



Modular Program Report

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 FDA requested use of modular program (MP) #4 to investigate use of Bupropion and Naltrexone. The query was run against the **Mini-Sentinel Distributed Database** and distributed on **February 23, 2012**.

Three different categories of users appear in these results: (1) Bupropion users, (2) Naltrexone users, and (3) Overlap users. Bupropion users are prevalent users of Bupropion during the study time period (January 1, 2005 to December 31, 2010). Naltrexone users are a subset of Bupropion users defined as one who ever used Naltrexone (not necessarily overlapping) during the same study time period. Overlap users are users of both Bupropion and Naltrexone where the days supplied after dispensings of both drugs overlap with each other.

Results presented in this report provide counts of prevalent users, dispensings, and total days supplied of Bupropion, Naltrexone, and overlapping use. Prevalent use was estimated with a drug washout period of 0 days. The maximum allowable treatment gap was set to 14 days, the minimum episode duration and the minimum episode days supplied were set to 1 day. The program was run from January 1, 2005 to December 31, 2010 for the entire time period and by year. All care settings were included in the query. Bupropion was identified as the study drug and Naltrexone the concomitant drug.

Please review the Notes below and refer to the Specifications table for request details.

Request ID MSY3_MPR3

Special Note Naltrexone users must have been users of Bupropion at some point during the query request period. However, the use of both products does not have to overlap for the Naltrexone category. Those users are given in the Overlapping category. The number of users, dispensings, and days supplied is only for Naltrexone in the Naltrexone category. Naltrexone users are a subset of the Bupropion users and the Overlapping users are a subset of the Naltrexone users.

Specifications Program parameter inputs and scenarios

Table 1 Three tables of the number of users, dispensings, and total days supplied for Bupropion, Naltrexone, and overlapping use as well as the number of days supplied per user, dispensings per user, and days supplied per dispensing. Includes the percent overlap use and concomitance intensity ratio

Figure 1 Five figures depicting the number of users, dispensings, and total days supplied for Bupropion, Naltrexone, and overlapping use as well as the number of days supplied per user, dispensings per user, and days supplied per dispensing

Table 2 Tables of the number of users, number of dispensings, and total days supplied for Bupropion, Naltrexone, and overlapping use by Year/Period, Age Group, and Sex. Includes the percent overlap use and concomitance intensity ratio

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.

Modular Program #4 Specifications

Modular Program #4 was used to investigate use of bupropion and concomitant use with naltrexone. Seven query periods were examined between January 1, 2005, and December 31, 2010, the enrollment gap was set at 45 days, and the episode gap (for drug/exposure) was set to 14 days. Age groups were split as follows: 0-17, 18-64, and 65+ years. In total, 7 different scenarios were examined in this report with differing query periods. See below for a description of each of these scenarios.

Scenario	Query Period	Study Drug	Washout* (days)	Concomitant Drug	Min. Days Supplied	Min. Episode Duration (days)	Care Setting
1	01/01/2005 to 12/31/2010	Bupropion	0	Naltrexone	1	1	IP, AV, ED
2	01/01/2005 to 12/31/2005	Bupropion	0	Naltrexone	1	1	IP, AV, ED
3	01/01/2006 to 12/31/2006	Bupropion	0	Naltrexone	1	1	IP, AV, ED
4	01/01/2007 to 12/31/2007	Bupropion	0	Naltrexone	1	1	IP, AV, ED
5	01/01/2008 to 12/31/2008	Bupropion	0	Naltrexone	1	1	IP, AV, ED
6	01/01/2009 to 12/31/2009	Bupropion	0	Naltrexone	1	1	IP, AV, ED
7	01/01/2010 to 12/31/2010	Bupropion	0	Naltrexone	1	1	IP, AV, ED

*Washout is applied to study drug only

Table 1a. Users, Dispensings, and Total Days Supplied for Bupropion, Naltrexone*, and Overlapping Use, by Year/Period

Year/Period	BUPROPION			NALTREXONE (among Bupropion Users)*		
	Users	Dispensings	Total Days Supplied	Users	Dispensings	Total Days Supplied
2005 - 2010	1,522,921	5,033,537	184,293,083	2,634	6,092	176,680
2005	391,246	1,576,523	59,793,445	492	1,366	40,861
2006	408,780	1,646,355	64,445,295	587	1,701	54,184
2007	409,137	1,695,195	66,127,411	614	1,781	55,252
2008	390,136	1,534,854	59,896,143	645	1,702	51,278
2009	519,961	1,758,001	67,935,107	1,028	2,583	77,781
2010	443,100	1,164,524	45,355,260	971	1,945	55,902

