



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 execution of Modular Program #3 (MP3), version 1, to investigate prevalent and incident use of Quinine Sulfate as well as incident Quinine Sulfate use among enrollees with a pre-existing diagnosis of malaria (ICD-9-CM: 084.0-084.6). The query was run against the Mini-Sentinel Distributed Database (MSDD) for the time period of January 1, 2006 through December 31, 2010. This request required a total of 15 runs of MP3 (10 runs for overall use and 5 runs for pre-existing malaria). The package was distributed to 17 Data Partners in multiple versions between March 23, 2012 and April 24, 2012. Though these versions were distributed at different times, the MSDD was consistent throughout the entire requesting time period. A separate request (MSY3_MPR10), which investigates thrombocytopenia related events following incident Quinine Sulfate or Diltiazem use, was sent out and reported in conjunction with this request.

Results presented in this report provide counts of prevalent and incident Quinine Sulfate users, dispensings, and total days supplied. A dispensing was considered incident if a user had not had a prior Quinine Sulfate dispensing in the prior 183 days. The program was run separately for each year, 2006-2010. Please see the Specifications for details about the exact parameters used in this request.

Request ID MSY3_MPR7

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<u>Table 2c</u>	Table showing the number of Quinine Sulfate users, dispensings, and days supplied among incident users with a pre-existing Malaria diagnosis as well as the number of days supplied per users, dispensings per user, and days supplied per dispensing for incident users with a pre-existing Malaria diagnosis by year and age group - January 1, 2006 - December 31, 2010.
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<u>Table 3b</u>	Table showing the number of incident Quinine Sulfate users, dispensings, and total days supplied as well as the number of days supplied per user, dispensings per user, and days supplied per dispensing for incident Quinine Sulfate use by year and sex - January 1, 2006 - December 31, 2010.

Overview (continued)

Table 4c

Table showing the number of Quinine Sulfate users, dispensings, and days supplied among incident users with a pre-existing Malaria diagnosis as well as the number of days supplied per users, dispensings per user, and days supplied per dispensing for incident users with a pre-existing Malaria diagnosis by year and sex - January 1, 2006 - December 31, 2010.

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 Specifications

Modular Program #3, version 1, was used to investigate the overall prevalent and incident use of Quinine Sulfate as well as incident Quinine Sulfate use among enrollees with a pre-existing diagnosis of malaria (ICD-9: 084.0-084.6). The query period was from January 1, 2006 through December 31, 2010. The episode gap was set to 14 days and both the minimum episode duration and minimum days supplied were set to 1 day. Age groups were split as follows: 00-19, 20-39, 40-64, 65+ years. In total, 3 different scenarios were examined in this report with 10 runs for overall use and 5 runs for pre-existing malaria. See below for a description of each of these scenarios.

Scenario	Drug/Exposure Criteria			Pre-Existing Condition Criteria				
	Incident exposure	Incident with respect to:	Washout Period (days)	Pre-Existing Condition	Lookback Type**	Lookback Period	Care Setting	Principal Diagnosis
1	Quinine Sulfate	Quinine Sulfate	0*	None	N/A	N/A	N/A	N/A
2	Quinine Sulfate	Quinine Sulfate	183	None	N/A	N/A	N/A	N/A
3	Quinine Sulfate	Quinine Sulfate	183	Malaria	Fixed	183	All	No

* A 0-day washout period estimates prevalent use in MP3

**A "Fixed" lookback type for pre-existing conditions scans for (Lookback period) days prior to the treatment episode index date for the pre-existing condition.

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.

Lookback Period (pre-existing condition) - number of days wherein a member is required to have evidence of pre-existing condition (diagnosis/procedure/drug dispensing).

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 considered.

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

Table 1a. Summary of Prevalent Quinine Sulfate Use in the MSDD between January 1, 2006 and December 31, 2010, by Year

	Users	Dispensings	Total Days Supplied	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing
2006	62,778	97,139	4,636,970	73.9	1.5	47.7
2007	32,561	46,249	1,967,159	60.4	1.4	42.5
2008	7,784	12,565	413,930	53.2	1.6	32.9
2009	7,103	10,205	327,538	46.1	1.4	32.1
2010	7,891	9,604	227,207	28.8	1.2	23.7

Figure 1a1. Number of Prevalent Quinine Sulfate Users and Dispensings between January 1, 2006 and December 31, 2010, by Year

