number of days members are at risk for an event during a treatment episode (calculated using number of days supplied plus any episode gaps and exposure extension periods).

Eligible Members - Number of members eligible for an incident treatment episode (defined by the exposure and event washout periods) with drug and medical coverage during the query period.

Enrollment Gap - number of days allowed between two consecutive enrollment periods without breaking a "continuously enrolled" sequence.

Episode Gap - number of days allowed between two (or more) consecutive treatment episodes to be considered the same treatment episode.

Exposure Extension Period - number of days post-treatment episode where outcomes/events are still attributed to a treatment episode.

Incidence type (drug/exposure)- Minimum incidence type will consider the first treatment episode in the query period as long as it is the first treatment episode in the user's entire available history. Single and Multiple incidence types will use the washout period to establish incidence; however, Single will only consider the first treatment episode whereas Multiple will consider all qualifying incident treatment episodes.

Incidence type (event/outcome)- Minimum incidence type considers the first event in a valid episode as long as it is the first event in the user's entire available history. Multiple incidence type uses the washout period to establish incidence and considers all qualifying incident treatment episodes. The program will only consider one event per episode, but the Multiple incidence type will consider more than one event per user if a user has more than one incident episode.

Inclusion/Exclusion Indicator - indicates whether condition(s) of interest are used for inclusion or exclusion criteria. A value of 1 instructs the program that members must have the condition of interest (inclusion criteria); a value of 0 instructs the program that members must not have the condition of interest (exclusion criteria).

Lookback Period Start and End - range of days relative to index that the program looks for inclusion/exclusion conditions of interest. For example, if the Inclusion/Exclusion Indicator =1, Lookback Period Start = -183 and Lookback Period End = 0, the cohort will only include members with the condition of interest present in the 183 days prior to and including the index date (the index date is day 0).

Member-Days - sum of all days a member is eligible for an incident treatment episode (i.e., days that the member meets all inclusion criteria such as incidence, pre-existing condition, and enrollment requirements).

Minimum Days Supplied - specifies a minimum number of days in length of the days supplied for the episode to be

Minimum Episode Duration - specifies a minimum number of days a treatment episode must have in order to be considered.

New Episodes - new treatment episodes; length of episode is determined by days supplied in one dispensing (or consecutive dispensings bridged by the episode gap).

New Users - number of members with incident exposure during the query period. A user may only be counted once in a query period.

Principal Diagnosis - diagnosis or condition established to be chiefly responsible for admission of the patient to the hospital. YES will only consider diagnoses flagged as Principal.

Query Period - period in which the modular program evaluates exposures of interest.

Total Days Supplied - number of days supplied for all dispensings in qualifying treatment episodes.

Washout Period (drug/exposure)** - number of days a user is required to have no evidence of prior exposure (drug dispensing/procedure) and continuous drug and medical coverage prior to an incident treatment episode.

Washout Period (event/outcome)** - number of days a user is required to have no evidence of a prior event (procedure/diagnosis) and continuous drug and medical coverage prior to an incident treatment episode.

*all terms may not be used in this report

Modular Program 3 Specifications for Query ID MSY4_MPR17

Modular Program #3 was used to investigate intracerebral hemorrhage (ICH) and gastrointestinal hemorrhage (GIH) diagnoses among new SSRI, SNRI, and tricyclics users with and without the criteria of a pre-existing condition of depression (please see Appendix A for a list of ICD-9-CM codes used in this request). The query period was from January 1, 2009 to December 31, 2011, and the enrollment gap was set at 45 days. Age groups were split as follows: 0-19, 20-34, 35-49, 50-64, 65-79, 80+. In total, 12 different scenarios were examined in this report with differing exposures of interest, events, and pre-existing condition requirements. See below for a description of each of these scenarios.

Scenario	Drug/Exposure								Inclusion/Exclusion Condition(s)							Event/Outcome				
	Incident exposure	Incident w/ respect to:	Washout (days)	incidence type*	Episode gap	Extension period	Min episode duration	Min days supplied	Condition	Inclusion/Exclusion Indicator	Lookback Start	Lookback End	Care Setting	Principal Dx	Event/Outcome	Washout (days)	incidence type**	Care Setting	Principal Dx	Blackout Period
1	SSRI	SSRI	183	Mult	0	0	0	0	None	---	---	---	---	---	GIH	183	Mult	All	No	0
2	SSRI	SSRI	183	Mult	0	0	0	0	None	---	---	---	---	---	ICH	183	Mult	All	No	0
3	SSRI	SSRI	183	Mult	0	0	0	0	Depression	1	-183	0	All	No	GIH	183	Mult	All	No	0
4	SSRI	SSRI	183	Mult	0	0	0	0	Depression	1	-183	0	All	No	ICH	183	Mult	All	No	0
5	SNRI	SNRI	183	Mult	0	0	0	0	None	---	---	---	---	---	GIH	183	Mult	All	No	0
6	SNRI	SNRI	183	Mult	0	0	0	0	None	---	---	---	---	---	ICH	183	Mult	All	No	0
7	SNRI	SNRI	183	Mult	0	0	0	0	Depression	1	-183	0	All	No	GIH	183	Mult	All	No	0
8	SNRI	SNRI	183	Mult	0	0	0	0	Depression	1	-183	0	All	No	ICH	183	Mult	All	No	0
9	Tricyclics	Tricyclics	183	Mult	0	0	0	0	None	---	---	---	---	---	GIH	183	Mult	All	No	0
10	Tricyclics	Tricyclics	183	Mult	0	0	0	0	None	---	---	---	---	---	ICH	183	Mult	All	No	0
11	Tricyclics	Tricyclics	183	Mult	0	0	0	0	Depression	1	-183	0	All	No	GIH	183	Mult	All	No	0
12	Tricyclics	Tricyclics	183	Mult	0	0	0	0	Depression	1	-183	0	All	No	ICH	183	Mult	All	No	0

NDC codes checked against First Data Bank's "National Drug Data File (NDDF®) Plus"
 ICD-9-CM diagnosis and procedure codes checked against "Ingenix 2012 ICD-9-CM Data File" provided by OptumInsight
 HCPCS codes checked against "Optum 2012 HCPCS Level II Data File" provided by OptumInsight
 CPT codes checked against "Optum 2012 Current Procedure Codes & Relative Values Data File" provided by OptumInsight

*A "multiple" incidence type for the exposure will consider all treatment episodes for a user during the query period that satisfies the washout period. A user may have more than one treatment episode.