Table 1b. Number of Days Supplied per User, Dispensings per User, and Days Supplied per Dispensing for Bupropion and Naltrexone*, by Year/Period

Year/Period	BUPROPION			NALTREXONE (among Bupropion Users)*		
	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing
2005 - 2010	121.01	3.31	36.61	67.08	2.31	29.00
2005	152.83	4.03	37.93	83.05	2.78	29.91
2006	157.65	4.03	39.14	92.31	2.90	31.85
2007	161.63	4.14	39.01	89.99	2.90	31.02
2008	153.53	3.93	39.02	79.50	2.64	30.13
2009	130.65	3.38	38.64	75.66	2.51	30.11
2010	102.36	2.63	38.95	57.57	2.00	28.74

Table 1c. Users and Total Days Supplied for Overlapping Use of Bupropion and Naltrexone, by Year/Period**

Year/Period	Overlap Users	Days Supplied Overlap	% Concomitant Overlapping Users (Unique Overlap Users/BUPROPION Unique Users)	Concomitance Intensity Ratio (Days Supplied Overlap/BUPROPION Total Days Supplied)
2005 - 2010	2,626	172,153	0.17%	0.09%
2005	491	39,791	0.13%	0.07%
2006	584	52,753	0.14%	0.08%
2007	612	53,664	0.15%	0.08%
2008	642	49,862	0.16%	0.08%
2009	1,025	75,464	0.20%	0.11%
2010	968	54,182	0.22%	0.12%

*Naltrexone use among the cohort of Bupropion users. Does not require overlapping use (see note**).