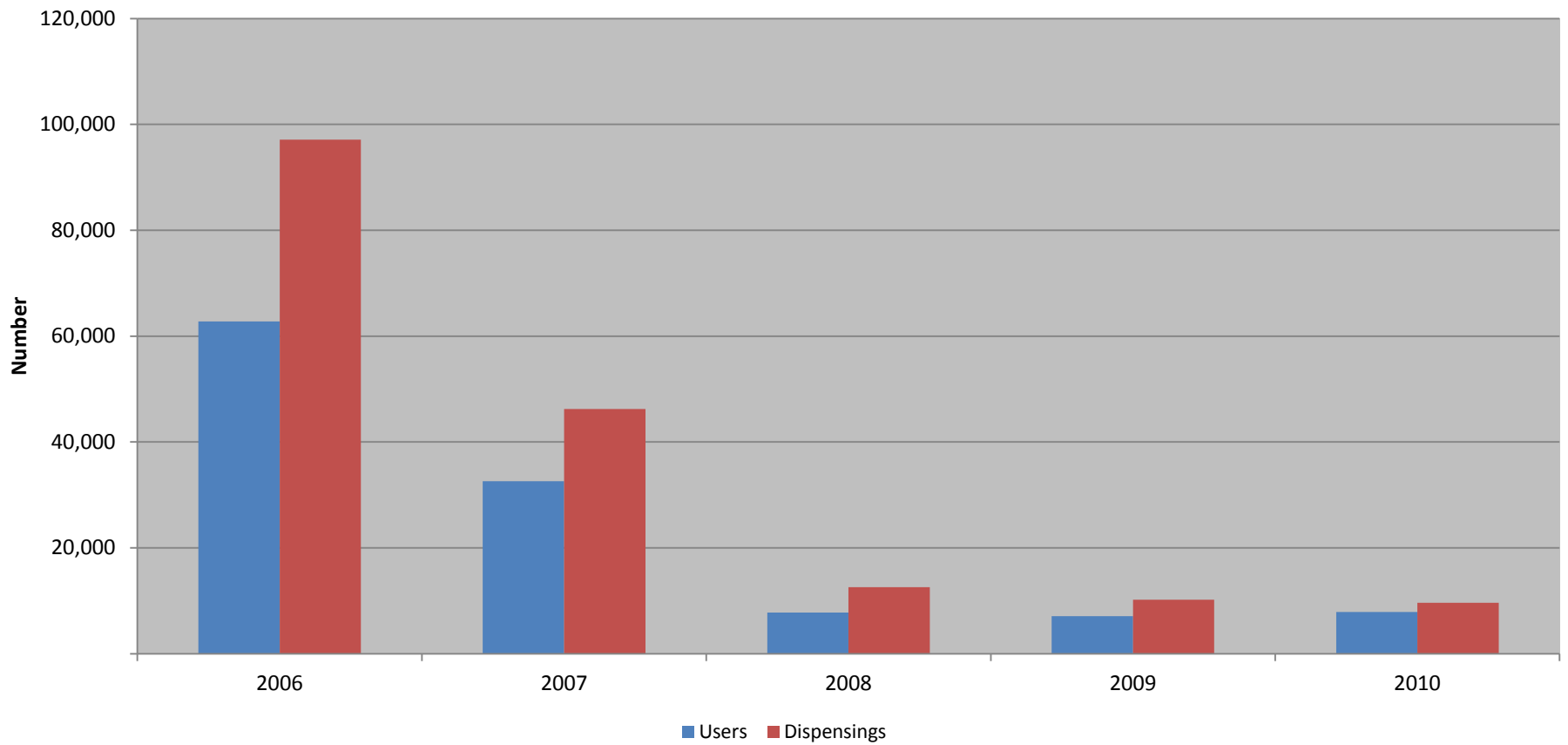


Figure 1a2. Prevalent Days Supplied per User, Days Supplied per Dispensing, and Dispensings per User between January 1, 2006 and December 31, 2010, by Year