**A "multiple" incidence type for the event will consider the first event for each episode that satisfies the Washout Period criteria of 183 days. There can be at most one event per episode, but a user may have multiple events if they have multiple episodes.

Table 1. Summary of Incident Anti-Depressant Use and Intracerebral and Gastrointestinal Bleeding in the MSDD between January 1, 2009 and December 31, 2011, by Drug Class and Outcome

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/100K Days at Risk
SNRIs													
<i>No Pre-Existing Criteria</i>													
Outcome of GIH	712,214	744,068	1,441,575	50,788,629	49,534,617	573	66,014,568	39,274,095,438	10.79	71.31	2.02	35.23	1.16
Outcome of ICH	713,032	745,017	1,443,052	50,836,421	49,604,001	242	66,016,962	39,288,425,501	10.80	71.30	2.02	35.23	0.49
<i>Pre-Existing Depression</i>													
Outcome of GIH	322,862	331,719	680,253	23,934,032	23,320,508	309	5,144,573	1,312,236,900	62.76	74.13	2.11	35.18	1.33
Outcome of ICH	323,370	332,299	681,186	23,963,861	23,361,742	125	5,145,569	1,313,984,893	62.84	74.11	2.11	35.18	0.54
SSRIs													
<i>No Pre-Existing Criteria</i>													
Outcome of GIH	2,800,664	3,016,101	5,748,523	217,465,130	210,634,069	2,523	64,336,986	37,405,819,415	43.53	77.65	2.05	37.83	1.20
Outcome of ICH	2,801,822	3,017,741	5,748,214	217,444,915	210,713,155	1,115	64,339,459	37,418,745,880	43.55	77.61	2.05	37.83	0.53
<i>Pre-Existing Depression</i>													
Outcome of GIH	1,072,924	1,117,617	2,249,998	86,869,565	84,003,869	1,061	3,966,681	764,931,107	270.48	80.97	2.10	38.61	1.26
Outcome of ICH	1,073,829	1,118,667	2,250,647	86,887,014	84,069,999	428	3,967,943	766,023,859	270.63	80.91	2.10	38.61	0.51
Tricyclics													
<i>No Pre-Existing Criteria</i>													
Outcome of GIH	727,654	772,432	1,153,708	42,325,531	41,440,866	548	66,325,331	39,468,463,947	10.97	58.17	1.59	36.69	1.32
Outcome of ICH	728,703	773,628	1,155,833	42,401,274	41,531,828	264	66,327,714	39,482,938,259	10.99	58.19	1.59	36.68	0.64
<i>Pre-Existing Depression</i>													
Outcome of GIH	134,071	138,694	230,477	8,317,668	8,109,804	159	5,452,900	1,472,384,998	24.59	62.04	1.72	36.09	1.96
Outcome of ICH	134,463	139,122	231,347	8,348,311	8,146,155	63	5,453,895	1,474,338,555	24.65	62.09	1.72	36.09	0.77

Figure 1a. Number of New Users, New Episodes, and Dispensings between January 1, 2009 and December 31, 2011 by Drug Class, Outcome, and Pre-existing Condition Requirements

