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	This report features the results from two modular program requests -- MPR25 and MPR10. Each request generated results from 2 runs of Mini-Sentinel Modular Program #1 [MP1] and 4 runs of Modular Program #3 (Version 1.2) [MP3]. There were a total of 4 runs of MP1 and 8 runs of MP3 between the 2 query requests. The MPR25 query for Clopidogrel was run against the Mini-Sentinel Distributed Database and distributed on October 18, 2011. The MPR10 query for Prasugrel was distributed on August 9, 2011. Except for the exposure of interest, both queries contained the same specifications. Three different categories of counts were generated: (1) Incident counts with washout period set to 183 days, (2) Incident counts with washout period set to 365 days, and (3) prevalent counts. Results from Modular Program # 1 provide counts of users of the drug interest regardless of any pre-existing conditions. The output was stratified by age group (0-74, 75+), sex, and year. These results are shown in Table 1 and Figure 1. Results from Modular Program # 3 provide the percent of new (incident) users of the drug of interest with a history of Transient Ischemic Attack (TIA) or stroke. The lookback period for TIA and stroke was set to 365 days. Only members with one or more diagnoses of TIA or stroke in the 365 days prior to first incident dispensing of Clopidogrel were considered. The maximum allowable treatment gap, minimum episode duration, and the minimum episode days supplied were set to zero. The program was run from July 1, 2009 to May 31, 2011. The output was stratified by age group (0-74, 75+), sex, and year. These results are shown in Table 2, Figure 2, Table 3, and Figure 3. Please review the Notes below and refer to the Modular Program request for specifications.
Request ID	MPR10, MPR25
Specifications	Specifications of Modular Program Requests MPR25 and MPR10.
Table 1	Two tables of aggregate counts (prevalent and incident) of users, days supplied, and dispensings by age group, sex, and year. Table 2a is for Clopidogrel users only and Table 2b is for Prasugrel users only.
Figure 1	Two graphs of aggregate counts (prevalent and incident) comparing Clopidogrel and Prasugrel days supplied per user, days supplied per dispensing and dispensings per user.
Table 2	Four tables of aggregate counts (prevalent and incident) of users of Clopidogrel and Prasugrel overall, by age group, sex, and year. Tables also include counts and percents of new Clopidogrel and Prasugrel users with a history of TIA or stroke.
Figure 2	Graphs of the percents of new Clopidogrel and Prasugrel users with a history of TIA or Stroke overall, by age group, sex, and year.

Overview	
Table 3	Two tables of aggregate counts and percents of new users of Clopidogrel and Prasugrel with a history of TIA or Stroke. Table 3a shows the 183-day washout period and Table 3b the 365-day washout period.
Figure 3	Graph of percent of new users of Clopidogrel and Prasugrel with a history of TIA or Stroke with 183- and 365-day washout periods.
Notes:	The program was run for the entire time period. When examining the yearly stratification in the incident output from Modular Program 3, note once an incident user is first encountered, this user will not be counted for subsequent years. 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 Specifications

Modular Program #1 was used to investigate the number of prevalent and incident users of clopidogrel (MPR25) and prasurgrel (MPR10). The query period was from July 1, 2009 to May 31, 2011. This request examined 2 age groups-- <75 and ≥75 years. Between MPR25 & MPR10 a total of 4 different scenarios were examined in this report with differing exposures of interest, outcomes of interest, and pre-existing condition criteria. See below for a description of each of these scenarios.

	Incident exposure	Incident w/ respect to (incidence criteria):	Washout (days)
MPR25 Scenarios:			
1	Clopidogrel	Clopidogrel	183
2	Clopidogrel	Clopidogrel	365
MPR10 Scenarios:			
3	Prasugrel	Prasugrel	183
4	Prasugrel	Prasugrel	365

Modular Program #3 was used to investigate the number of new users of clopidogrel (MPR25) and prasurgrel (MPR10) with a pre-existing condition of Transient Ischemic Attack (TIA, ICD-9-CM 439.5) and stroke (ICD-9-CM 431, 432, 433, 434). The query period was from July 1, 2009 to May 31, 2011. The episode gap (for drug/exposure) was not utilized and thus set to 0 days. This request examined 2 age groups-- <75 and ≥75 years. Between MPR25 & MPR10 a total of 8 different scenarios were examined in this report with differing exposures of interest, outcomes of interest, and pre-existing condition criteria. See below for a description of each of these scenarios.

	Drug/Exposure					Pre-Existing Condition						Event/Outcome
	Incident exposure	Incident w/ respect to (incidence criteria):	Washout (days)	Min episode duration	Min days supplied	Pre-Existing Condition	Code Type	Lookback period (days)	Lookback Type	Care Setting	Principal Dx Only?	Event/Outcome
MPR25 Scenarios:												
1	Clopidogrel	Clopidogrel	183	0	0	TIA	ICD-9	365	F	ED	No	N/A
2	Clopidogrel	Clopidogrel	365	0	0	TIA	ICD-9	365	F	ED	No	N/A
3	Clopidogrel	Clopidogrel	183	0	0	Stroke	ICD-9	365	F	ED	No	N/A
4	Clopidogrel	Clopidogrel	365	0	0	Stroke	ICD-9	365	F	ED	No	N/A
MPR10 Scenarios:												
5	Prasugrel	Prasugrel	183	0	0	TIA	ICD-9	365	F	ED	No	N/A
6	Prasugrel	Prasugrel	365	0	0	TIA	ICD-9	365	F	ED	No	N/A
7	Prasugrel	Prasugrel	183	0	0	Stroke	ICD-9	365	F	ED	No	N/A
8	Prasugrel	Prasugrel	365	0	0	Stroke	ICD-9	365	F	ED	No	N/A