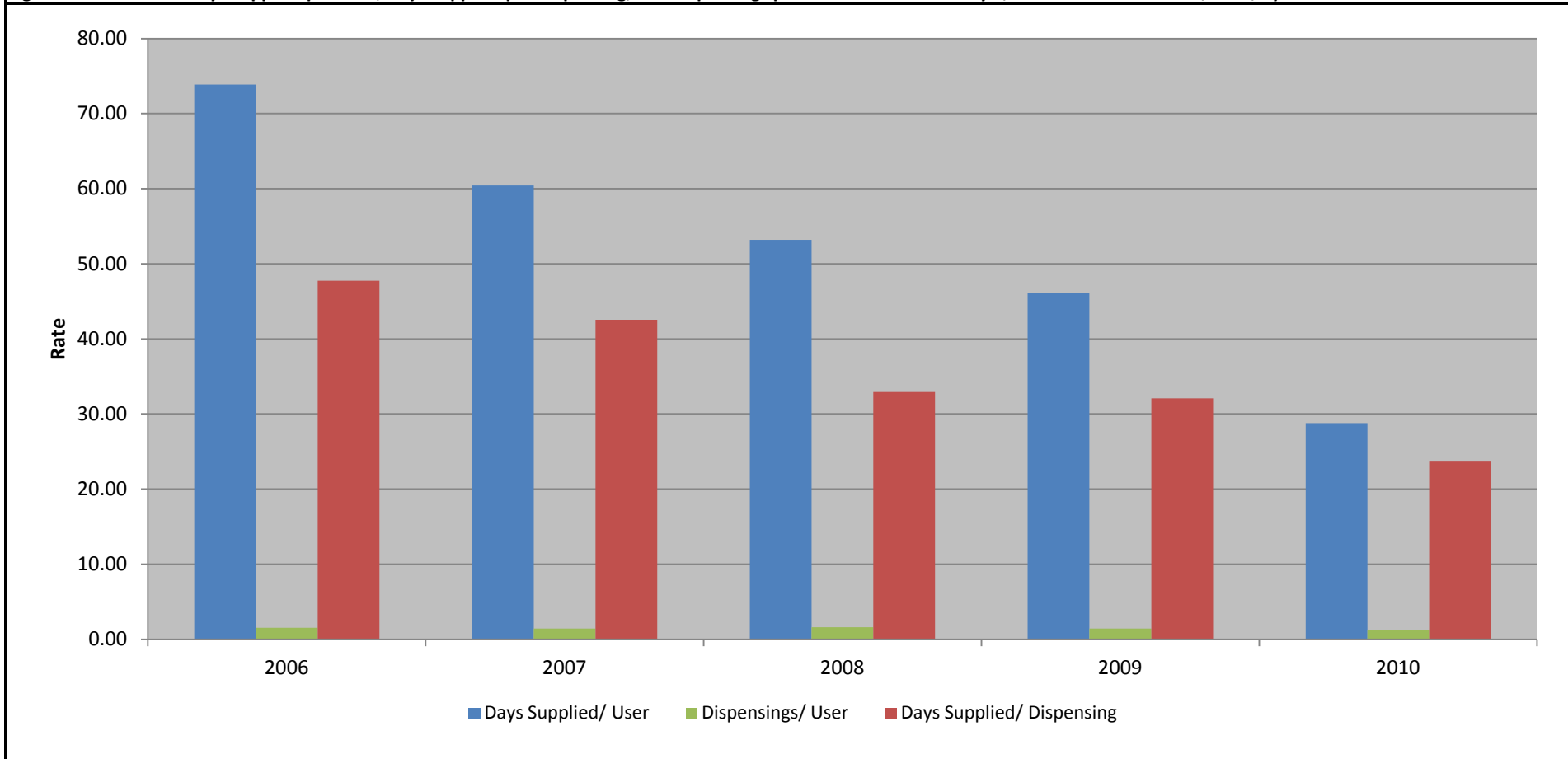


Table 1b. Summary of Incidence Quinine Sulfate Use in the MSDD between January 1, 2006 and December 31, 2010, by Year

	New Users	Dispensings	Total Days Supplied	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing
2006	35,121	56,284	2,389,899	68.0	1.6	42.5
2007	11,077	16,073	616,680	55.7	1.5	38.4
2008	3,520	5,520	176,318	50.1	1.6	31.9
2009	2,913	3,837	87,919	30.2	1.3	22.9
2010	5,643	6,252	108,830	19.3	1.1	17.4

Figure 1b1. Summary of Incidence Quinine Sulfate Use in the MSDD between January 1, 2006 and December 31, 2010, by Year