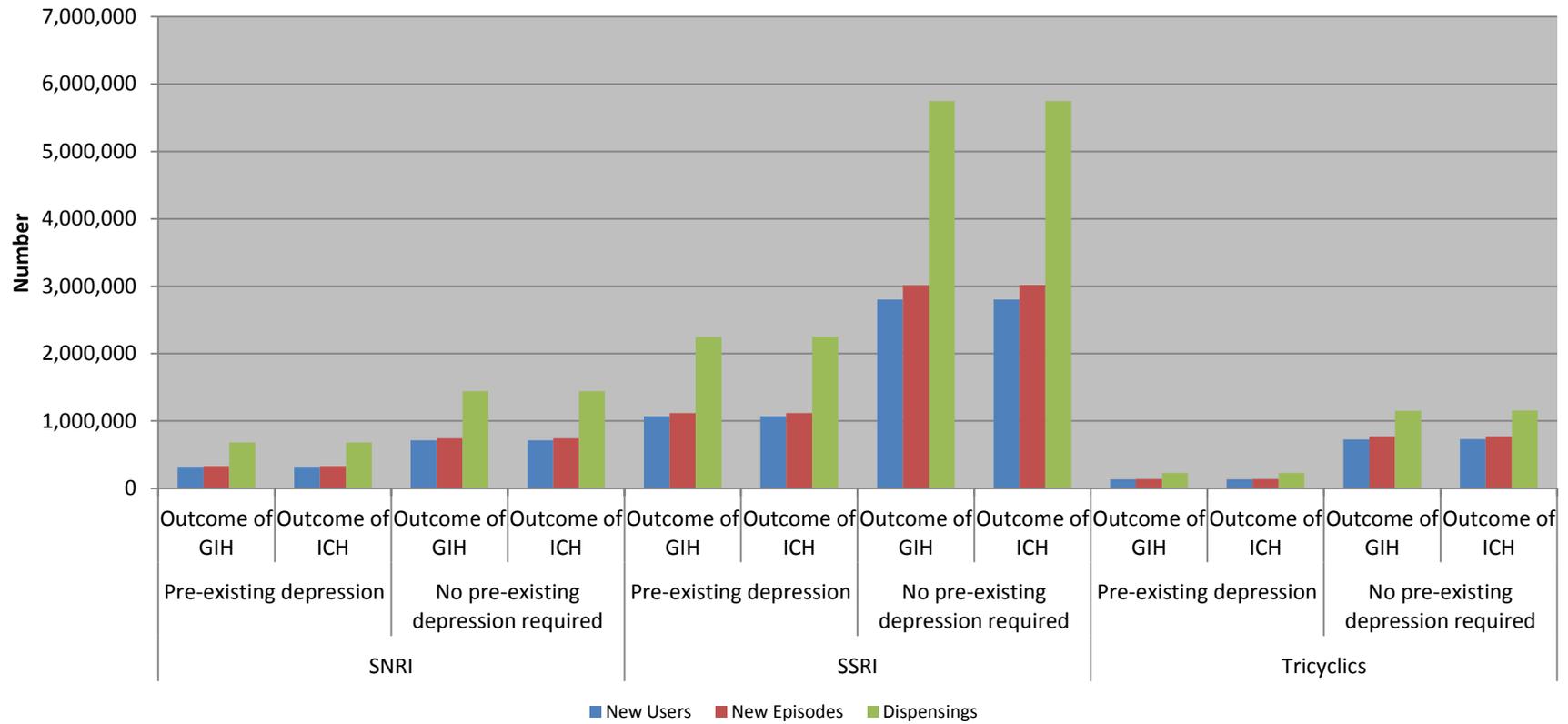


Figure 1b. New Users per 1,000 Eligible Members, Dispensings per User, and New Events per 100,000 Days at Risk between January 1, 2009 and December 31, 2011 by Drug Class, Outcome, and Pre-existing Condition Requirements

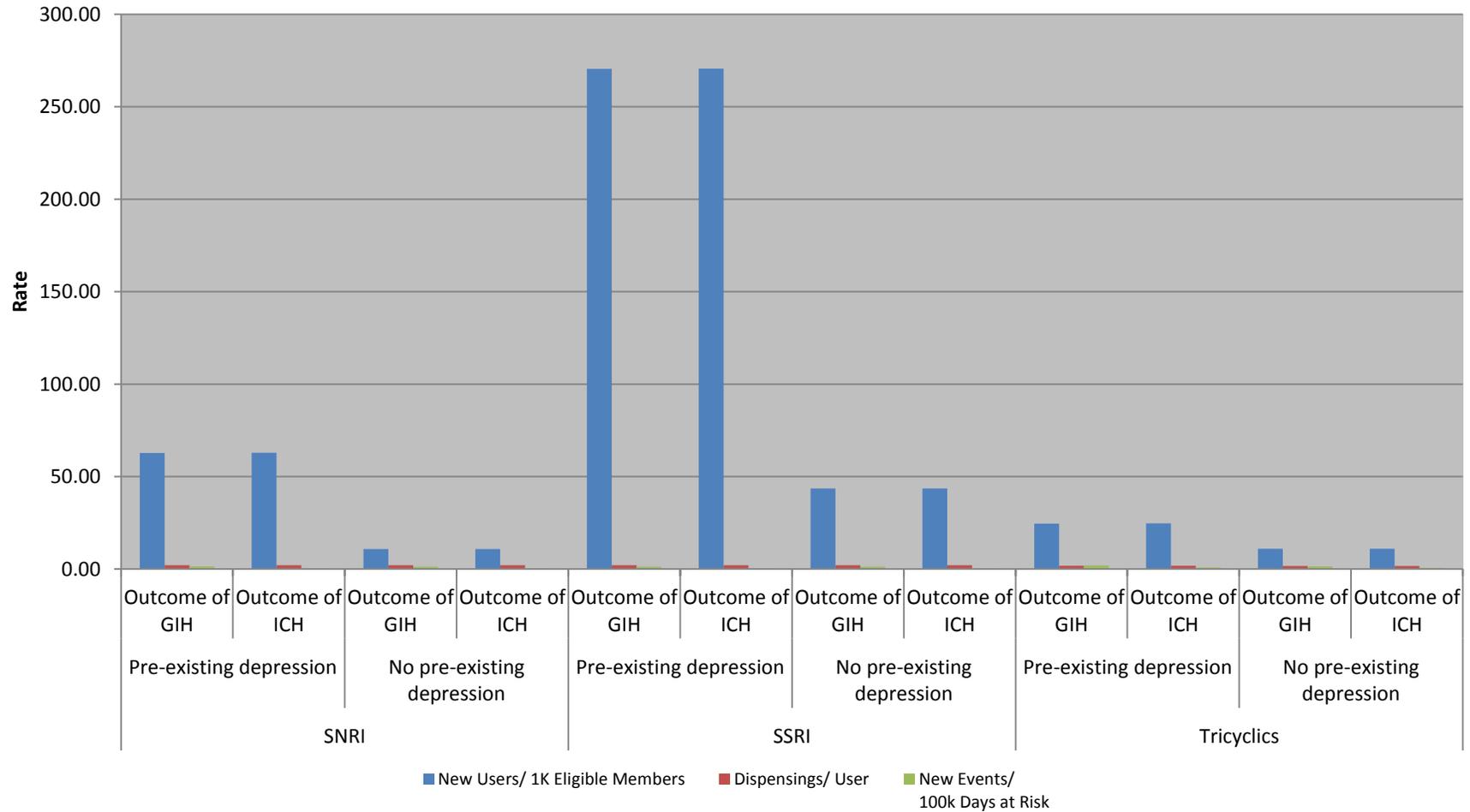


Figure 1c. Days Supplied per User and Days Supplied per Dispensing between January 1, 2009 and December 31, 2011 by Drug Class, Outcome, and Pre-existing Condition Requirements