NDC codes checked against First Data Bank's "National Drug Data File (NDDF®) Plus"
ICD-9-CM diagnosis and procedure codes checked against "Ingenix 2011 ICD-9-CM Data File" provided by OptumInsight
HCPCS codes checked against "Optum 2011 HCPCS Level II Data File" provided by OptumInsight
CPT codes checked against "Optum 2011 Current Procedure Codes & Relative Values Data File" provided by OptumInsight

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Table 1a. Number of Prevalent and New Clopidogrel Users (Regardless of Pre-Existing Conditions), Number of Dispensings, and Total Days Supplied Overall by Washout Period (WO), Age Group, Sex, and Year

			PREVALENT	INCIDENT (183-DAY WO)	INCIDENT (365-DAY WO)
Overall		***Unique Patients***	***662,284***	***186,838***	***153,191***
		Dispensings	***4,695,750***	***920,110***	***768,666***
		Total Days Supplied	***182,122,337***	***35,261,701***	***28,861,978***
AGE GROUP	0 to 74	Unique Patients	413,196	114,846	91,817
		Dispensings	2,865,483	565,925	462,886
		Total Days Supplied	112,013,447	21,839,820	17,566,033
	75+	Unique Patients	249,088	71,992	61,374
SEX	Female	Unique Patients	293,980	81,573	67,410
		Dispensings	2,126,945	405,522	340,378
		Total Days Supplied	79,929,827	15,073,064	12,392,563
	Male	Unique Patients	368,007	105,162	85,696
		Dispensings	2,566,270	513,918	427,720
		Total Days Supplied	102,099,309	20,164,064	16,449,510
	Unknown	Unique Patients	297	103	85
		Dispensings	2,535	670	568
		Total Days Supplied	93,201	24,573	19,905
YEAR	2009	Unique Patients	425,396	71,000	53,189
		Dispensings	1,533,828	170,550	134,200
		Total Days Supplied	58,259,757	6,374,977	4,811,777
	2010	Unique Patients	508,480	153,359	126,412
		Dispensings	2,882,468	671,959	567,023
		Total Days Supplied	112,058,708	25,680,798	21,301,238
	2011	Unique Patients	237,419	62,591	53,906
		Dispensings	279,454	77,601	67,443
		Total Days Supplied	11,803,872	3,205,926	2,748,963

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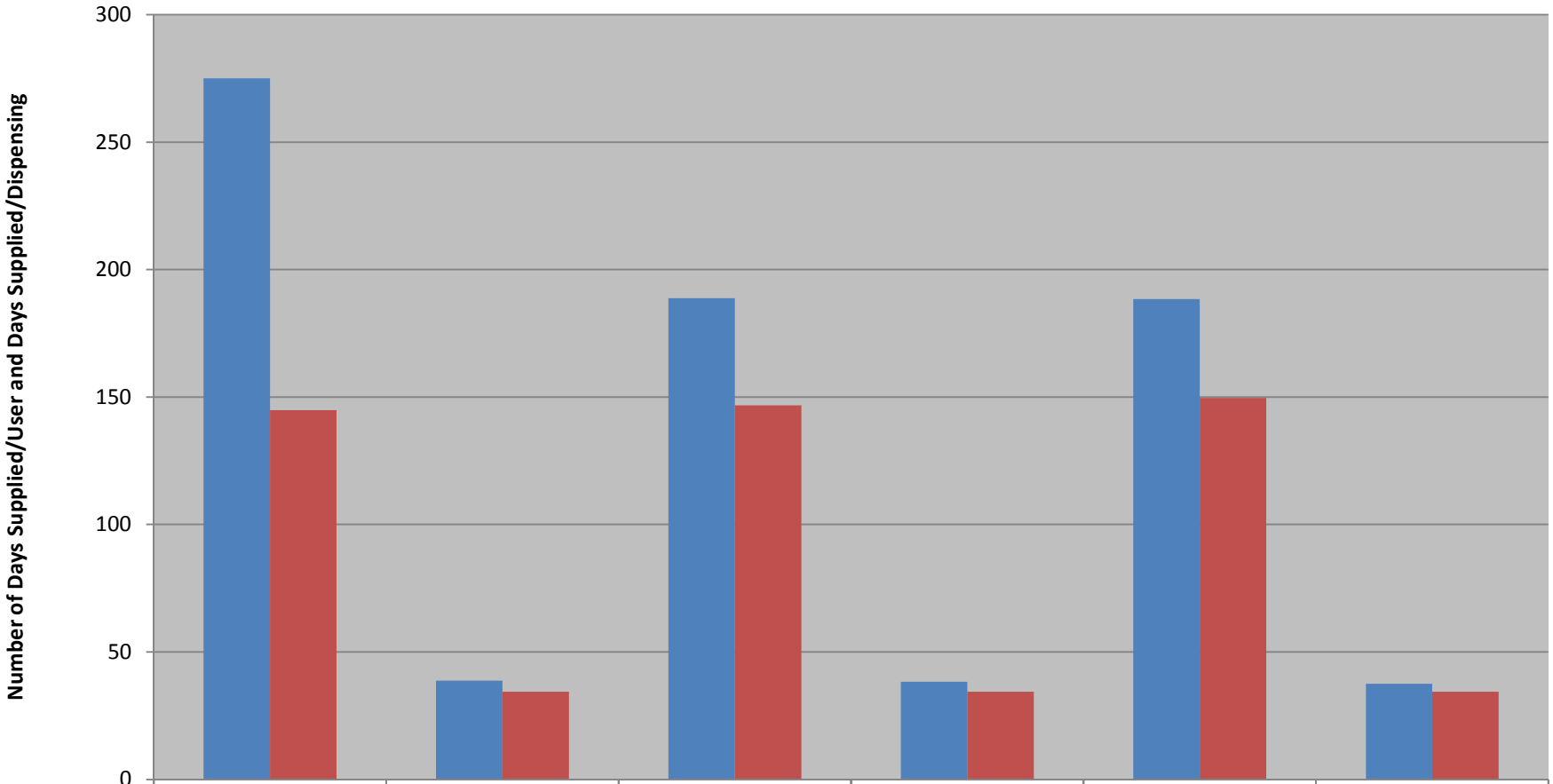
Table 1b. Number of Prevalent and New Prasugrel Users (Regardless of Pre-Existing Conditions), Number of Dispensings, and Total Days Supplied Overall, by Age Group, by Sex, and by Year