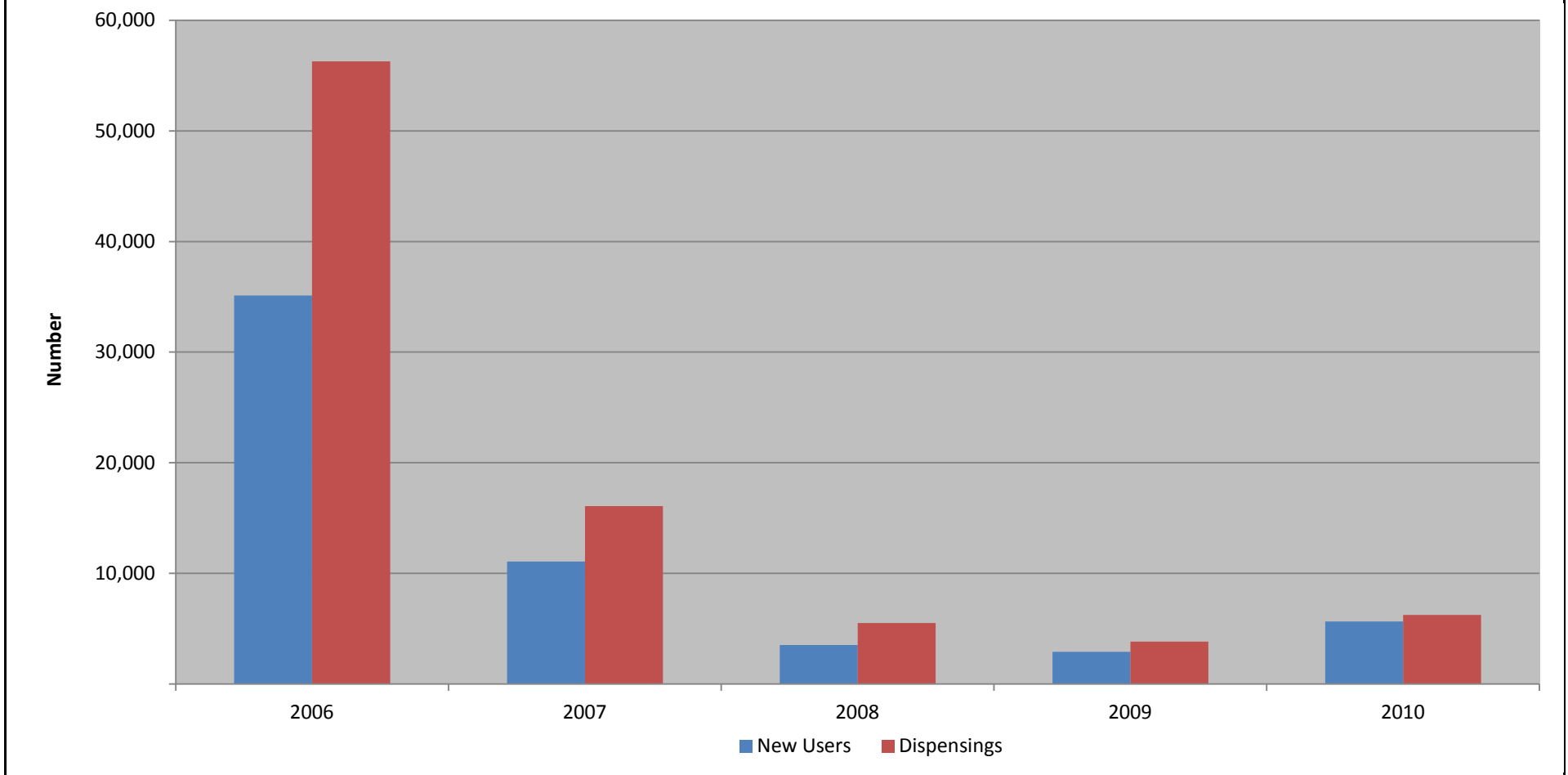


Figure 1b2. Incidence Days Supplied per User, Days Supplied per Dispensing, and Dispensings per User between January 1, 2006 and December 31, 2010, by Year

