



Ministry of Defence

Ad Hoc Statistical Bulletin

UK Armed Forces prescribed Mefloquine Hydrochloride and subsequent presentation to MOD Specialist Mental Health Services, 1 April 2007 – 30 September 2015

Date 22 September 2016

Overview

This is the second ad hoc statistical bulletin presenting information on UK Armed Forces personnel who were prescribed Mefloquine Hydrochloride (Mefloquine). The first ad hoc statistical bulletin published on 8 January 2016 presented information on prescriptions of Mefloquine Hydrochloride (Mefloquine) to UK Armed Forces personnel.

This ad hoc statistical bulletin provides information on the number of UK Armed Forces personnel prescribed Mefloquine Hydrochloride (Mefloquine) and other antimalarial drugs and subsequent presentations to MOD Specialist Mental Health Services for a mental health disorder.

This bulletin has been provided in response to recent media coverage and to ensure the public has equal access to the information.

Mefloquine (marketed in UK as Lariam) is used to prevent or treat malaria by killing the blood phase of the parasites. It may be currently prescribed as prophylaxis for military personnel deployed to areas with a recognised risk of malaria. This includes regions within a number of countries for example Kenya, the Congo, Guinea, Ghana, and Sierra Leone. Mefloquine is one of the four main chemoprophylaxis drugs that are available for use in UK to prevent malaria. Others include Doxycycline; Chloroquine; Proguanil; and Atovaquone (when combined with Proguanil it is marketed as Malarone). All of these drugs have a recognised profile of side effects and there have been reported neuropsychological side effects of Mefloquine.

Malaria is a serious febrile illness. If malaria is not diagnosed and treated promptly it can be fatal, specifically if the *P.falciparum* strain is contracted. The Government therefore has a duty of care to provide members of our Armed Forces with appropriately tested and effective methods of chemoprophylaxis. The exact choice of drug offered to personnel depends on a number of factors, including the region the individual is deploying to, their health and any past history of side effects. Taking antimalarial tablets when visiting an area where there is a malaria risk can reduce the risk of malaria by about 90%.

Issued by: Head of Defence Statistics (Health) | MoD | Abbey Wood | Oak 0 West | Bristol | BS34 8JH
Telephone: 030679 84423 Email: DefStrat-Stat-Health-Hd@mod.uk

Press office: 020721 83253

Link to stats: <https://www.gov.uk/government/statistics/mod-national-and-official-statistics-by-topic>

Results

Number of prescriptions by drug type to mental health presentation analysis

Between 01 April 2007 and 30 September 2015, **17,623** UK Regular Armed Forces personnel were prescribed Mefloquine Hydrochloride and **99,081** UK Regular Armed Forces personnel were prescribed a different antimalarial drug. Of these:

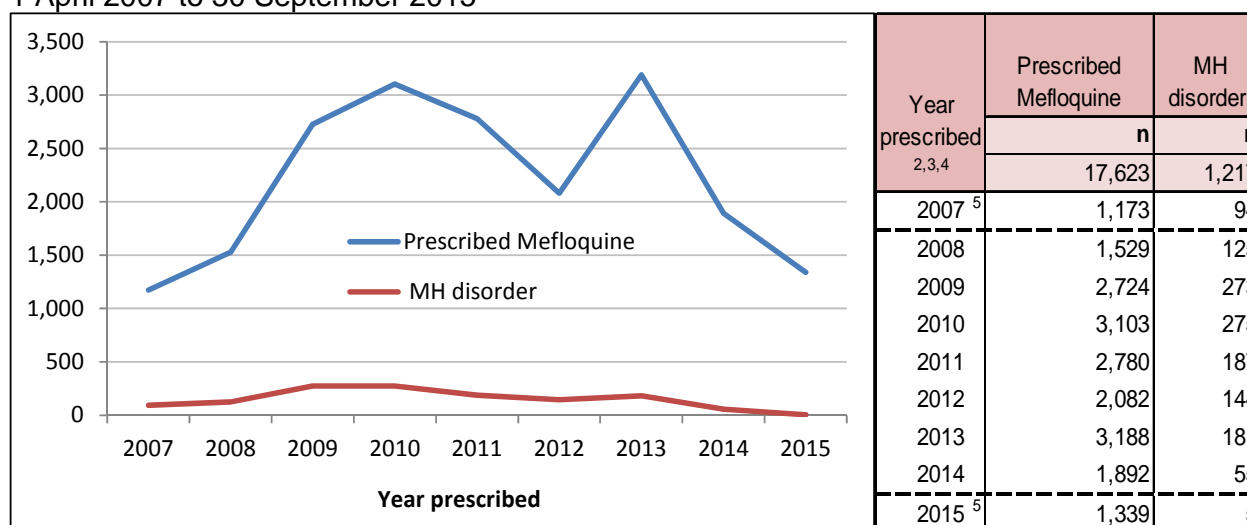
- **6.9% (n=1,217)** of those prescribed Mefloquine Hydrochloride subsequently had an initial assessment for a mental health disorder at MOD Specialist Mental Health Services^a.
- **7.9% (n=7,825)** of those prescribed other antimalarial drugs subsequently had an initial assessment for a mental health disorder at MOD Specialist Mental Health Services.