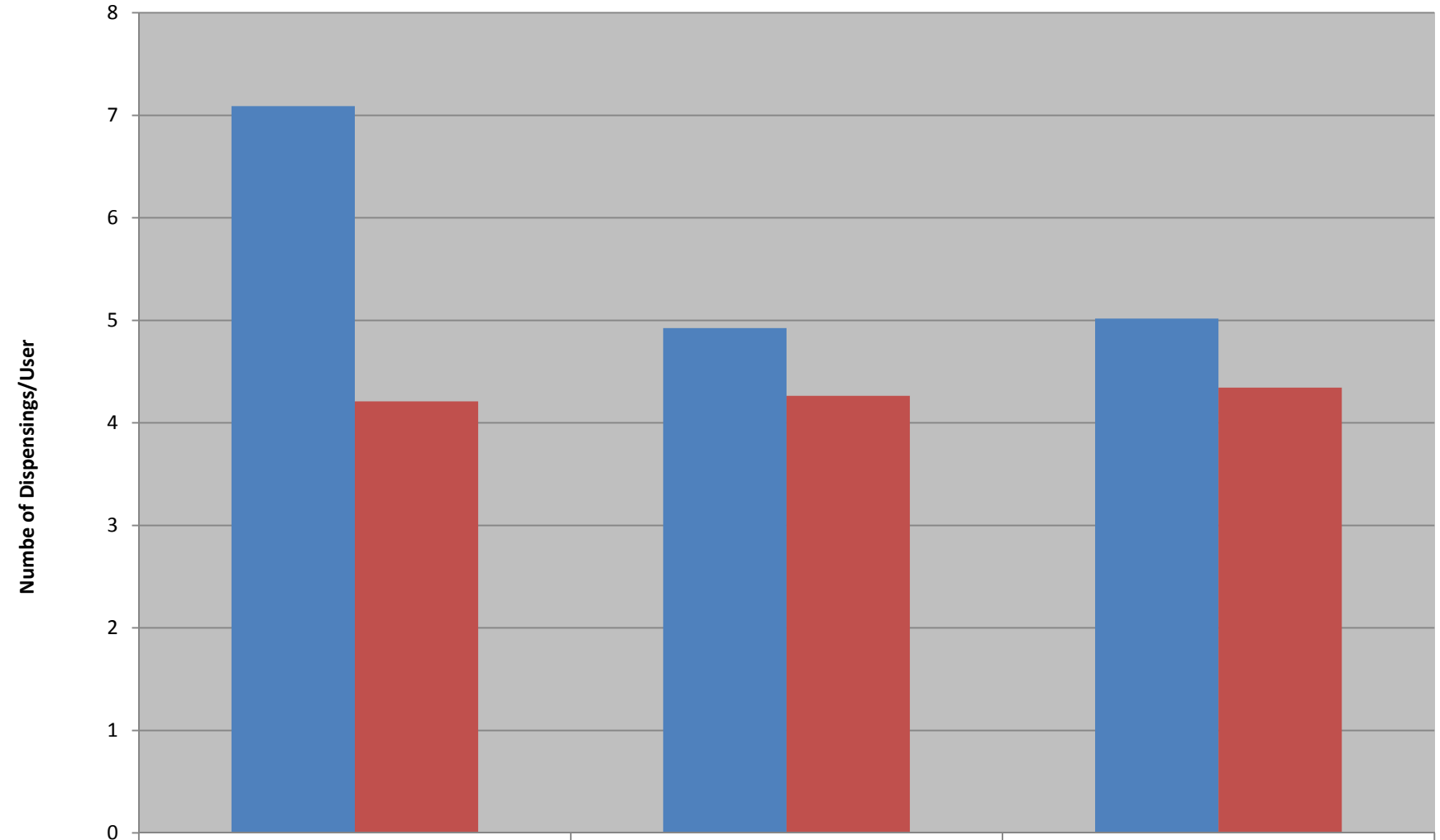
			Prevalent Use	New Use (183 WO)	New Use (365 WO)
Overall		***Unique Patients***	***9,509***	***7,850***	***6,997***
		Dispensings	***40,030***	***33,474***	***30,386***
		Total Days Supplied	***1,377,295***	***1,151,797***	***1,046,930***
AGE GROUP	0 to 74	Unique Patients	8,477	6,950	6,173
		Dispensings	36,295	30,288	27,388
		Total Days Supplied	1,249,750	1,041,801	943,149
	75+	Unique Patients	1,032	900	824
		Dispensings	3,735	3,186	2,998
		Total Days Supplied	127,545	109,996	103,781
SEX	Female	Unique Patients	2,640	2,191	1,930
		Dispensings	10,388	8,684	7,769
		Total Days Supplied	349,857	292,444	261,939
	Male	Unique Patients	6,854	5,644	5,053
		Dispensings	29,568	24,716	22,548
		Total Days Supplied	1,024,918	856,833	782,621
	Unknown	Unique Patients	15	15	14
		Dispensings	74	74	69
		Total Days Supplied	2,520	2,520	2,370
YEAR	2009	Unique Patients	1,080	994	885
		Dispensings	2,100	1,930	1,717
		Total Days Supplied	64,317	59,497	53,246
	2010	Unique Patients	8,656	7,202	6,423
		Dispensings	34,707	28,979	26,359
		Total Days Supplied	1,189,086	994,274	905,155
	2011	Unique Patients	2,751	2,238	2,007
		Dispensings	3,223	2,565	2,310
		Total Days Supplied	123,892	98,026	88,529