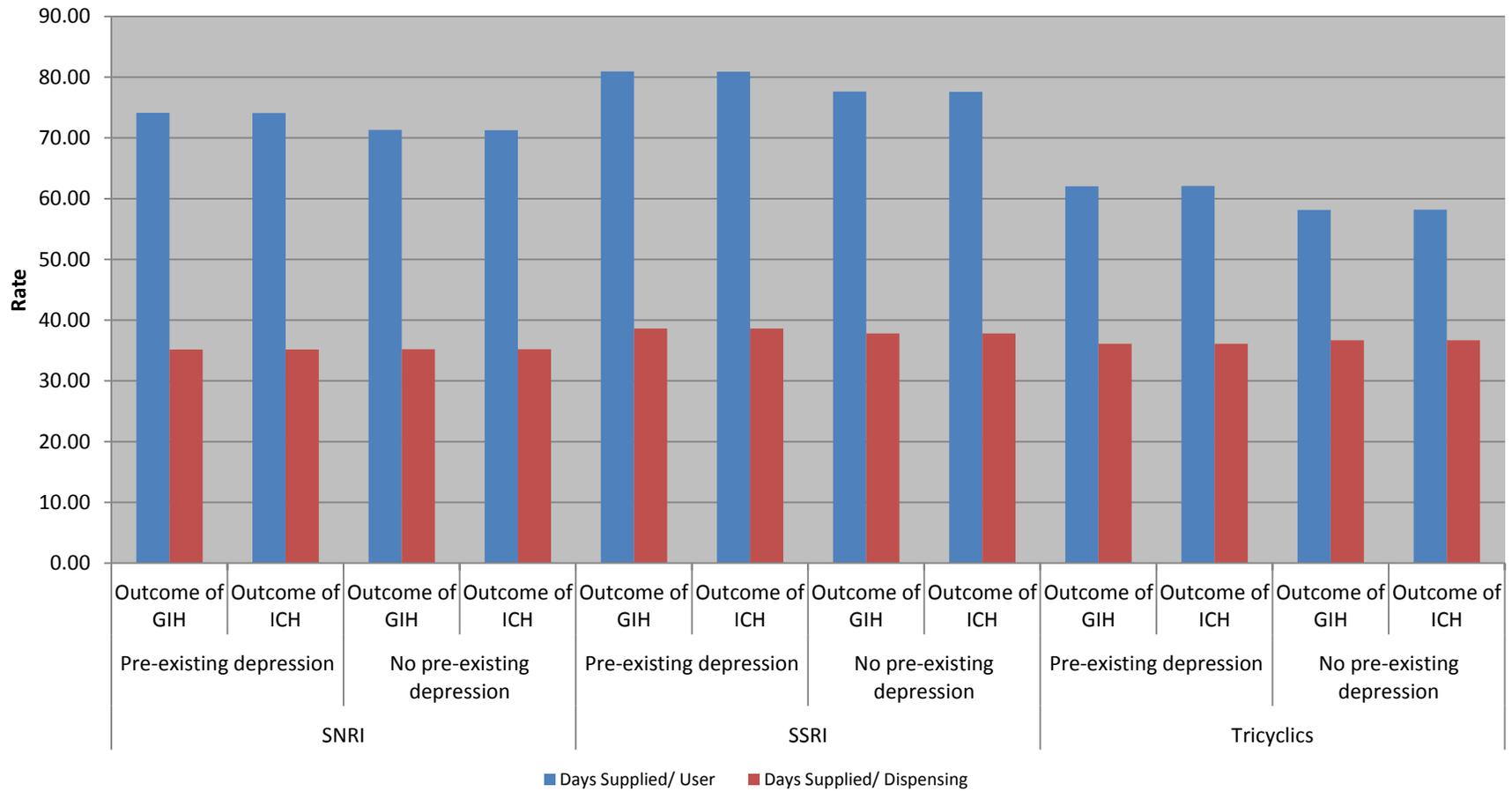


Table 2. Summary of Incident Anti-Depressant Use and Intracerebral and Gastrointestinal Bleeding in the MSDD between January 1, 2009 and December 31, 2011, by Drug Class, Outcome, and Age Group