It is not possible from centrally held data to identify whether the mental health episode was associated with being prescribed an antimalarial drug.

As an individual may have been prescribed an antimalarial drug in a number of years, the sum of each year may not equal the total number of UK Regular Armed Forces personnel prescribed over the whole period in **Tables 1** and **2**. Please also note that some personnel may have been prescribed both Mefloquine Hydrochloride and another antimalarial drug, these personnel have been counted within each year prescribed as well as for each drug they were prescribed in.

Figure 1 & Table 1: UK Regular¹ Armed Forces personnel prescribed Mefloquine Hydrochloride^{2,3,4} and subsequently assessed as having a mental health disorder at MOD Specialist Mental Health Services. Numbers.

1 April 2007 to 30 September 2015



Source: Defence Medical Information Capability Programme (DMICP), Joint Personnel Administration (JPA)

1. As recorded on JPA as at the time of prescription

2. As recorded on DMICP, extracted 8 February 2016.

3. Personnel have been counted in each year they were prescribed, thus the sum of all years will not equal the overall number of personnel prescribed i.e. if personnel were prescribed in 2008 and 2010, they would be counted once in each year they were prescribed in the table above but only once in the overall total.

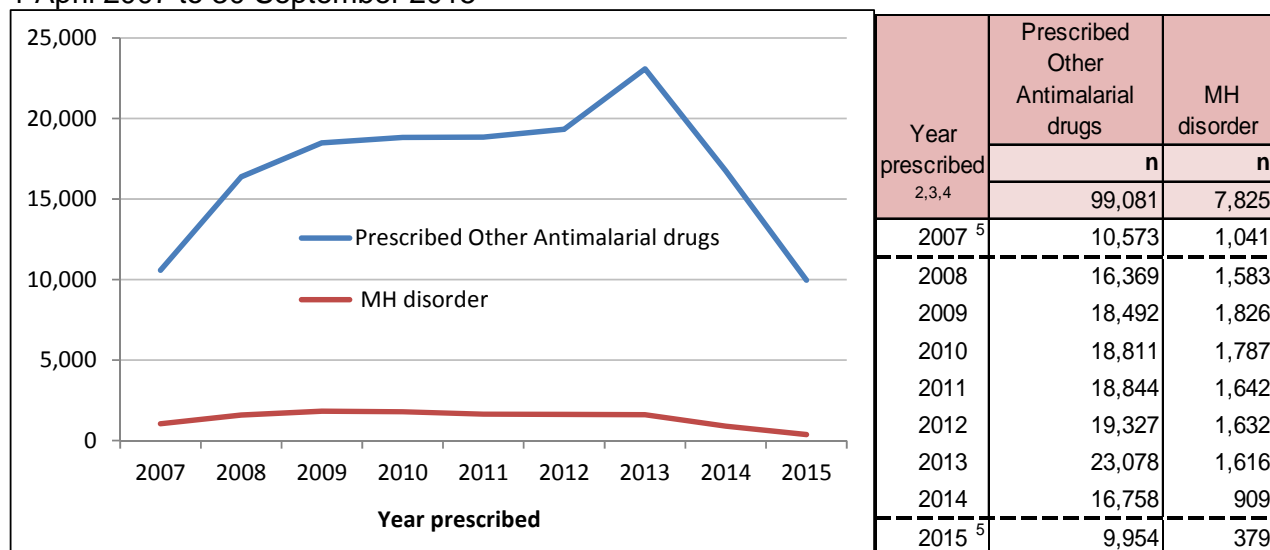
4. Personnel have been counted in each year they have been prescribed an antimalarial drug and subsequently assessed for a mental health disorder, regardless of the year in which their mental health assessment took place. i.e. If someone was prescribed in 2007 and their subsequent assessment for a mental health disorder was in 2010, they will be counted in 2007 as this is the year in which they were prescribed the drug.