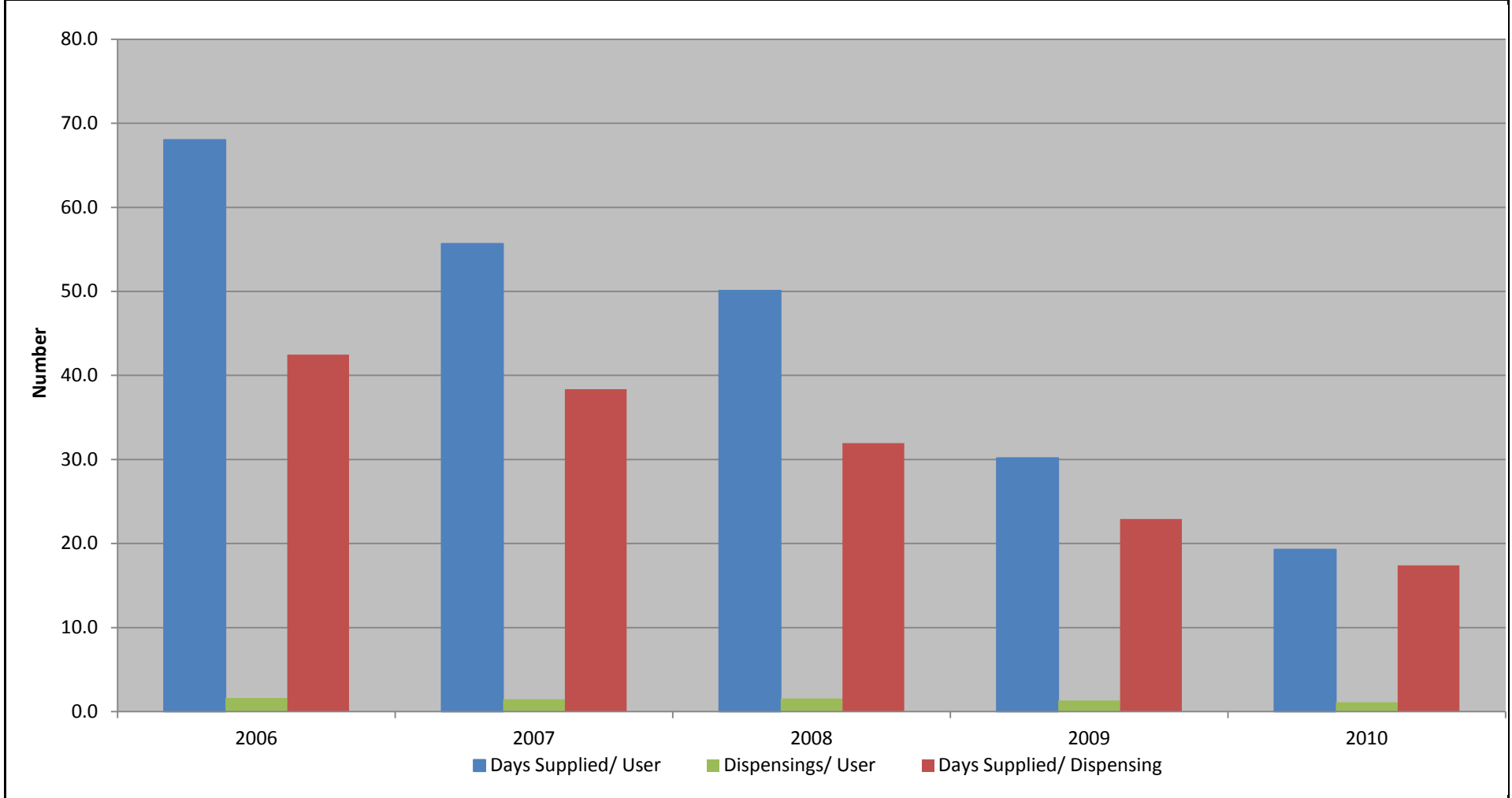


Table 1c. Summary of Incidence Quinine Sulfate Use in the MSDD between January 1, 2006 and December 31, 2010 with a Pre-Existing Malaria Diagnosis by Year

	New Users	Dispensings	Total Days Supplied	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing
2006	45	47	298	6.6	1.0	6.3
2007	27	27	182	6.7	1.0	6.7
2008	14	14	76	5.4	1.0	5.4
2009	26	26	165	6.3	1.0	6.3
2010	17	17	99	5.8	1.0	5.8

Figure 1c1. Number of Prevalent Quinine Sulfate Users and Dispensings between January 1, 2006 and December 31, 2010 with a Pre-Existing Malaria Diagnosis by Year