**Days supplied after dispensings of Bupropion and Naltrexone must overlap to be considered overlapping use.

Figure 1a. Number of Bupropion Users, by Year/Period

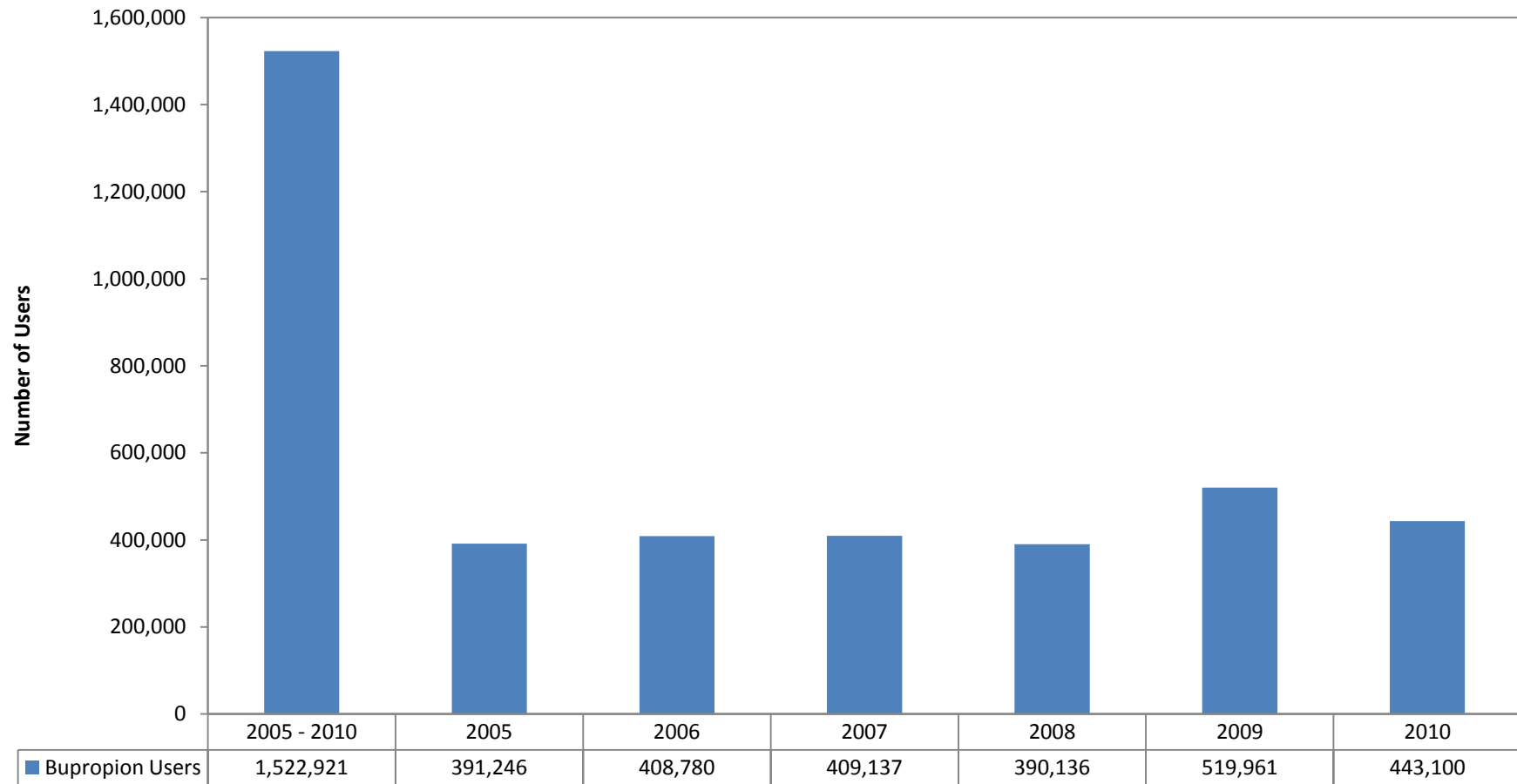
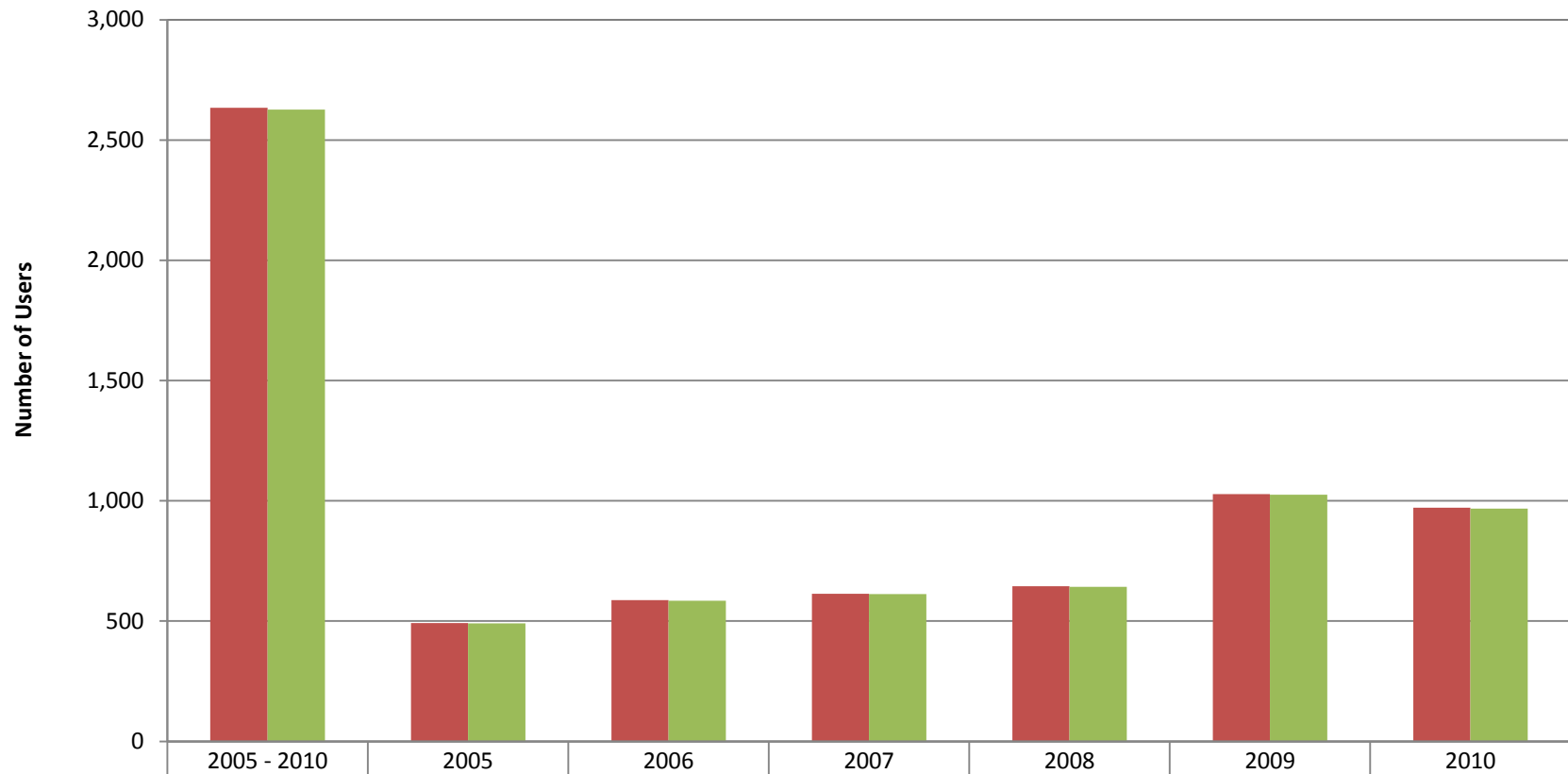