5. From 1 April 2007 to 30 September 2015

^a This includes outpatient appointments at Departments for Community Mental Health (DCMH) and admissions to MOD In-Patient contractors

Figure 2 & Table 2: UK Regular¹ Armed Forces personnel prescribed Other Antimalarial² drugs and subsequently assessed as having a mental health disorder at MOD Specialist Mental Health Services³, Numbers.

1 April 2007 to 30 September 2015



Source: DMICP, JPA

1. As recorded on JPA as at the time of prescription

2. As recorded on DMICP, extracted 8 February 2016.

3. Personnel have been counted in each year they were prescribed, thus the sum of all years will not equal the overall number of personnel prescribed i.e. if personnel were prescribed in 2008 and 2010, they would be counted once in each year they were prescribed in the table above but only once in the overall total.

4. Personnel have been counted in each year they have been prescribed an antimalarial drug and subsequently assessed for a mental health disorder, regardless of the year in which their mental health assessment took place. i.e. If someone was prescribed in 2007 and their subsequent assessment for a mental health disorder was in 2010, they will be counted in 2007 as this is the year in which they were prescribed the drug.

5. From 1 April 2007 to 30 September 2015

Figure 1 and **Figure 2** show that the number of personnel who were assessed as having a mental health disorder following prescription of either Mefloquine Hydrochloride or other antimalarial drugs has remained stable over time. A number of the personnel prescribed Mefloquine Hydrochloride or other antimalarial drugs may not have been assessed with a mental health disorders at the time the data was extracted but may present with a mental health disorder in future years, thus the reduction seen in mental health presentations for prescriptions in more recent years are likely to change. The time between prescription and presentation with a Mental Health disorder is presented in the next section.

Service personnel prescribed antimalarial drugs in 2009 and 2010 had the highest number of mental health assessments. It is not possible from centrally held data to determine whether the reason for mental health assessment was due to the prescription of an antimalarial drug or caused by other factors such as deployment on operations; for example this time period corresponds with the highest number of deaths and casualties UK Armed Forces sustained in Afghanistan.

Time from prescription to presentation with a mental health disorder

Table 3 and **Table 4** below present the total number of personnel prescribed antimalarial drugs that were subsequently assessed as having a mental health disorder. Personnel were counted in each year they were prescribed and the year they subsequently first presented with a mental health disorder.

Table 3: UK Regular¹ Armed Forces personnel prescribed Mefloquine Hydrochloride² by year of prescription and year subsequently assessed as having a mental health disorder at MOD Specialist Mental Health Services. Numbers.

1 April 2007 to 30 September 2015

Year prescribed Mefloquine Hydrochloride	Year in which assessed with a MH Disorder									
	All	2007	2008	2009	2010	2011	2012	2013	2014	2015
	1,217	0	23	53	99	150	209	267	300	238
2007 ³	94	0	16	10	11	14	11	14	13	5
2008	125	-	7	15	23	20	23	15	14	8
2009	273	-	-	28	42	37	46	51	42	27
2010	275	-	-	-	23	54	51	66	48	33
2011	187	-	-	-	-	25	57	36	42	27
2012	144	-	-	-	-	-	21	54	35	34
2013	181	-	-	-	-	-	-	31	83	67
2014	55	-	-	-	-	-	-	-	23	32
2015 ³	5	-	-	-	-	-	-	-	-	5

Source: DMICP, JPA

1. As recorded on JPA as at the time of prescription

2. As recorded on DMICP, extracted 8 February 2016.

3. From 1 April 2007 to 30 September 2015

4. Personnel were counted once in each year they were prescribed and subsequently assessed as having a MH disorder.

Table 4: UK Regular¹ Armed Forces personnel prescribed Other Antimalarial drugs by year of prescription and year subsequently assessed as having a mental health disorder at MOD Specialist Mental Health Services. Number.