Figure 1a. Number of Days Supplied per User and Days Supplied per Dispensing for Clopidogrel and Prasugrel (Regardless of Pre-Existing Conditions)



	Prevalent Use		New Use (183-Day Washout)		New Use (365-Day Washout)	
	Days Supplied per User	Days per Dispensing	Days Supplied per User	Days per Dispensing	Days Supplied per User	Days per Dispensing
Clopidogrel	275.0	38.8	188.7	38.3	188.4	37.5
Prasugrel	144.8	34.4	146.7	34.4	149.6	34.5

Figure 1b. Number of Dispensings per User for Clopidogrel and Prasugrel (Regardless of Pre-Existing Conditions)



	Prevalent Use	New Use (183-Day Washout)	New Use (365-Day Washout)
Clopidogrel	7.1	4.9	5.0
Prasugrel	4.2	4.3	4.3

Table 2a. 183-Day Washout Period - Counts and Percents of New Users of Clopidogrel with a History of TIA or Stroke Overall, by Age Group, by Sex, and by Year						
		Number (%) of New Users (183-Day Washout Period):				
			With History of TIA[2]		With History of Stroke[2]	
		Total[1]	N	%	N	%
Overall		***186,838***	***12,585***	***6.7%***	***27,919***	***14.9%***
AGE GROUP	0 to 74	114,846	7,154	6.2%	16,440	14.3%
	75+	71,992	5,431	7.5%	11,479	15.9%
SEX	Female	81,573	6,391	7.8%	12,741	15.6%
	Male	105,162	6,190	5.9%	15,162	14.4%
	Unknown	103	4	3.9%	16	15.5%
	2011	62,591	630	1.0%	1,420	2.3%

Table 2b. 365-Day Washout Period - Counts and Percents of New Users of Clopidogrel with a History of TIA or Stroke Overall, by Age Group, by Sex, and by Year						
		Number (%) of New Users (365-Day Washout Period):				
			With History of TIA[2]		With History of Stroke[2]	
		Total[1]	N	%	N	%
Overall		***153,191***	***11,815***	***7.7%***	***25,820***	***16.9%***
AGE GROUP	0 to 74	91,817	6,732	7.3%	15,235	16.6%
	75+	61,374	5,083	8.3%	10,585	17.2%
SEX	Female	67,410	5,991	8.9%	11,829	17.5%
	Male	85,696	5,821	6.8%	13,976	16.3%
	Unknown	85	3	3.5%	15	17.6%
YEAR	2009	53,189	3,910	7.4%	8,454	15.9%
	2010	126,412	7,275	5.8%	15,949	12.6%
	2011	53,906	630	1.2%	1,417	2.6%

Notes:

[1] Data from Table 1

[2] The lookup period for TIA and stroke was set to 365 days prior to treatment initiation. Only members with one or more diagnosis of TIA or stroke in the 365 days prior to the Clopidogrel index date were considered.

Table 2c. 183-Day Washout Period - Counts and Percents of New Users of Prasugrel with a History of TIA or Stroke Overall, by Age Group, by Sex, and by Year						
		Number (%) of New Users (183-Day Washout Period):				
			With History of TIA[4]		With History of Stroke[4]	
		Total[3]	N	%	N	%
Overall		***8,045***	***135***	***1.7%***	***547***	***6.8%***
AGE GROUP	0 to 74	7,134	113	1.6%	466	6.5%
	75+	911	22	2.4%	81	8.9%
SEX	Female	2,228	44	2.0%	172	7.7%
	Male	5,802	91	1.6%	372	6.4%
	Unknown	15	0	0.0%	3	20.0%
YEAR	2009	1,002	20	2.0%	62	6.2%
	2010	7,394	108	1.5%	467	6.3%
	2011	2,380	7	0.3%	18	0.8%

Table 2d. 365-Day Washout Period - Counts and Percents of New Users of Prasugrel with a History of TIA or Stroke Overall, by Age Group, by Sex, and by Year						
		Number (%) of New Users (365-Day Washout Period):				
			With History of TIA[4]		With History of Stroke[4]	
		Total[3]	N	%	N	%
Overall		***7,184***	***135***	***1.9%***	***545***	***7.6%***
AGE GROUP	0 to 74	6,349	113	1.8%	464	7.3%
	75+	835	22	2.6%	81	9.7%
SEX	Female	1,966	44	2.2%	172	8.7%
	Male	5,204	91	1.7%	370	7.1%
	Unknown	14	0	0.0%	3	21.4%
YEAR	2009	892	20	2.2%	62	7.0%
	2010	6,607	108	1.6%	465	7.0%
	2011	2,143	7	0.3%	18	0.8%

Notes:

[3] Data from Table 1

[4] The lookup period for TIA and stroke was set to 365 days prior to treatment initiation. Only members with one or more diagnosis of TIA or stroke in the 365 days prior to the Prasugrel index date were considered.