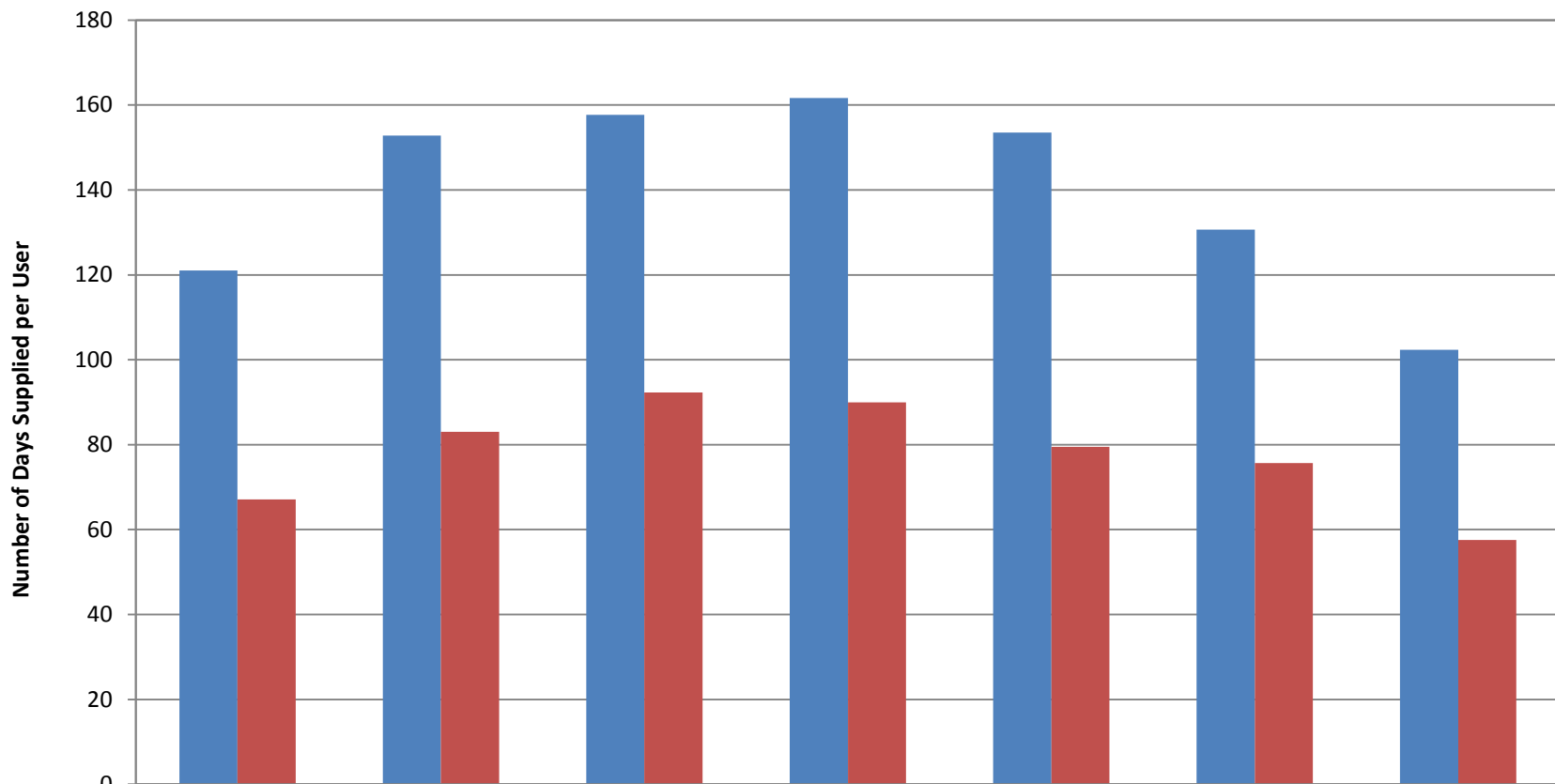
Figure 1b. Number of Naltrexone Users (among Bupropion Users)* and Overlapping Users, by Year/Period



Naltrexone Users	2,634	492	587	614	645	1,028	971
Overlapping Users	2,626	491	584	612	642	1,025	968

*Naltrexone use among the cohort of Bupropion users. Does not require overlapping use.