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/100K Days at Risk
SNRIs													
<i>No Pre-Existing Criteria</i>													
Outcome of GIH													
0 to 19	22,639	23,141	45,597	1,458,394	1,425,941	10	17,794,973	10,104,214,067	1.27	64.42	2.01	31.98	0.70
20 to 34	137,698	142,517	253,277	8,141,594	7,929,203	84	16,330,747	7,557,824,648	8.43	59.13	1.84	32.15	1.06
35 to 49	250,839	261,268	494,293	16,770,414	16,359,144	130	17,088,964	9,223,526,523	14.68	66.86	1.97	33.93	0.79
50 to 64	232,618	243,030	491,995	18,235,149	17,776,656	198	14,187,275	8,353,164,045	16.40	78.39	2.12	37.06	1.11
65 to 79	56,410	59,003	120,656	4,893,626	4,786,230	102	4,863,639	3,054,896,932	11.60	86.75	2.14	40.56	2.13
80+	14,615	15,109	35,757	1,289,452	1,257,443	49	1,465,354	980,469,223	9.97	88.23	2.45	36.06	3.90
Outcome of ICH													
0 to 19	22,670	23,173	45,649	1,460,055	1,427,845	0	17,795,270	10,105,598,416	1.27	64.40	2.01	31.98	0.00
20 to 34	137,951	142,794	253,663	8,153,232	7,942,723	14	16,331,803	7,560,516,181	8.45	59.10	1.84	32.14	0.18
35 to 49	251,114	261,582	494,862	16,788,476	16,383,901	31	17,089,744	9,226,412,811	14.69	66.86	1.97	33.93	0.19
50 to 64	232,815	243,273	492,324	18,246,864	17,798,272	86	14,187,793	8,356,634,232	16.41	78.37	2.11	37.06	0.48
65 to 79	56,445	59,048	120,692	4,894,248	4,788,465	67	4,863,937	3,057,356,774	11.60	86.71	2.14	40.55	1.40
80+	14,653	15,147	35,862	1,293,546	1,262,795	44	1,465,485	981,907,087	10.00	88.28	2.45	36.07	3.48
<i>Pre-Existing Depression</i>													
Outcome of GIH													
0 to 19	12,815	13,024	26,770	859,238	840,238	8	479,488	112,171,768	26.73	67.05	2.09	32.10	0.95
20 to 34	67,480	68,836	127,171	4,117,404	4,005,925	48	1,138,457	236,228,027	59.27	61.02	1.88	32.38	1.20
35 to 49	114,210	117,068	233,071	7,938,388	7,736,652	76	1,592,830	374,781,753	71.70	69.51	2.04	34.06	0.98
50 to 64	98,499	101,322	220,422	8,173,518	7,956,455	103	1,449,700	376,317,090	67.94	82.98	2.24	37.08	1.29
65 to 79	24,205	24,963	55,626	2,228,122	2,179,071	53	529,574	149,444,550	45.71	92.05	2.30	40.06	2.43
80+	6,384	6,506	17,193	617,362	602,167	21	224,790	63,293,712	28.40	96.70	2.69	35.91	3.49
Outcome of ICH													
0 to 19	12,843	13,054	26,822	860,868	842,073	0	479,623	112,300,590	26.78	67.03	2.09	32.10	0.00
20 to 34	67,651	69,017	127,411	4,124,561	4,013,976	7	1,138,986	236,586,450	59.40	60.97	1.88	32.37	0.17
35 to 49	114,385	117,269	233,369	7,947,962	7,749,306	17	1,593,269	375,253,598	71.79	69.48	2.04	34.06	0.22
50 to 64	98,608	101,453	220,594	8,178,730	7,969,155	50	1,449,780	376,746,106	68.02	82.94	2.24	37.08	0.63
65 to 79	24,219	24,982	55,714	2,230,471	2,181,267	30	529,535	149,676,025	45.74	92.10	2.30	40.03	1.38
80+	6,402	6,524	17,276	621,269	605,965	21	224,802	63,422,124	28.48	97.04	2.70	35.96	3.47

Table 2. Summary of Incident Anti-Depressant Use and Intracerebral and Gastrointestinal Bleeding in the MSDD between January 1, 2009 and December 31, 2011, by Drug Class, Outcome, and Age Group

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/100K Days at Risk
SSRIs													
<i>No Pre-Existing Criteria</i>													
Outcome of GIH													
0 to 19	257,251	270,777	550,642	18,432,628	17,863,807	162	17,689,224	9,970,342,486	14.54	71.65	2.14	33.47	0.91
20 to 34	692,309	739,632	1,277,240	44,217,676	42,666,006	370	15,987,046	7,226,823,174	43.30	63.87	1.84	34.62	0.87
35 to 49	859,952	922,648	1,695,647	62,159,262	60,234,271	486	16,521,668	8,688,033,769	52.05	72.28	1.97	36.66	0.81
50 to 64	679,596	728,560	1,439,270	57,962,205	56,211,469	583	13,595,391	7,804,960,196	49.99	85.29	2.12	40.27	1.04
65 to 79	231,787	249,940	529,019	24,146,365	23,457,694	552	4,615,313	2,825,329,357	50.22	104.17	2.28	45.64	2.35
80+	97,885	104,544	256,705	10,546,994	10,200,822	370	1,376,048	890,330,433	71.13	107.75	2.62	41.09	3.63
Outcome of ICH													
0 to 19	257,460	271,016	550,984	18,444,803	17,884,994	9	17,689,525	9,971,599,066	14.55	71.64	2.14	33.48	0.05
20 to 34	692,977	740,429	1,278,346	44,253,926	42,714,986	65	15,988,093	7,229,204,342	43.34	63.86	1.84	34.62	0.15
35 to 49	860,395	923,192	1,696,175	62,175,577	60,273,212	118	16,522,448	8,690,594,426	52.07	72.26	1.97	36.66	0.20
50 to 64	679,568	728,641	1,438,232	57,921,691	56,194,786	293	13,595,926	7,808,112,767	49.98	85.23	2.12	40.27	0.52
65 to 79	231,675	249,869	528,078	24,110,507	23,444,011	335	4,615,625	2,827,580,726	50.19	104.07	2.28	45.66	1.43
80+	97,903	104,594	256,399	10,538,411	10,201,166	295	1,376,209	891,654,553	71.14	107.64	2.62	41.10	2.89
<i>Pre-Existing Depression</i>													
Outcome of GIH													
0 to 19	110,639	114,276	232,271	7,931,894	7,664,669	73	398,263	65,039,734	277.80	71.69	2.10	34.15	0.95
20 to 34	258,410	267,480	478,565	17,045,825	16,420,006	155	883,210	133,748,990	292.58	65.96	1.85	35.62	0.94
35 to 49	320,739	332,808	651,341	24,347,319	23,539,295	221	1,231,229	226,834,254	260.50	75.91	2.03	37.38	0.94
50 to 64	255,083	264,989	562,261	23,075,500	22,347,041	232	1,091,803	229,565,032	233.63	90.46	2.20	41.04	1.04
65 to 79	92,564	96,987	220,130	10,064,948	9,778,732	225	367,838	77,117,896	251.64	108.74	2.38	45.72	2.30
80+	39,342	41,077	105,430	4,404,079	4,254,126	155	157,617	32,625,201	249.61	111.94	2.68	41.77	3.64
Outcome of ICH													
0 to 19	110,759	114,406	232,484	7,939,319	7,675,739	2	398,406	65,102,683	278.01	71.68	2.10	34.15	0.03
20 to 34	258,744	267,850	479,094	17,062,597	16,442,980	21	883,763	133,962,441	292.78	65.94	1.85	35.61	0.13
35 to 49	321,069	333,170	651,837	24,363,509	23,565,623	40	1,231,702	227,141,502	260.67	75.88	2.03	37.38	0.17
50 to 64	255,194	265,142	562,039	23,065,091	22,348,563	115	1,091,994	229,854,422	233.70	90.38	2.20	41.04	0.51
65 to 79	92,599	97,026	220,026	10,061,560	9,787,115	126	367,835	77,256,428	251.74	108.66	2.38	45.73	1.29
80+	39,333	41,073	105,167	4,394,938	4,249,979	124	157,673	32,706,383	249.46	111.74	2.67	41.79	2.92