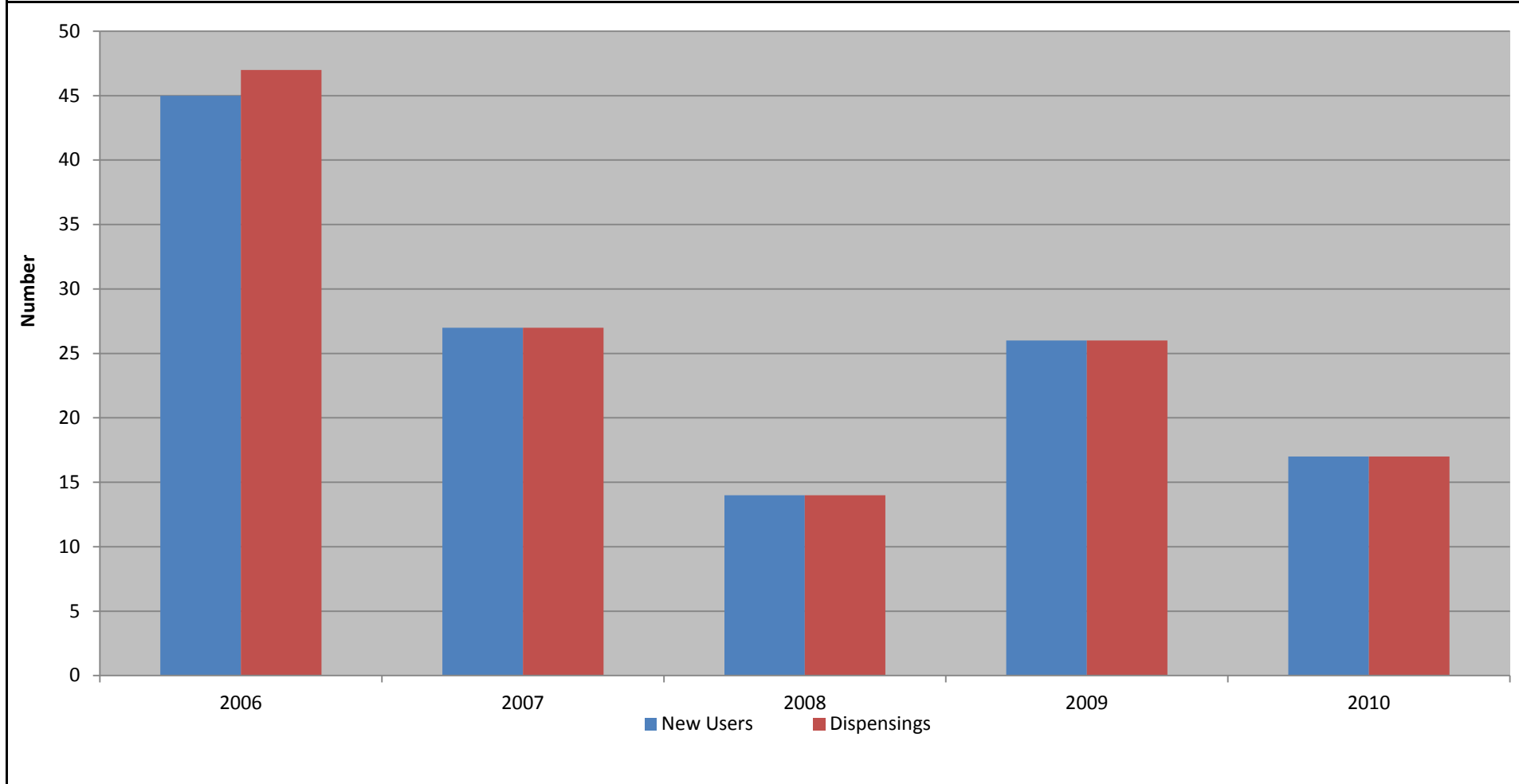


Figure 1c2. Prevalent Days Supplied per User, Days Supplied per Dispensing, and Dispensings per User between January 1, 2006 and December 31, 2010 with a Pre-Existing Malaria Diagnosis by Year

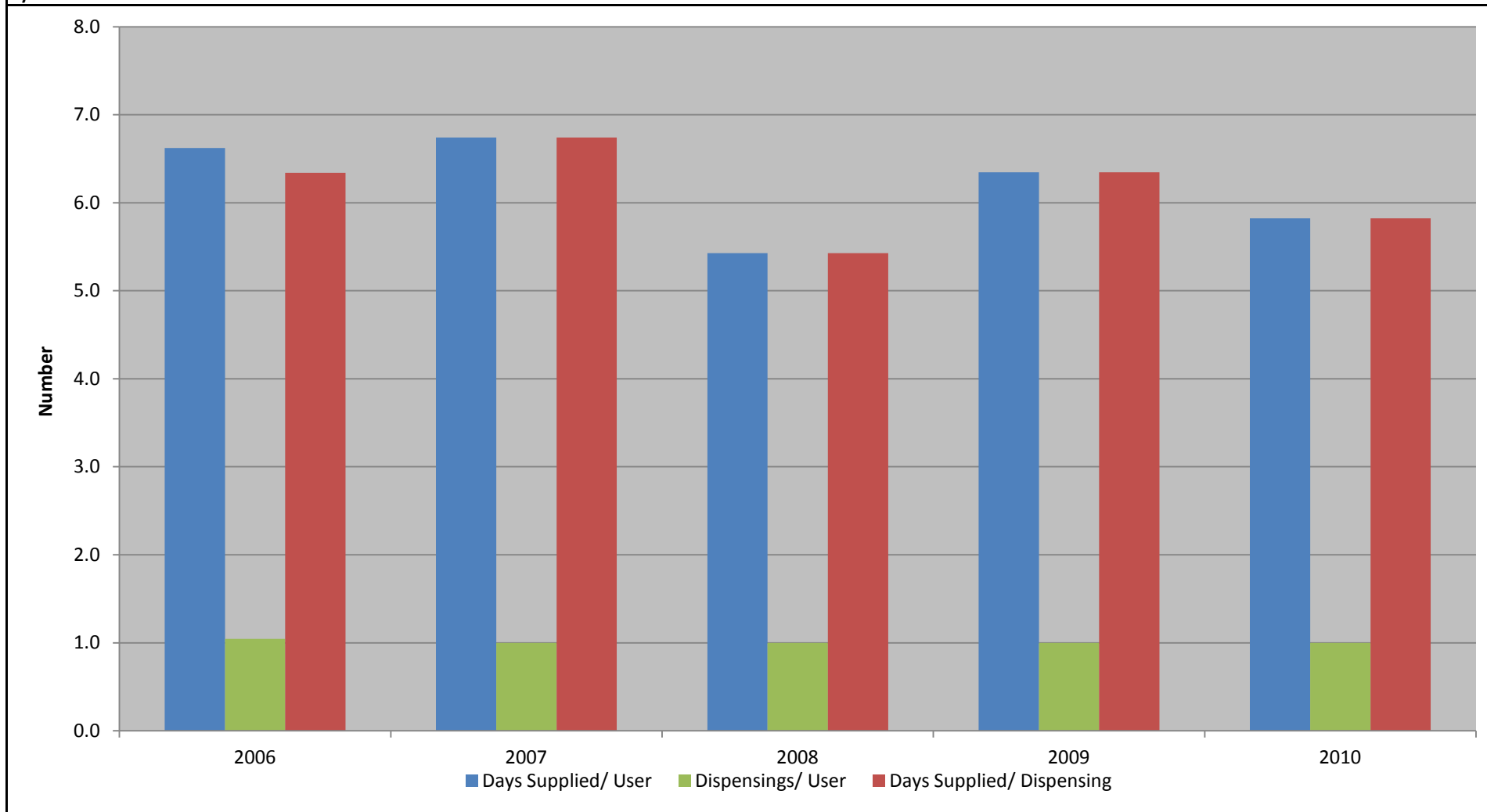


Table 2a. Summary of Prevalent Quinine Sulfate Use in the MSDD between January 1, 2006 and December 31, 2010, by Year and Age Group