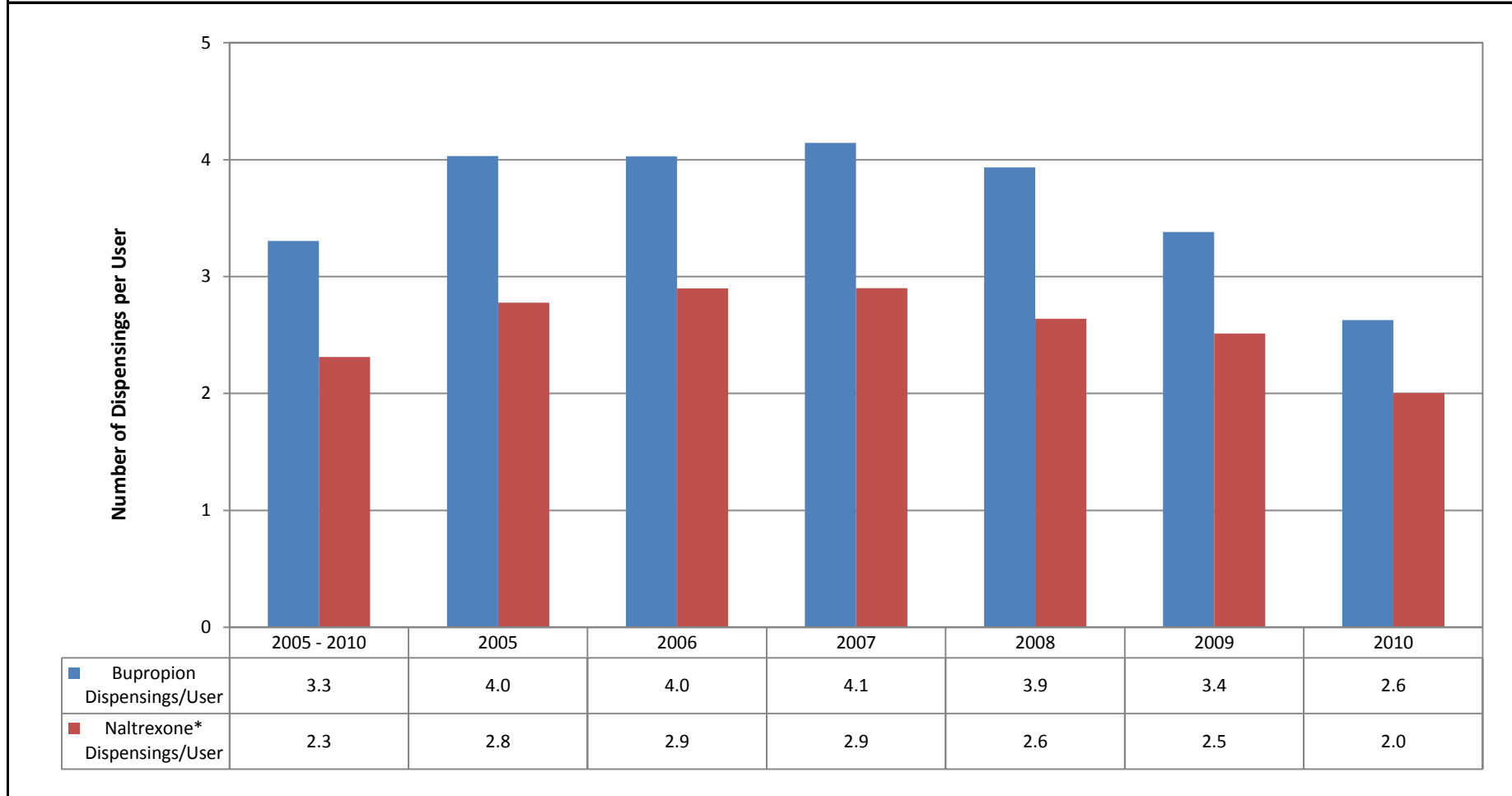
Figure 1c. Days Supplied per User of Bupropion and Naltrexone*, by Year/Period