1 April 2007 to 30 September 2015

Year prescribed Other Anti-Malarial drugs	Year in which assessed with a MH Disorder									
	All	2007	2008	2009	2010	2011	2012	2013	2014	2015
	7,825	32	282	546	866	1,139	1,719	2,133	2,407	1,895
2007 ³	1,041	32	162	154	122	130	137	115	118	71
2008	1,583	-	120	242	229	212	227	205	210	130
2009	1,826	-	-	150	344	277	309	286	231	183
2010	1,787	-	-	-	171	339	383	340	284	190
2011	1,642	-	-	-	-	181	415	394	289	217
2012	1,632	-	-	-	-	-	248	477	413	281
2013	1,616	-	-	-	-	-	-	316	598	391
2014	909	-	-	-	-	-	-	-	264	314
2015 ³	379	-	-	-	-	-	-	-	-	118

Source: DMICP, JPA

1. As recorded on JPA as at the time of prescription

2. As recorded on DMICP, extracted 8 February 2016.

3. From 1 April 2007 to 30 September 2015

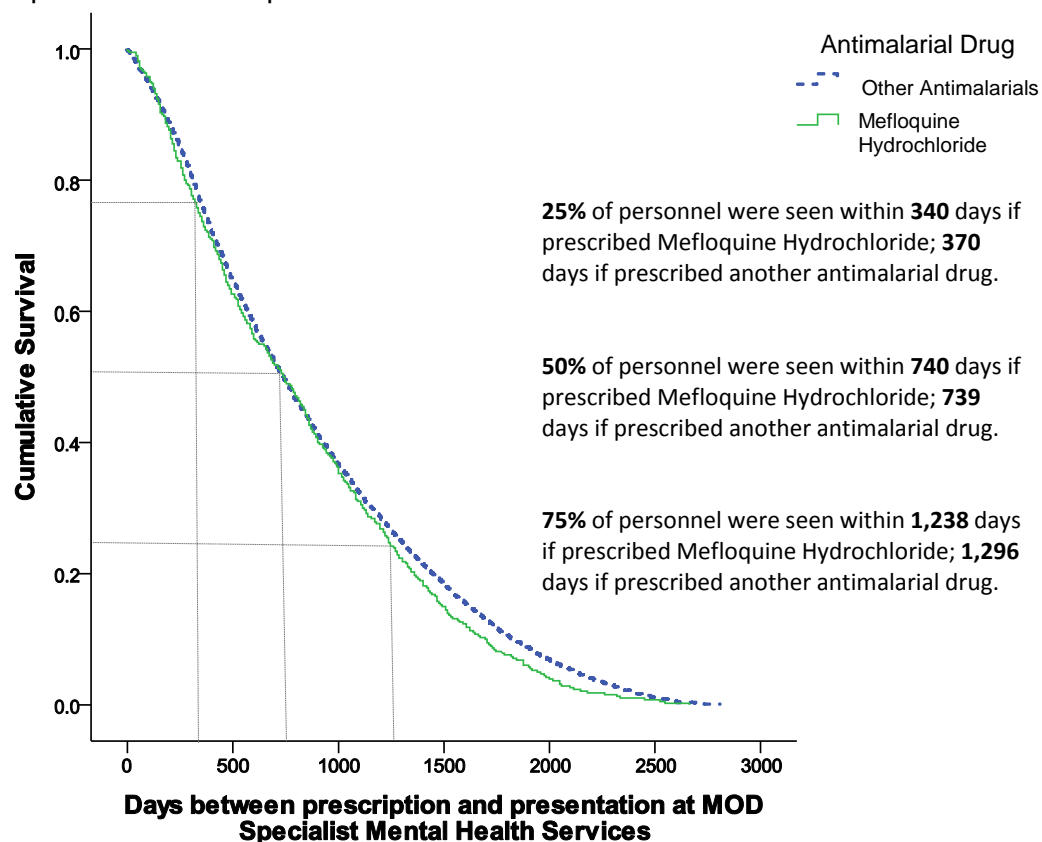
4. Personnel were counted once in each year they were prescribed and subsequently assessed as having a MH disorder.

Table 3 and **Table 4** show that UK Armed Forces personnel present to MOD Specialist Mental Health Services over a long period of time thus there was no time point post prescription when personnel were more likely to be diagnosed with a mental health disorder.