	Users	Dispensings	Total Days Supplied	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing
2006	62,778	97,139	4,636,970	73.9	1.5	47.7
00 to 19	91	127	3,895	42.8	1.4	30.7
20 to 39	2,129	2,743	89,614	42.1	1.3	32.7
40 to 64	28,274	43,131	1,821,408	64.4	1.5	42.2
65+	32,284	51,138	2,722,053	84.3	1.6	53.2
2007	32,561	46,249	1,967,159	60.4	1.4	42.5
00 to 19	36	36	895	24.9	1.0	24.9
20 to 39	792	1,001	30,272	38.2	1.3	30.2
40 to 64	14,218	20,507	785,183	55.2	1.4	38.3
65+	17,515	24,705	1,150,809	65.7	1.4	46.6
2008	7,784	12,565	413,930	53.2	1.6	32.9
00 to 19	6	6	153	25.5	1.0	25.5
20 to 39	142	210	5,598	39.4	1.5	26.7
40 to 64	2,922	4,918	157,075	53.8	1.7	31.9
65+	4,714	7,431	251,104	53.3	1.6	33.8
2009	7,103	10,205	327,538	46.1	1.4	32.1
00 to 19	146	150	1,586	10.9	1.0	10.6
20 to 39	683	729	10,110	14.8	1.1	13.9
40 to 64	3,268	4,703	137,610	42.1	1.4	29.3
65+	3,006	4,623	178,232	59.3	1.5	38.6
2010	7,891	9,604	227,207	28.8	1.2	23.7
00 to 19	282	286	3,029	10.7	1.0	10.6
20 to 39	1,419	1,442	16,125	11.4	1.0	11.2
40 to 64	4,106	4,836	102,680	25.0	1.2	21.2
65+	2,084	3,040	105,373	50.6	1.5	34.7

Table 2b. Summary of Incidence Quinine Sulfate Use in the MSDD between January 1, 2006 and December 31, 2010, by Year and Age Group

	New Users	Dispensings	Total Days Supplied	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing
2006	35,121	56,284	2,389,899	68.0	1.6	42.5
00 to 19	68	99	2,941	43.3	1.5	29.7
20 to 39	1,513	2,039	63,183	41.8	1.3	31.0
40 to 64	16,908	27,278	1,046,774	61.9	1.6	38.4
65+	16,632	26,868	1,277,001	76.8	1.6	47.5
2007	11,077	16,073	616,680	55.7	1.5	38.4
00 to 19	26	30	602	23.2	1.2	20.1
20 to 39	461	684	19,645	42.6	1.5	28.7
40 to 64	5,436	8,050	274,567	50.5	1.5	34.1
65+	5,154	7,309	321,866	62.4	1.4	44.0
2008	3,520	5,520	176,318	50.1	1.6	31.9
00 to 19	2	2	33	16.5	1.0	16.5
20 to 39	78	97	2,360	30.3	1.2	24.3
40 to 64	1,161	1,896	59,630	51.4	1.6	31.5
65+	2,279	3,525	114,295	50.2	1.5	32.4
2009	2,913	3,837	87,919	30.2	1.3	22.9
00 to 19	120	121	1,231	10.3	1.0	10.2
20 to 39	499	512	6,110	12.2	1.0	11.9
40 to 64	1,550	2,057	44,378	28.6	1.3	21.6
65+	744	1,147	36,200	48.7	1.5	31.6
2010	5,643	6,252	108,830	19.3	1.1	17.4
00 to 19	236	241	2,513	10.6	1.0	10.4
20 to 39	1,158	1,174	12,626	10.9	1.0	10.8
40 to 64	3,070	3,394	57,262	18.7	1.1	16.9
65+	1,179	1,443	36,429	30.9	1.2	25.2

Table 2c. Summary of Incidence Quinine Sulfate Use in the MSDD between January 1, 2006 and December 31, 2010 with a Pre-Existing Malaria Diagnosis by Year and Age Group

	New Users	Dispensings	Total Days Supplied	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing
2006	45	47	298	6.6	1.0	6.3
00 to 19	1	1	3	3.0	1.0	3.0
20 to 39	15	17	96	6.4	1.1	5.6
40 to 64	26	26	183	7.0	1.0	7.0
65+	3	3	16	5.3	1.0	5.3
2007	27	27	182	6.7	1.0	6.7
00 to 19	4	4	38	9.5	1.0	9.5
20 to 39	16	16	96	6.0	1.0	6.0
40 to 64	7	7	48	6.9	1.0	6.9
65+	0	0	0	---	---	---
2008	14	14	76	5.4	1.0	5.4
00 to 19	1	1	3	3.0	1.0	3.0
20 to 39	5	5	31	6.2	1.0	6.2
40 to 64	8	8	42	5.3	1.0	5.3
65+	0	0	0	---	---	---
2009	26	26	165	6.3	1.0	6.3
00 to 19	1	1	7	7.0	1.0	7.0
20 to 39	9	9	64	7.1	1.0	7.1
40 to 64	16	16	94	5.9	1.0	5.9
65+	0	0	0	---	---	---
2010	17	17	99	5.8	1.0	5.8
00 to 19	0	0	0	---	---	---
20 to 39	3	3	19	6.3	1.0	6.3
40 to 64	13	13	77	5.9	1.0	5.9
65+	1	1	3	3.0	1.0	3.0