■ Bupropion Days Supplied/User	121.0	152.8	157.7	161.6	153.5	130.7	102.4
■ Naltrexone* Days Supplied/User	67.1	83.1	92.3	90.0	79.5	75.7	57.6

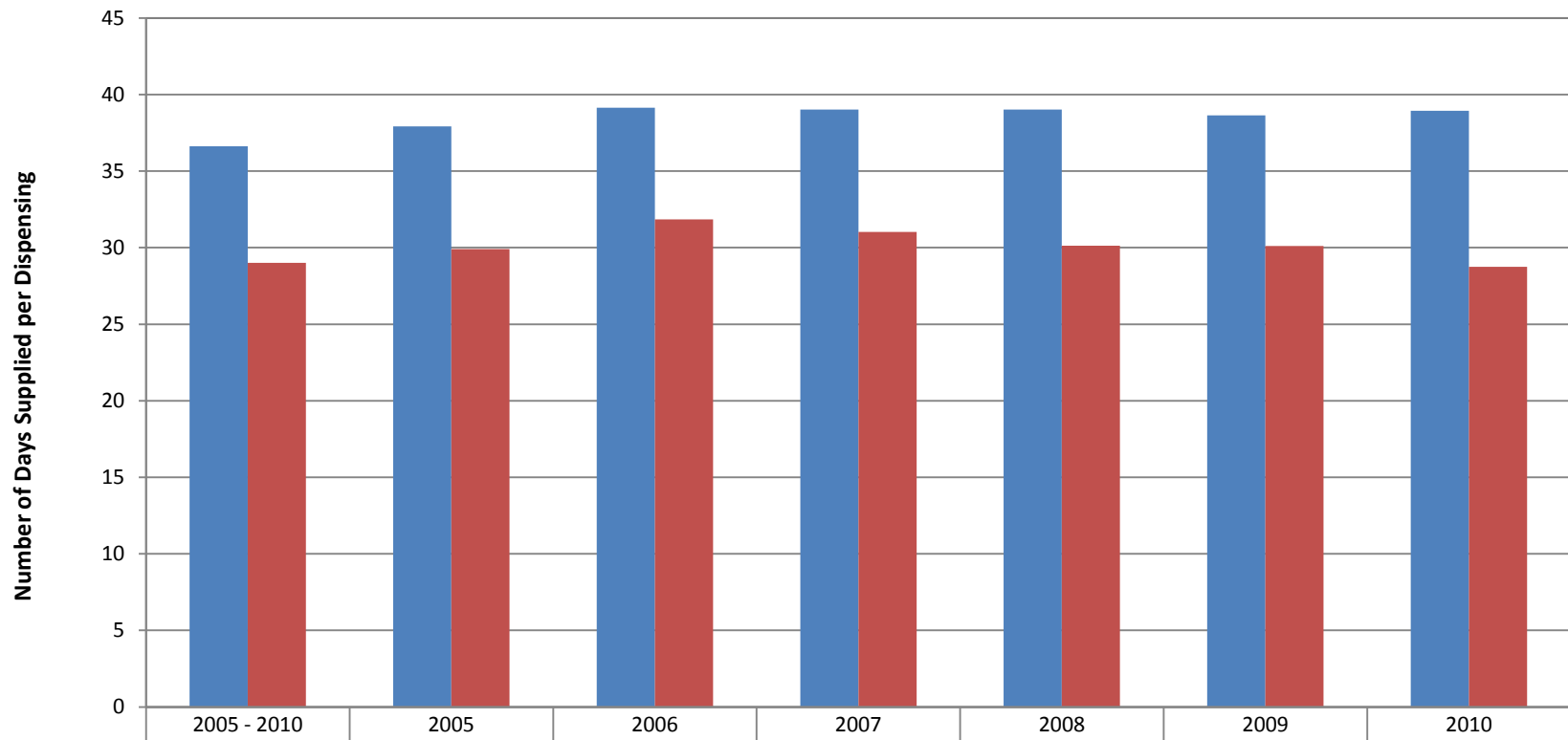
*Naltrexone use among the cohort of Bupropion users. Does not require overlapping use.

Figure 1d. Dispensings per User of Bupropion and Naltrexone*, by Year/Period



*Naltrexone use among the cohort of Bupropion users. Does not require overlapping use.