Figure 3 presents the time between the first antimalarial prescription and subsequent presentation for a mental health disorder at MOD Specialist Mental Health Services. All subsequent prescriptions and presentations to MOD Specialist Mental Health Services have been excluded from the analysis to remove the potential effect drug accumulation has to an individual over time. Thus numbers presented in **Figure 3** are a subset of those presented in **Tables 1 to 4**.

Figure 3: Time between first antimalarial prescription and assessment of having a mental disorder at MOD Specialist Mental Health Services.

1 April 2007 to 30 September 2015



Source: DMICP, DS Database

Kaplan-Meier estimate based on **n=994** UK AF personnel prescribed mefloquine hydrochloride who subsequently presented with a mental health disorder and **n= 6,456** personnel prescribed other antimalarial drugs who subsequently presented with a mental health disorder at MOD Specialist Services between 01 April 2007 and 30 September 2015.

UK Armed Forces personnel were counted once for their first prescription and all subsequent prescriptions have been excluded from the analysis

A statistical test to compare the time from prescription to first assessment for a mental disorder between the two antimalarial drug groups showed a statistically significant difference^b. However, further analysis showed no significant difference^c in time to presentation between the two groups up to 1,000 days after prescription and the statistical difference between the two groups was the result of mental health presentations more than 2.5 years post antimalarial prescription.

^b Log-Rank test; $p=0.004$.

^c Log-Rank test; $p=0.938$.

Limitations

There are a number of imitations that need to be taken into consideration when interpreting these findings:

- There were a minimum of 12,900 UK Armed Forces personnel who were deployed on Operations who were prescribed an antimalarial where the drug name was not available in the primary care data warehouse and were therefore excluded from the analysis, thus, numbers of those prescribed Mefloquine and other antimalarial drugs were the minimum.
- Only personnel assessed as having a mental health disorder at MOD Specialist Mental Health Services were included in the analysis; thus missing from this data were any Service personnel who hadn't been referred to a DCMH/MOD In-Patient provider i.e. Service personnel who may have been seen by a MOD General Practitioner or accessed private healthcare and any veteran who may have sought care after leaving service.
- Personnel who attended but were assessed as not having a mental health disorder at MOD Specialist Mental Health Services were excluded from the analysis.
- The Doxycycline data includes prescriptions issued for anti-malarial purposes and where it has been prescribed as an antibiotic. To differentiate between an anti-malarial or antibiotic prescription for Doxycycline would require a complex algorithm and a review of patient notes, which has not been done.
- The number of prescriptions presented should be treated as **minimum** for the following reasons:
 - UK Armed Forces personnel who leave the Armed Forces and subsequently register at a MOD medical centre as a civilian were not included in the numbers presented.
 - It is possible that UK Armed Forces personnel were prescribed an antimalarial drug prior to their medical record being held in the electronic patient record; therefore these records were not available centrally.
 - If antimalarial drug prescriptions were recorded as free text only in the patient medical record the information does not transfer into the central data warehouse and thus were not accessible for inclusion in the numbers presented.
 - If antimalarial drugs were issued via a Patient Specific Direction, the name of the drug prescribed was not transferred into the central data warehouse and thus were not accessible for inclusion in the numbers presented.
 - If the antimalarial drug was prescribed by the NHS it has not been included in the numbers presented.

Background notes

This ad hoc statistical bulletin has been released in response to the recent media coverage on the prescribing of Mefloquine in the UK Armed Forces and subsequent mental health presentations. This statistical bulletin ensures MOD is open and transparent about the methodology and quality of any statistics and that equal access is given to all, as required by the Code of Practice for Official Statistics.

The MOD use a range of prevention drugs in line with the guidance provided by Public Health England's Advisory Committee on Malaria Prevention (ACMP) to ensure the treatment provided is going to be the most effective.

The Ministry of Defence needs to be able to use the most appropriate drug for the areas to where our people deploy to help ensure their protection against this disease. The choice of prescribed treatment depends upon a number of factors including:

- the region to which personnel are being deployed.
- The individual's medical history, for example, past history of side effects or contraindications to the drug.

Drug options include Chloroquine; Chloroquine plus Proguanil; Mefloquine (Lariam); Doxycycline; and Atovaquone plus Proguanil (Malarone®).

Data sources

UK Armed Forces personnel include Regular trained and untrained personnel.