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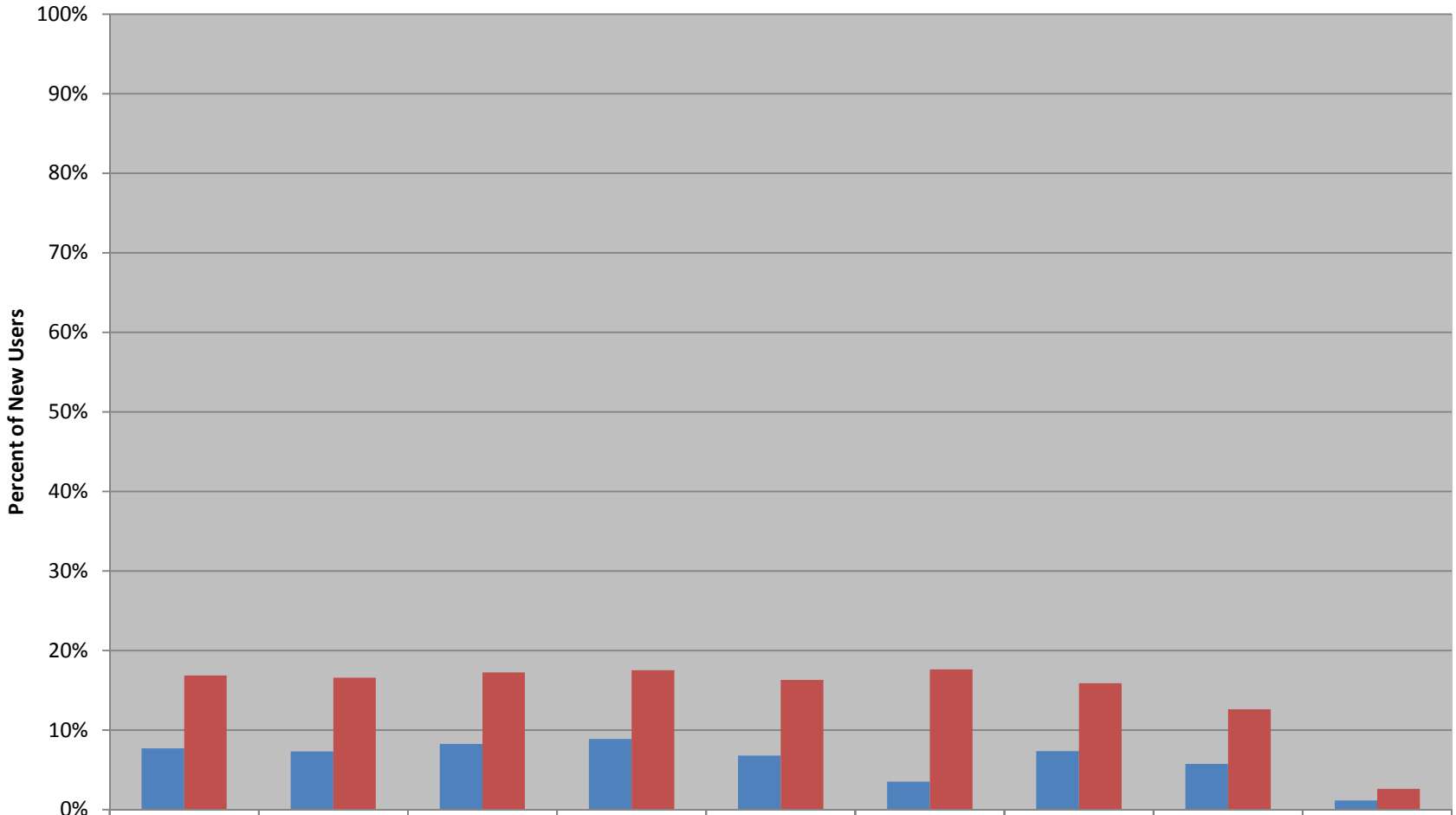
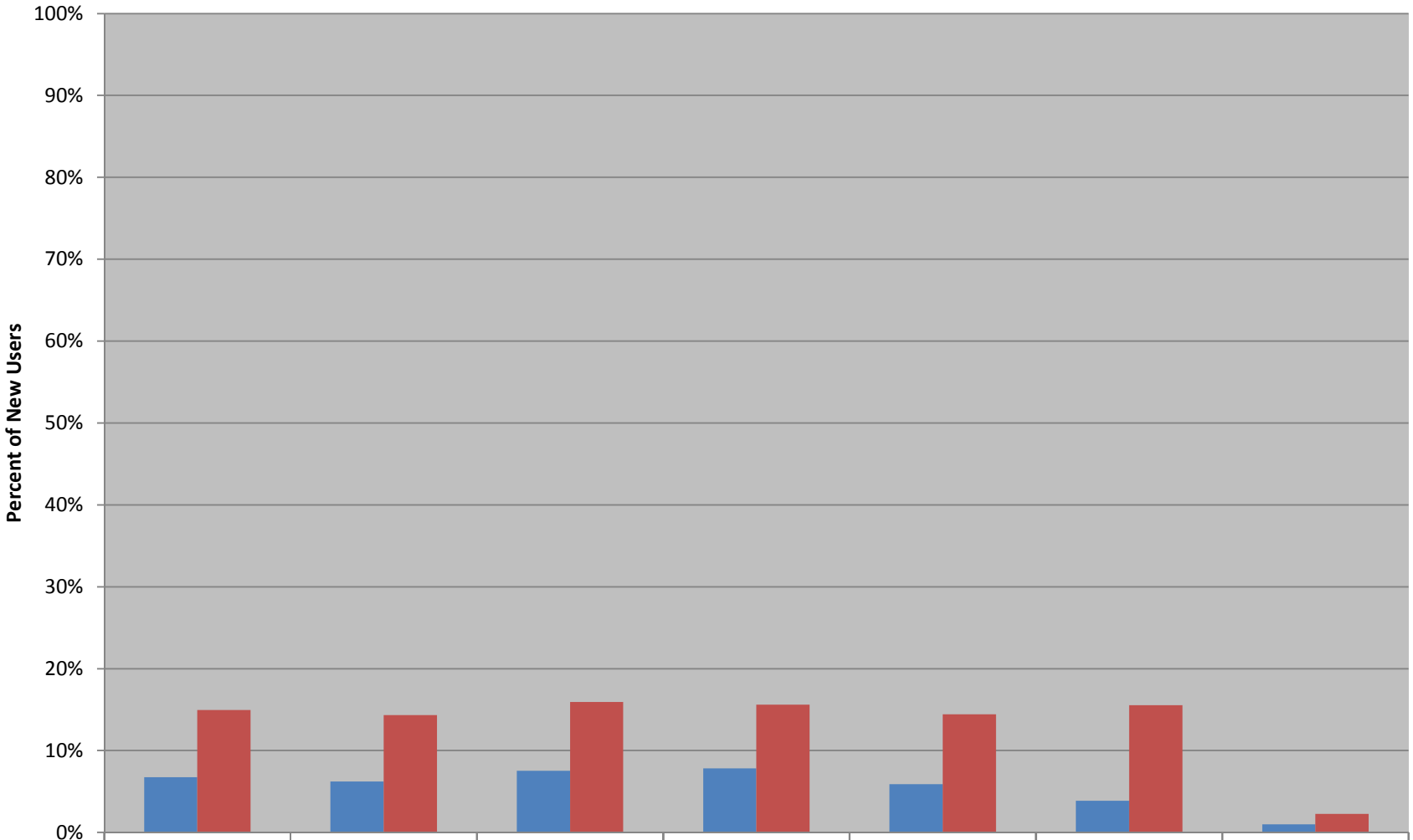
Figure 2a. 183-Day Washout Period - Percent of New Users of Clopidogrel with a History of TIA or Stroke: Overall, by Age Group, Sex, and Year