Table 2. Summary of Incident Anti-Depressant Use and Intracerebral and Gastrointestinal Bleeding in the MSDD between January 1, 2009 and December 31, 2011, by Drug Class, Outcome, and Age Group

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/100K Days at Risk
Tricyclics													
<i>No Pre-Existing Criteria</i>													
Outcome of GIH													
0 to 19	55,239	57,600	83,482	2,743,174	2,691,353	30	17,793,519	10,093,129,634	3.10	49.66	1.51	32.86	1.11
20 to 34	126,360	131,876	180,525	5,981,631	5,836,060	66	16,391,655	7,593,850,213	7.71	47.34	1.43	33.13	1.13
35 to 49	211,710	223,606	328,082	11,420,056	11,171,296	123	17,247,205	9,329,701,415	12.28	53.94	1.55	34.81	1.10
50 to 64	223,837	238,059	368,902	13,877,537	13,580,741	162	14,332,294	8,447,451,855	15.62	62.00	1.65	37.62	1.19
65 to 79	88,674	94,591	149,848	6,488,913	6,378,189	107	4,856,500	3,033,282,137	18.26	73.18	1.69	43.30	1.68
80+	25,178	26,700	42,869	1,814,220	1,783,227	60	1,459,384	971,048,693	17.25	72.06	1.70	42.32	3.36
Outcome of ICH													
0 to 19	55,336	57,704	83,601	2,747,584	2,696,079	10	17,793,813	10,094,495,685	3.11	49.65	1.51	32.87	0.37
20 to 34	126,658	132,221	180,988	5,995,934	5,851,831	20	16,392,735	7,596,585,996	7.73	47.34	1.43	33.13	0.34
35 to 49	211,997	223,927	328,720	11,440,716	11,193,458	46	17,247,989	9,332,674,710	12.29	53.97	1.55	34.80	0.41
50 to 64	224,053	238,313	369,456	13,897,222	13,608,154	85	14,332,799	8,450,999,278	15.63	62.03	1.65	37.62	0.62
65 to 79	88,790	94,718	150,138	6,502,084	6,394,884	64	4,856,784	3,035,720,091	18.28	73.23	1.69	43.31	1.00
80+	25,220	26,745	42,930	1,817,734	1,787,422	39	1,459,520	972,462,499	17.28	72.08	1.70	42.34	2.18
<i>Pre-Existing Depression</i>													
Outcome of GIH													
0 to 19	5,862	5,971	9,373	303,074	296,549	3	482,965	114,881,682	12.14	51.70	1.60	32.33	1.01
20 to 34	23,750	24,307	35,549	1,159,996	1,125,221	22	1,195,308	262,448,951	19.87	48.84	1.50	32.63	1.96
35 to 49	42,641	43,962	72,296	2,475,850	2,409,033	47	1,724,629	435,461,382	24.72	58.06	1.70	34.25	1.95
50 to 64	43,745	45,330	78,796	2,916,950	2,844,547	54	1,578,343	436,991,244	27.72	66.68	1.80	37.02	1.90
65 to 79	14,646	15,194	27,316	1,169,511	1,147,553	26	545,690	157,633,096	26.84	79.85	1.87	42.81	2.27
80+	3,810	3,930	7,147	292,287	286,901	7	227,352	64,968,643	16.76	76.72	1.88	40.90	2.44
Outcome of ICH													
0 to 19	5,889	5,999	9,401	304,033	297,470	2	483,101	115,012,229	12.19	51.63	1.60	32.34	0.67
20 to 34	23,861	24,426	35,720	1,165,086	1,130,566	6	1,195,852	262,853,793	19.95	48.83	1.50	32.62	0.53
35 to 49	42,776	44,105	72,581	2,485,276	2,420,736	12	1,725,076	436,001,454	24.80	58.10	1.70	34.24	0.50
50 to 64	43,822	45,423	79,048	2,926,045	2,856,344	24	1,578,426	437,492,872	27.76	66.77	1.80	37.02	0.84
65 to 79	14,683	15,235	27,437	1,174,964	1,153,642	10	545,645	157,877,818	26.91	80.02	1.87	42.82	0.87
80+	3,815	3,934	7,160	292,907	287,397	9	227,363	65,100,389	16.78	76.78	1.88	40.91	3.13

Table 3. Summary of Incident Anti-Depressant Use and Intracerebral and Gastrointestinal Bleeding in the MSDD between January 1, 2009 and December 31, 2011, by Drug Class, Outcome, and Sex