DMICP commenced during 2007 and comprises an integrated primary Health Record (iHR) for clinical use and a pseudo-anonymised central data warehouse. Prior to 2007 medical records were kept locally at each individual medical centre. By 2010, DMICP was available in the UK and the majority of Germany. Rollout to other overseas locations commenced in November 2011.

Mental Health

UK Armed Forces personnel have access to specialist mental health services via referrals made by their GP, provided through MOD Department of Community Mental Health (DCMH) or the MOD in-patient provider. DCMH are specialised psychiatric services based on community mental health teams closely located with primary care services at MOD sites in the UK and abroad.

DCMH staff record the initial mental health assessment during a patient's first appointment, based on presenting complaints. The information is based on a clinician's diagnosis at initial assessment and final diagnoses may differ as some patients do not present the full range of symptoms, signs or clinical history during their first appointment. Data presents those assessed with a mental disorder at initial appointment.

All UK based and aero-medically evacuated Service personnel based overseas requiring in-patient admission are treated by one of eight NHS trusts in the UK which are part of a consortium headed by the South Staffordshire and Shropshire NHS Foundation trust (SSSFT). UK based Service personnel from British Forces Germany (BFG) were treated at Guys and St Thomas Hospital in the UK up until April 2013 and from this date, at Gilead IV hospital, Bielefeld, under a contract with Soldiers, Sailors and Airmen Family Association (SSAFA) through the Limited Liability Partnership. Data is received monthly direct from SSSFT and SSAFA. See Background Quality Report for the UK Armed Forces Mental Health Report for further information on data sources found at www.gov.uk.

Please note, an individual may have had more than one episode of care, the data provides the first appointment following a prescription for an antimalarial drug.

Prescriptions

UK Armed Forces personnel include trained and untrained personnel; UK Armed Forces full time Regulars including Nursing Services and Gurkhas.

Information presented relates to the number of personnel prescribed antimalarial drugs not the total number of prescriptions. Individuals may have received more than one prescription however; they have only been counted once in each year for each drug prescribed. For example, an individual prescribed Mefloquine and another antimalarial drug in 2010 was counted once for Mefloquine and once for other antimalarial drugs. However, if they were prescribed Mefloquine

twice in 2010, they were counted only once. Therefore the sum of each year may not equal the total number of UK Armed Forces personnel prescribed over the whole period.

Data on prescriptions for all antimalarial drugs were derived from the DMICP data warehouse. Data were extracted as at 8 February 2016 to provide more up to date information than previously published.

Searches in DMICP for antimalarial drug names which include Avloclor, Chloroquine Phosphate, Chloroquine Phosphate and Proguanil, Chloroquine Sulfate, Doxycycline Hyclate, Doxycycline Monohydrate, Malarone, Nivaquine, Paludrine, Paludrine/Avloclor, Proguanil and Atovaquone, Proguanil Hydrochloride, Lariam and Mefloquine Hydrochloride were conducted.

Please note if the drug prescriptions were recorded as free text only in the patient medical record the information does not transfer into the central data warehouse, thus was not available for analysis. It would require many hours of a medics time to review the patient records to code the information and thus make the information centrally available; in the timeframe required to provide the analysis, this was deemed to be disproportionate effort.

DMICP is a live record system and data presented may vary from figures previously released.

The data on Mefloquine and other Antimalarial drugs presented was based on personnel who had been prescribed the drug; it does not ensure the individual took the drug.

Methodology

Number of prescriptions by drug type to mental health presentation analysis

Personnel have been counted once in each year they were prescribed the antimalarial drug, for example, if personnel were prescribed Mefloquine Hydrochloride in 2010 and also prescribed another antimalarial drug in 2010, they will be counted once in each year for each prescription. (Tables 1–4 and Figures 1-2)

Personnel who were subsequently assessed as having a mental health disorder following prescription of an antimalarial drug have been counted once within the year they were prescribed (Tables 3-4).

Time from prescription to mental health presentation analysis

In order to assess whether there were differences in time to presentation with a mental disorder following prescription between the two groups: Mefloquine Hydrochloride and other antimalarial drugs, a Kaplan-Meier estimate was conducted. The analysis included the first antimalarial prescription and first subsequent presentation for a mental health disorder at MOD Specialist Mental Health Services (n=994 for Mefloquine Hydrochloride, n=6,456 for other antimalarial drugs). All subsequent prescriptions and presentations to MOD Specialist Mental Health Services have been excluded from the analysis to remove the potential effect drug accumulation has to an individual over time. Thus numbers presented in **Figure 3** are a subset of those presented in **Tables 1 to 4**.