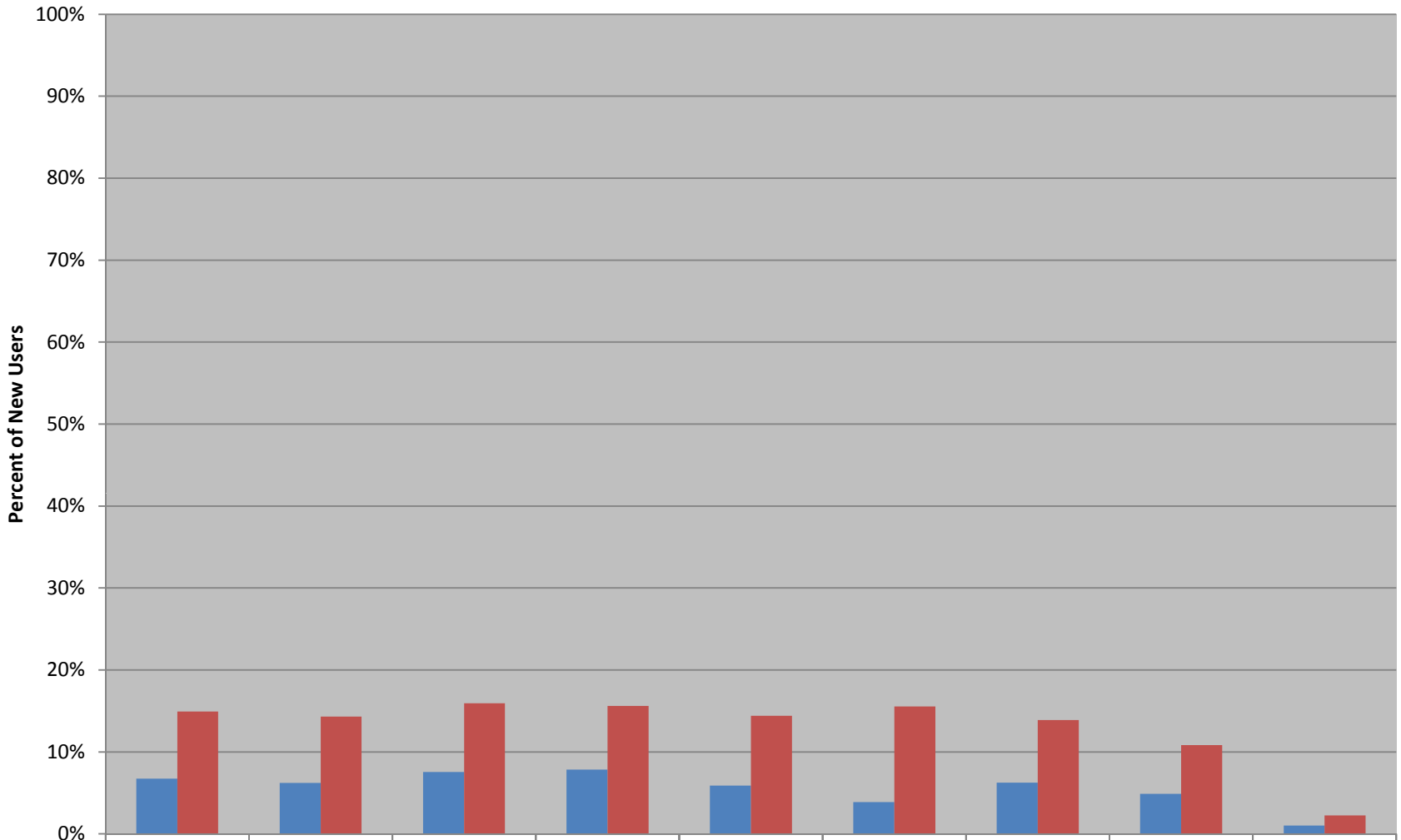
	Overall	Age Group		Sex			Year		
		0 to 74	75+	Female	Male	Unknown	2009	2010	2011
TIA	7.71%	7.33%	8.28%	8.89%	6.79%	3.53%	7.35%	5.75%	1.17%
Stroke	16.85%	16.59%	17.25%	17.55%	16.31%	17.65%	15.89%	12.62%	2.63%