Figure 1e. Days Supplied per Dispensing for Bupropion and Naltrexone*, by Year/Period



■ Bupropion Days Supplied/Dispensing	36.6	37.9	39.1	39.0	39.0	38.6	38.9
■ Naltrexone* Days Supplied/Dispensing	29.0	29.9	31.9	31.0	30.1	30.1	28.7

*Naltrexone use among the cohort of Bupropion users. Does not require overlapping use.

Table 2a. Unique Users, Dispensings, and Total Days Supplied for Bupropion and Naltrexone*, by Year/Period, Age Group, and Sex								
		BUPROPION			NALTREXONE (among Bupropion Users)*			
Year/Period		Unique Users	Dispensings	Total Days Supplied	Unique Users	Dispensings	Total Days Supplied	
2005 - 2010	Overall	1,522,921	5,033,537	184,293,083	2,634	6,092	176,680	
	Age Group	0 to 17	49,855	181,037	6,141,437	67	197	5,459
		18 to 64	1,377,110	4,532,141	164,679,107	2,489	5,710	165,105
		65+	95,956	320,359	13,472,539	78	185	6,116
	Sex	Female	998,190	3,355,546	122,942,778	1,402	3,231	93,592
		Male	523,068	1,672,716	61,183,064	1,231	2,860	83,058
		Unknown	1,663	5,275	167,241	1	1	30
2005	Overall	391,246	1,576,523	59,793,445	492	1,366	40,861	
	Age Group	0 to 17	13,846	60,545	2,122,795	14	45	1,214
		18 to 64	358,580	1,438,001	54,062,983	466	1,295	38,979
		65+	18,820	77,977	3,607,667	12	26	668
	Sex	Female	256,745	1,051,454	39,931,466	282	769	22,533
		Male	134,070	523,448	19,809,823	210	597	18,328
		Unknown	431	1,621	52,156	0	0	0
2006	Overall	408,780	1,646,355	64,445,295	587	1,701	54,184	
	Age Group	0 to 17	13,350	58,856	2,056,776	17	52	1,440
		18 to 64	373,149	1,492,521	57,781,731	555	1,587	48,460
		65+	22,281	94,978	4,606,788	15	62	4,284
	Sex	Female	269,413	1,103,761	43,201,946	313	804	23,874
		Male	138,897	540,939	21,189,740	273	896	30,280
		Unknown	470	1,655	53,609	1	1	30
2007	Overall	409,137	1,695,195	66,127,411	614	1,781	55,252	
	Age Group	0 to 17	11,725	49,381	1,713,030	11	44	1,211
		18 to 64	367,499	1,511,906	58,376,051	576	1,668	50,374
		65+	29,913	133,908	6,038,330	27	69	3,667
	Sex	Female	275,124	1,148,286	44,792,392	311	886	27,249
		Male	133,562	545,288	21,282,877	303	895	28,003
		Unknown	451	1,621	52,142	0	0	0

*Naltrexone use among the cohort of Bupropion users. Does not require overlapping use.

Table 2a cont. Unique Users, Dispensings, and Total Days Supplied for Bupropion and Naltrexone*, by Year/Period, Age Group, and Sex								
		BUPROPION			NALTREXONE (among Bupropion Users)*			
Year/Period		Unique Users	Dispensings	Total Days Supplied	Unique Users	Dispensings	Total Days Supplied	
2008	Overall	390,136	1,534,854	59,896,143	645	1,702	51,278	
	Age Group	0 to 17	10,279	40,420	1,395,435	6	32	831
		18 to 64	346,991	1,356,361	52,284,167	612	1,581	47,216
		65+	32,866	138,073	6,216,541	27	89	3,231
	Sex	Female	263,792	1,041,139	40,657,382	331	846	25,112
		Male	125,883	492,053	19,186,189	314	856	26,166
Unknown		461	1,662	52,572	0	0	0	
2009	Overall	519,961	1,758,001	67,935,107	1,028	2,583	77,781	
	Age Group	0 to 17	11,918	42,366	1,443,382	19	74	2,184
		18 to 64	466,351	1,568,960	59,715,282	967	2,381	71,349
		65+	41,692	146,675	6,776,443	42	128	4,248
	Sex	Female	349,815	1,189,728	46,007,217	554	1,325	40,221
		Male	169,742	566,804	21,881,157	474	1,258	37,560
Unknown		404	1,469	46,733	0	0	0	
2010	Overall	443,100	1,164,524	45,355,260	971	1,945	55,902	
	Age Group	0 to 17	9,400	26,034	886,695	18	50	1,312
		18 to 64	394,151	1,036,266	39,679,974	911	1,758	50,285
		65+	39,549	102,224	4,788,591	42	137	4,305
	Sex	Female	298,195	786,591	30,701,589	551	1,091	31,613
		Male	144,545	377,066	14,625,059	420	854	24,289
Unknown		360	867	28,612	0	0	0	

*Naltrexone use among the cohort of Bupropion users. Does not require overlapping use.