Table 3a. Summary of Prevalent Quinine Sulfate Use in the MSDD between January 1, 2006 and December 31, 2010, by Year and Sex

	Users	Dispensings	Total Days Supplied	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing
2006	62,778	97,139	4,636,970	73.9	1.5	47.7
Female	38,513	59,337	2,834,817	73.6	1.5	47.8
Male	24,236	37,754	1,800,688	74.3	1.6	47.7
Unknown	29	48	1,465	50.5	1.7	30.5
2007	32,561	46,249	1,967,159	60.4	1.4	42.5
Female	19,510	27,757	1,181,746	60.6	1.4	42.6
Male	13,042	18,481	785,065	60.2	1.4	42.5
Unknown	9	11	348	38.7	1.2	31.6
2008	7,784	12,565	413,930	53.2	1.6	32.9
Female	4,602	7,580	249,354	54.2	1.6	32.9
Male	3,175	4,975	164,103	51.7	1.6	33.0
Unknown	7	10	473	67.6	1.4	47.3
2009	7,103	10,205	327,538	46.1	1.4	32.1
Female	4,396	6,313	202,774	46.1	1.4	32.1
Male	2,703	3,888	124,707	46.1	1.4	32.1
Unknown	4	4	57	14.3	1.0	14.3
2010	7,891	9,604	227,207	28.8	1.2	23.7
Female	5,053	6,132	142,754	28.3	1.2	23.3
Male	2,830	3,464	84,368	29.8	1.2	24.4
Unknown	8	8	85	10.6	1.0	10.6

Table 3b. Summary of Incidence Quinine Sulfate Use in the MSDD between January 1, 2006 and December 31, 2010, by Year and Sex

	New Users	Dispensings	Total Days Supplied	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing
2006	35,121	56,284	2,389,899	68.0	1.6	42.5
Female	21,461	33,970	1,452,575	67.7	1.6	42.8
Male	13,642	22,283	936,490	68.6	1.6	42.0
Unknown	18	31	834	46.3	1.7	26.9
2007	11,077	16,073	616,680	55.7	1.5	38.4
Female	6,497	9,388	361,629	55.7	1.4	38.5
Male	4,575	6,679	254,841	55.7	1.5	38.2
Unknown	5	6	210	42.0	1.2	35.0
2008	3,520	5,520	176,318	50.1	1.6	31.9
Female	2,026	3,241	103,312	51.0	1.6	31.9
Male	1,491	2,275	72,886	48.9	1.5	32.0
Unknown	3	4	120	40.0	1.3	30.0
2009	2,913	3,837	87,919	30.2	1.3	22.9
Female	1,814	2,340	50,496	27.8	1.3	21.6
Male	1,095	1,493	37,366	34.1	1.4	25.0
Unknown	4	4	57	14.3	1.0	14.3
2010	5,643	6,252	108,830	19.3	1.1	17.4
Female	3,645	3,977	66,516	18.2	1.1	16.7
Male	1,992	2,269	42,249	21.2	1.1	18.6
Unknown	6	6	65	10.8	1.0	10.8

Table 3c. Summary of Incidence Quinine Sulfate Use in the MSDD between January 1, 2006 and December 31, 2010 with a Pre-Existing Malaria Diagnosis by Year and Sex

	New Users	Dispensings	Total Days Supplied	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing
2006	45	47	298	6.6	1.0	6.3
Female	11	11	71	6.5	1.0	6.5
Male	34	36	227	6.7	1.1	6.3
Unknown	0	0	0	---	---	---
2007	27	27	182	6.7	1.0	6.7
Female	10	10	69	6.9	1.0	6.9
Male	17	17	113	6.6	1.0	6.6
Unknown	0	0	0	---	---	---
2008	14	14	76	5.4	1.0	5.4
Female	3	3	20	6.7	1.0	6.7
Male	11	11	56	5.1	1.0	5.1
Unknown	0	0	0	---	---	---
2009	26	26	165	6.3	1.0	6.3
Female	10	10	65	6.5	1.0	6.5
Male	16	16	100	6.3	1.0	6.3
Unknown	0	0	0	---	---	---
2010	17	17	99	5.8	1.0	5.8
Female	7	7	33	4.7	1.0	4.7
Male	10	10	66	6.6	1.0	6.6
Unknown	0	0	0	---	---	---