Figure 2b. 365-Day Washout Period - Percent of New Users of Clopidogrel with a History of TIA or Stroke: Overall, by Age Group, Sex, and Year



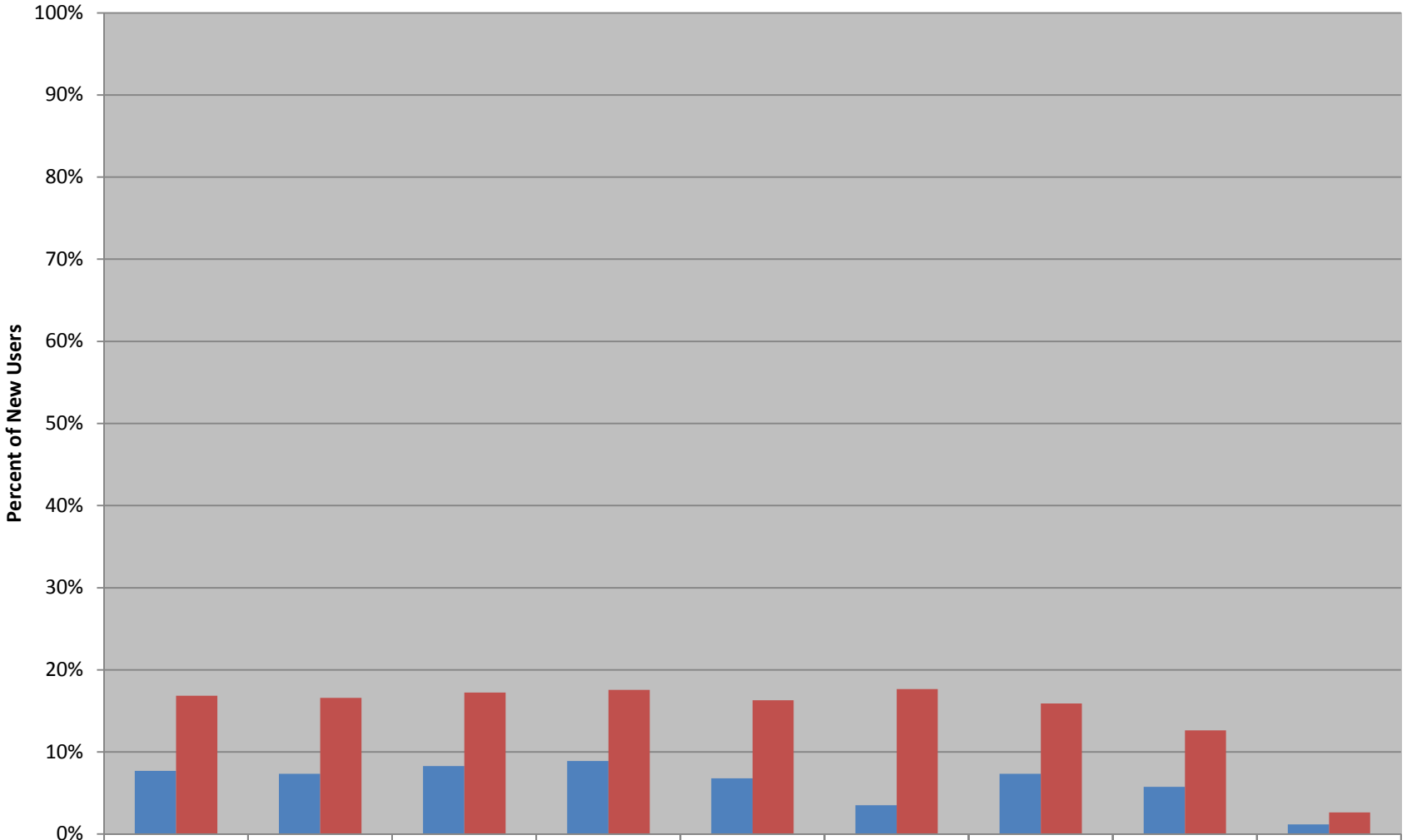
	Overall	Age Group		Sex			
		0 to 74	75+	Female	Male	Unknown	2011
TIA	6.74%	6.23%	7.54%	7.83%	5.89%	3.88%	1.01%
Stroke	14.94%	14.31%	15.94%	15.62%	14.42%	15.53%	2.27%

Figure 2c. 183-Day Washout Period - Percent of New Users of Prasugrel with a History of TIA or Stroke: Overall, by Age Group, Sex, and Year



	Overall	Age Group		Sex			Year		
		0 to 74	75+	Female	Male	Unknown	2009	2010	2011
TIA	6.74%	6.23%	7.54%	7.83%	5.89%	3.88%	6.25%	4.90%	1.01%
Stroke	14.9%	14.3%	15.9%	15.6%	14.4%	15.5%	13.9%	10.8%	2.3%

Figure 2d. 365-Day Washout Period - Percent of New Users of Prasugrel with a History of TIA or Stroke: Overall, by Age Group, Sex, and Year