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/100K Days at Risk
SNRIs													
<i>No Pre-Existing Criteria</i>													
Outcome of GIH													
Female	519,189	543,386	1,047,429	37,045,830	36,132,882	386	33,490,501	20,019,350,233	15.50	71.35	2.02	35.37	1.07
Male	192,290	199,922	392,673	13,693,033	13,353,423	187	32,441,159	19,203,406,637	5.93	71.21	2.04	34.87	1.40
Unknown	735	760	1,473	49,766	48,312	0	82,908	51,338,568	8.87	67.71	2.00	33.79	0.00
Outcome of ICH													
Female	519,789	544,077	1,048,498	37,078,469	36,184,082	133	33,491,649	20,026,360,725	15.52	71.33	2.02	35.36	0.37
Male	192,508	200,180	393,082	13,708,216	13,371,637	109	32,442,404	19,210,718,317	5.93	71.21	2.04	34.87	0.82
Unknown	735	760	1,472	49,736	48,282	0	82,909	51,346,459	8.87	67.67	2.00	33.79	0.00
<i>Pre-Existing Depression</i>													
Outcome of GIH													
Female	233,830	240,510	490,342	17,318,106	16,876,159	216	3,452,297	893,124,263	67.73	74.06	2.10	35.32	1.28
Male	88,719	90,892	189,294	6,595,713	6,424,720	93	1,687,594	418,002,494	52.57	74.34	2.13	34.84	1.45
Unknown	313	317	617	20,213	19,629	0	4,682	1,110,143	66.85	64.58	1.97	32.76	0.00
Outcome of ICH													
Female	234,199	240,927	491,011	17,338,826	16,907,711	64	3,453,065	894,249,582	67.82	74.03	2.10	35.31	0.38
Male	88,859	91,056	189,560	6,604,882	6,434,462	61	1,687,823	418,624,862	52.65	74.33	2.13	34.84	0.95
Unknown	312	316	615	20,153	19,569	0	4,681	1,110,449	66.65	64.59	1.97	32.77	0.00
SSRIs													
<i>No Pre-Existing Criteria</i>													
Outcome of GIH													
Female	1,884,664	2,040,585	3,840,764	145,998,310	141,462,542	1,427	32,342,187	18,744,972,444	58.27	77.47	2.04	38.01	1.01
Male	913,000	972,338	1,901,966	71,271,039	68,982,337	1,095	31,913,104	18,611,193,186	28.61	78.06	2.08	37.47	1.59
Unknown	3,000	3,178	5,793	195,781	189,190	1	81,695	49,653,785	36.72	65.26	1.93	33.80	0.53
Outcome of ICH													
Female	1,885,551	2,041,817	3,841,650	146,031,033	141,552,807	643	32,343,407	18,751,058,468	58.30	77.45	2.04	38.01	0.45
Male	913,268	972,744	1,900,770	71,218,071	68,971,160	470	31,914,356	18,618,026,726	28.62	77.98	2.08	37.47	0.68
Unknown	3,003	3,180	5,794	195,811	189,188	2	81,696	49,660,686	36.76	65.21	1.93	33.80	1.06
<i>Pre-Existing Depression</i>													
Outcome of GIH													
Female	729,928	762,459	1,522,826	59,051,353	57,123,413	628	2,627,912	511,551,490	277.76	80.90	2.09	38.78	1.10
Male	341,981	354,121	725,087	27,748,646	26,813,742	432	1,335,018	252,716,486	256.16	81.14	2.12	38.27	1.61
Unknown	1,015	1,037	2,085	69,566	66,714	1	3,751	663,131	270.59	68.54	2.05	33.36	1.50

Table 3. Summary of Incident Anti-Depressant Use and Intracerebral and Gastrointestinal Bleeding in the MSDD between January 1, 2009 and December 31, 2011, by Drug Class, Outcome, and Sex

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/100K Days at Risk
Tricyclics													
<i>No Pre-Existing Depression</i>													
Outcome of GIH													
Female	496,931	529,160	789,901	29,097,262	28,485,342	336	33,731,387	20,180,189,466	14.73	58.55	1.59	36.84	1.18
Male	230,139	242,659	362,832	13,197,012	12,924,861	212	32,510,773	19,236,698,729	7.08	57.34	1.58	36.37	1.64
Unknown	584	613	975	31,257	30,663	0	83,171	51,575,752	7.02	53.52	1.67	32.06	0.00
Outcome of ICH													
Female	497,648	529,976	791,457	29,151,345	28,547,673	156	33,732,541	20,187,344,889	14.75	58.58	1.59	36.83	0.55
Male	230,471	243,039	363,401	13,218,672	12,953,616	107	32,512,001	19,244,009,200	7.09	57.36	1.58	36.37	0.83
Unknown	584	613	975	31,257	30,539	1	83,172	51,584,170	7.02	53.52	1.67	32.06	3.27
<i>Pre-Existing Depression</i>													
Outcome of GIH													
Female	99,692	103,314	170,638	6,202,725	6,047,213	107	3,684,007	1,012,075,141	27.06	62.22	1.71	36.35	1.77
Male	34,293	35,290	59,683	2,110,254	2,057,947	52	1,763,931	459,061,822	19.44	61.54	1.74	35.36	2.53
Unknown	86	90	156	4,689	4,644	0	4,962	1,248,035	17.33	54.52	1.81	30.06	0.00
Outcome of ICH													
Female	99,975	103,620	171,319	6,226,151	6,073,763	38	3,684,763	1,013,352,800	27.13	62.28	1.71	36.34	0.63
Male	34,403	35,413	59,873	2,117,501	2,067,750	25	1,764,169	459,737,440	19.50	61.55	1.74	35.37	1.21
Unknown	85	89	155	4,659	4,642	0	4,963	1,248,315	17.13	54.81	1.82	30.06	0.00

Table 4. Summary of Incident Anti-Depressant Use and Intracerebral and Gastrointestinal Bleeding in the MSDD between January 1, 2009 and December 31, 2011, by Drug Class, Outcome, and Year