The Kaplan-Meier estimate used the number of days between the date of first prescription for an antimalarial drug and the date of initial assessment at MOD Specialist Mental Health Services for each individual included in the analysis.

A log-rank test is a hypothesis test to compare the survival distributions of two samples. The log-rank test statistic compares estimates of the hazard functions of the two groups at each observed event time. It is constructed by computing the observed and expected number of events in one of the groups at each observed event time and then adding these to obtain an overall summary across all-time points where there is an event. The log-rank test was used in this analysis to determine if there was a significant difference in the distribution of time between the date of first prescription and the date of initial assessment for a mental disorder at MOD Specialist Mental Health Services for Mefloquine Hydrochloride and other antimalarial drugs.

The timelines in **Figure 3** were computed by calculating the proportion of each cohort that had not presented for a mental disorder at a certain point in time for example, at 340 days 25% of personnel prescribed with Mefloquine Hydrochloride had presented with a mental disorder, therefore 75% of that cohort still had not presented up to this time (days between prescription and presentation at MOD Specialist Mental Health Services = 340, Cumulative Survival = 0.75).

Table 5 presents the Percentiles table from this analysis.

Table 5: Percentiles of days between prescription and initial assessment for mental disorder, by antimalarial drug.

1 April 2007 – 30 September 2015

	Percentiles		
	25%	50%	75%
	Estimate (days)	Estimate (days)	Estimate (days)
Anti-malarial drug			
Mefloquine Hydrochloride	1,238	740	340
Other Anti-malarial	1,296	739	370

Source: DMICP, DS Database

Glossary:

Antimalarial drugs - include Chloroquine; Chloroquine plus Proguanil; Mefloquine (Lariam); Doxycycline; and Atovaquone plus Proguanil (Malarone®).

Defence Medical Information Capability Programme (DMICP) - The DMICP programme commenced during 2007 and comprises an integrated primary Health Record (iHR) for clinical use and a pseudo-anonymised central data warehouse.

Malaria – Malaria is a mosquito-borne infectious disease of humans and other animals caused by parasitic protozoans (a group of single-celled microorganisms) belonging to the genus *Plasmodium*.

Mefloquine Hydrochloride - Mefloquine is used to prevent or treat certain types of malaria. It works by killing the parasites that cause malaria. It is used to prevent malaria in people who are in areas where there is an increased risk of getting malaria.

MOD Specialist Mental Health Services - encompass the delivery of care through MOD's Department for Community Mental Health (DCMH) for outpatient care, and all admissions to the MOD's in-patient care contractor. It does not cover mental health care for patients treated wholly in the primary care setting by GPs.

Other Antimalarial drugs – where the term is used in this adhoc statistics release it includes: Chloroquine; Chloroquine plus Proguanil; Doxycycline; and Atovaquone plus Proguanil (Malarone®). It excludes Mefloquine Hydrochloride (Lariam).

UK Regulars - are full time Service personnel, including Nursing Services and Gurkhas, but excluding FTRS personnel, Naval activated Reservists, mobilised Reservists, Military Provost Guarding Service (MPGS) and Non Regular Permanent Service (NRPS). Unless otherwise stated, includes trained and untrained personnel.

Further information

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Defence Statistics (Health)

Telephone: 030679 84423

Email: DefStrat-Stat-Health-PQ-FOI@mod.uk

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Defence Expenditure Analysis	030 679 34531	DefStrat-Econ-ESES-DEA-Hd@mod.uk
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Tri-Service Manpower	020 7807 8896	DefStrat-Stat-Tri-Hd@mod.uk
Civilian Manpower	020 7218 1359	DefStrat-Stat-Civ-Hd@mod.uk
Health Information	030 6798 4423	DefStrat-Stat-Health-Hd@mod.uk

If you wish to correspond by mail, our postal address is:

Defence Statistics (Health)
Ministry of Defence
Abbey Wood North
Oak 0 West
#6028
Bristol
BS34 8JH

For general MOD enquiries, please call: 020 7218 9000