	Overall	Age Group		Sex			Year		
		0 to 74	75+	Female	Male	Unknown	2009	2010	2011
TIA	7.71%	7.33%	8.28%	8.89%	6.79%	3.53%	7.35%	5.75%	1.17%
Stroke	16.85%	16.59%	17.25%	17.55%	16.31%	17.65%	15.89%	12.62%	2.63%

Table 3a. Number of New Users of Clopidogrel and Prasugrel with a History of TIA or Stroke: 183-Day Washout Period					
	Number (%) of New Users (183-Day Washout Period):				
		With History of TIA[2]		With History of Stroke[2]	
	Total[1]	N	%	N	%
Clopidogrel	*186,838*	*12,585*	*6.7%*	*27,919*	*14.9%*
Prasugrel	*7,850*	*134*	*1.7%*	*542*	*6.9%*

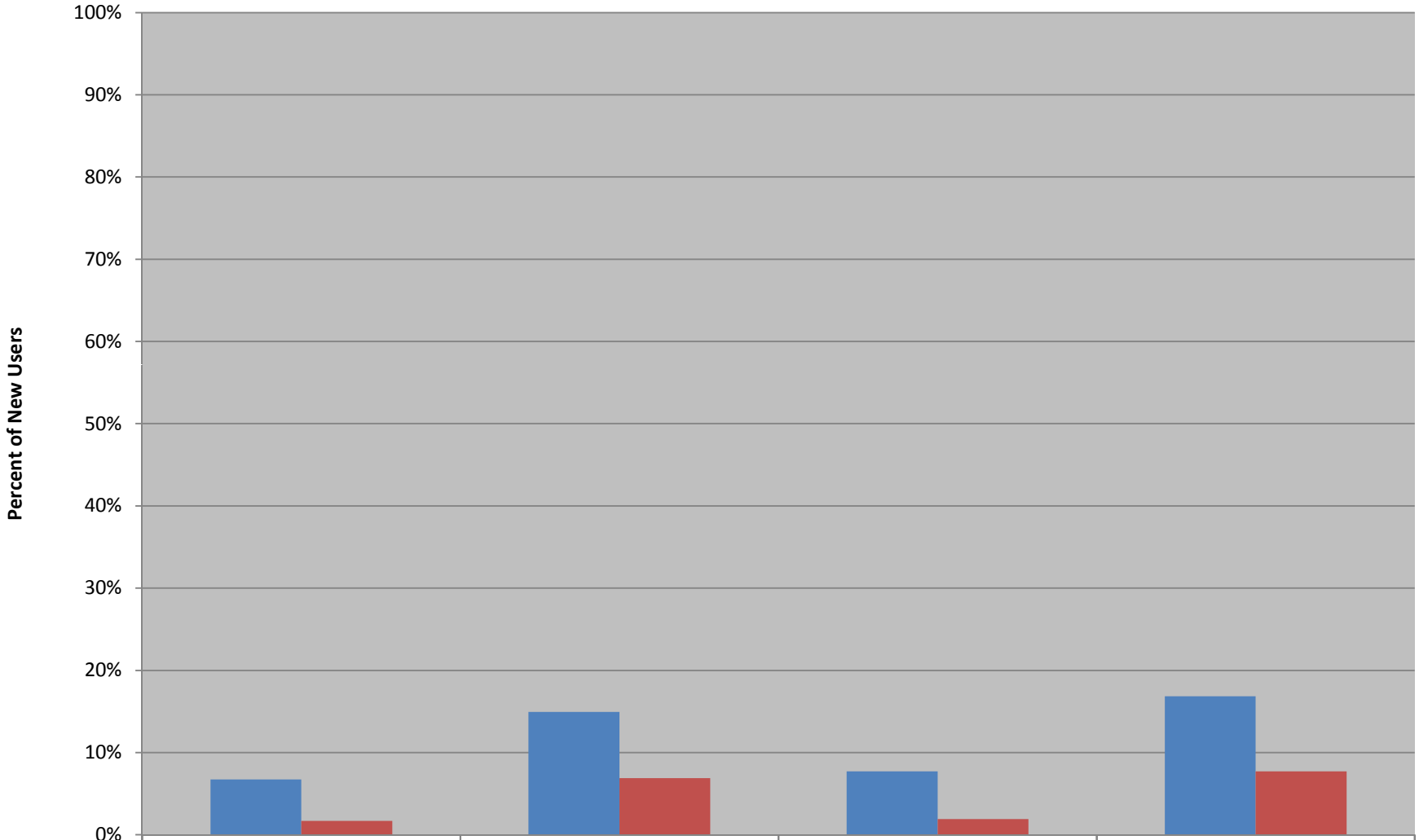
Table 3b. Overall Counts and Percents of New Users of Clopidogrel and Prasugrel with a History of TIA or Stroke: 365-Day Washout Period					
	Number (%) of New Users (365-Day Washout Period):				
Clopidogrel	*153,191*	*11,815*	*7.7%*	25,820	*16.9%*
Prasugrel	*6,997*	*134*	*1.9%*	*540*	*7.7%*

Notes:

[1] Data from Table 1

[2] The lookup period for TIA and stroke was set to 365 days prior to treatment initiation. Only members with one or more diagnosis of TIA or stroke in the 365 days prior to the index date were considered.

Figure 3. Percent of New Clopidogrel and Prasugrel Users w/ History of TIA or Stroke - 183 and 365-Day Washout Periods



	183-Day Washout		365-Day Washout	
	TIA	Stroke	TIA	Stroke
Clopidogrel	6.7%	14.9%	7.7%	16.9%
Prasugrel	1.7%	6.9%	1.9%	7.7%