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/100K Days at Risk
SNRIs													
<i>No Pre-Existing Criteria</i>													
Outcome of GIH													
2009	279,313	280,568	575,902	20,575,923	20,074,988	204	47,444,569	13,556,777,263	5.89	73.67	2.06	35.73	1.02
2010	244,146	245,211	501,526	17,637,472	17,201,386	209	45,658,237	13,100,100,254	5.35	72.24	2.05	35.17	1.22
2011	217,555	218,289	364,147	12,575,234	12,258,243	160	44,113,511	12,617,217,921	4.93	57.80	1.67	34.53	1.31
Outcome of ICH													
2009	279,668	280,933	576,600	20,598,533	20,106,155	98	47,446,443	13,561,717,472	5.89	73.65	2.06	35.72	0.49
2010	244,473	245,542	502,001	17,652,298	17,222,924	85	45,660,077	13,104,896,025	5.35	72.21	2.05	35.16	0.49
2011	217,804	218,542	364,451	12,585,590	12,274,922	59	44,114,980	12,621,812,004	4.94	57.78	1.67	34.53	0.48
<i>Pre-Existing Depression</i>													
Outcome of GIH													
2009	122,958	123,282	269,062	9,642,350	9,398,641	101	2,744,069	437,948,128	44.81	78.42	2.19	35.84	1.07
2010	110,509	110,812	240,282	8,428,950	8,212,536	126	2,730,550	442,769,379	40.47	76.27	2.17	35.08	1.53
2011	97,415	97,625	170,909	5,862,732	5,709,331	82	2,609,464	431,519,393	37.33	60.18	1.75	34.30	1.44
Outcome of ICH													
2009	123,169	123,496	269,413	9,653,395	9,414,058	49	2,744,952	438,508,960	44.87	78.38	2.19	35.83	0.52
2010	110,706	111,013	240,623	8,439,699	8,226,058	49	2,731,451	443,368,542	40.53	76.24	2.17	35.07	0.60
2011	97,580	97,790	171,150	5,870,767	5,721,626	27	2,610,270	432,107,391	37.38	60.16	1.75	34.30	0.47
SSRIs													
<i>No Pre-Existing Criteria</i>													
Outcome of GIH													
2009	1,083,635	1,091,717	2,211,273	84,314,034	81,767,641	951	45,929,885	12,915,258,355	23.59	77.81	2.04	38.13	1.16
2010	1,020,886	1,028,180	2,052,954	77,533,504	75,139,754	876	44,176,087	12,478,436,882	23.11	75.95	2.01	37.77	1.17
2011	891,162	896,204	1,484,296	55,617,592	53,726,674	696	42,658,545	12,012,124,178	20.89	62.41	1.67	37.47	1.30
Outcome of ICH													
2009	1,084,150	1,092,252	2,210,708	84,277,756	81,778,664	412	45,931,884	12,919,735,235	23.60	77.74	2.04	38.12	0.50
2010	1,021,363	1,028,684	2,052,630	77,524,987	75,163,694	410	44,177,960	12,482,786,840	23.12	75.90	2.01	37.77	0.55
2011	891,747	896,805	1,484,876	55,642,172	53,770,797	293	42,660,127	12,016,223,805	20.90	62.40	1.67	37.47	0.54
<i>Pre-Existing Depression</i>													
Outcome of GIH													
2009	396,726	398,229	859,799	33,735,537	32,671,919	388	1,969,632	256,886,554	201.42	85.03	2.17	39.24	1.19
2010	382,376	383,869	808,668	31,114,277	30,098,936	376	1,947,060	258,105,000	196.39	81.37	2.11	38.48	1.25
2011	334,514	335,519	581,531	22,019,751	21,233,014	297	1,839,704	249,939,553	181.83	65.83	1.74	37.87	1.40

Table 4. Summary of Incident Anti-Depressant Use and Intracerebral and Gastrointestinal Bleeding in the MSDD between January 1, 2009 and December 31, 2011, by Drug Class, Outcome, and Year

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/100K Days at Risk
Tricyclics													
<i>No Pre-Existing Criteria</i>													
Outcome of GIH													
2009	271,246	273,239	424,517	15,713,374	15,393,727	205	47,690,104	13,625,126,598	5.69	57.93	1.57	37.01	1.33
2010	261,404	263,242	408,318	14,944,250	14,636,953	190	45,905,492	13,166,876,184	5.69	57.17	1.56	36.60	1.30
2011	234,542	235,951	320,873	11,667,907	11,410,186	153	44,346,951	12,676,461,165	5.29	49.75	1.37	36.36	1.34
Outcome of ICH													
2009	271,636	273,637	425,338	15,742,405	15,431,760	101	47,691,969	13,630,126,101	5.70	57.95	1.57	37.01	0.65
2010	261,790	263,633	409,042	14,970,877	14,667,359	87	45,907,353	13,171,726,994	5.70	57.19	1.56	36.60	0.59
2011	234,943	236,358	321,453	11,687,992	11,432,709	76	44,348,443	12,681,085,164	5.30	49.75	1.37	36.36	0.66
<i>Pre-Existing Depression</i>													
Outcome of GIH													
2009	46,626	46,791	82,660	3,013,324	2,941,888	56	2,959,542	492,976,059	15.75	64.63	1.77	36.45	1.90
2010	47,529	47,724	82,677	2,990,021	2,916,215	57	2,948,314	497,511,444	16.12	62.91	1.74	36.17	1.95
2011	44,028	44,179	65,140	2,314,323	2,251,701	46	2,813,309	481,897,495	15.65	52.56	1.48	35.53	2.04
Outcome of ICH													
2009	46,773	46,939	83,050	3,027,916	2,959,693	27	2,960,467	493,614,489	15.80	64.74	1.78	36.46	0.91
2010	47,662	47,860	82,941	2,998,772	2,926,514	19	2,949,217	498,181,130	16.16	62.92	1.74	36.16	0.65
2011	44,169	44,323	65,356	2,321,623	2,259,948	17	2,814,153	482,542,936	15.70	52.56	1.48	35.52	0.75