Table 2b. Unique Users, Dispensings, and Total Days Supplied for Overlapping Use of Bupropion and Naltrexone, by Year/Period, Age Group, and Sex						
Year/Period			Unique Overlap Users	Days Supplied Overlap*	% Concomitant Overlapping Users (Unique Overlap Users/ BUPROPION Unique Users)	Concomitance Intensity Ratio (Days Supplied Overlap/ BUPROPION Total Days Supplied)
2005 - 2010	Overall		2,626	172,153	0.17%	0.09%
	Age Group	0 to 17	67	5,340	0.13%	0.09%
		18 to 64	2,481	160,939	0.18%	0.10%
		65+	78	5,874	0.08%	0.04%
	Sex	Female	1,398	90,998	0.14%	0.07%
		Male	1,227	81,125	0.23%	0.13%
Unknown		1	30	0.06%	0.02%	
2005	Overall		491	39,791	0.13%	0.07%
	Age Group	0 to 17	14	1,165	0.10%	0.05%
		18 to 64	465	37,979	0.13%	0.07%
		65+	12	647	0.06%	0.02%
	Sex	Female	281	22,007	0.11%	0.06%
		Male	210	17,784	0.16%	0.09%
Unknown		0	0	0.00%	0.00%	
2006	Overall		584	52,753	0.14%	0.08%
	Age Group	0 to 17	17	1,395	0.13%	0.07%
		18 to 64	552	47,161	0.15%	0.08%
		65+	15	4,197	0.07%	0.09%
	Sex	Female	312	23,185	0.12%	0.05%
		Male	271	29,538	0.20%	0.14%
Unknown		1	30	0.21%	0.06%	
2007	Overall		612	53,664	0.15%	0.08%
	Age Group	0 to 17	11	1,202	0.09%	0.07%
		18 to 64	574	48,869	0.16%	0.08%
		65+	27	3,593	0.09%	0.06%
	Sex	Female	309	26,364	0.11%	0.06%
		Male	303	27,300	0.23%	0.13%
Unknown		0	0	0.00%	0.00%	

*Days supplied after dispensings of Bupropion and Naltrexone must overlap to be considered overlapping use.

Table 2b cont. Unique Users, Dispensings, and Total Days Supplied for Overlapping Use of Bupropion and Naltrexone, by Year/Period, Age Group, and Sex						
Year/Period		Unique Overlap Users	Days Supplied Overlap*	Percent Concomitant Overlapping Users (Unique Overlap Users/ BUPROPION Unique Users)	Concomitance Intensity Ratio (Days Supplied Overlap/ BUPROPION Total Days Supplied)	
2008	Overall	642	49,862	0.16%	0.08%	
	Age Group	0 to 17	6	806	0.06%	0.06%
		18 to 64	609	45,891	0.18%	0.09%
		65+	27	3,165	0.08%	0.05%
	Sex	Female	330	24,337	0.13%	0.06%
		Male	312	25,525	0.25%	0.13%
		Unknown	0	0	0.00%	0.00%
2009	Overall	1,025	75,464	0.20%	0.11%	
	Age Group	0 to 17	19	2,149	0.16%	0.15%
		18 to 64	964	69,224	0.21%	0.12%
		65+	42	4,091	0.10%	0.06%
	Sex	Female	551	38,850	0.16%	0.08%
		Male	474	36,614	0.28%	0.17%
		Unknown	0	0	0.00%	0.00%
2010	Overall	968	54,182	0.22%	0.12%	
	Age Group	0 to 17	18	1,291	0.19%	0.15%
		18 to 64	908	48,836	0.23%	0.12%
		65+	42	4,055	0.11%	0.08%
	Sex	Female	550	30,607	0.18%	0.10%
		Male	418	23,575	0.29%	0.16%
		Unknown	0	0	0.00%	0.00%

*Days supplied after dispensings of Bupropion and Naltrexone must overlap to be considered overlapping use.