Ministry of Defence

Mefloquine Prescribing in the UK Armed Forces 12 September 2016 – 31 March 2017

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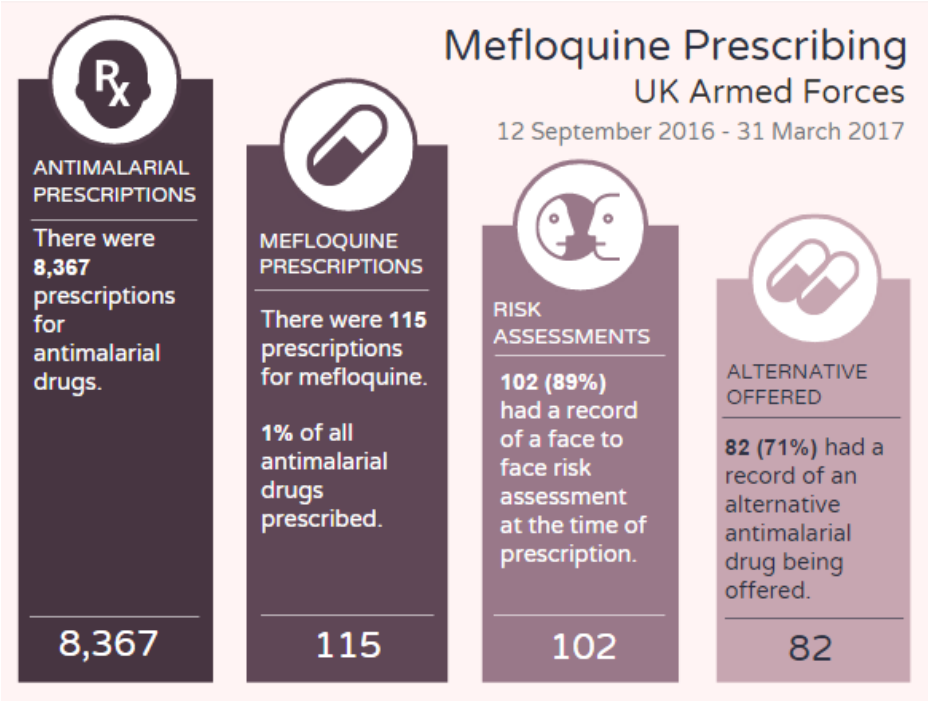
Mefloquine (also known as Lariam) is used to prevent or treat malaria. It may be prescribed as one of a number of alternative chemoprophylactic drugs for military personnel deployed to areas where there is a high risk of chloroquine resistant malaria. This biannual Official Statistic provides information on the number of mefloquine prescriptions given to UK Armed Forces personnel at MOD medical facilities covering the period 12 September 2016 to 31 March 2017. This first edition of the statistic also presents the results of a clinical audit (carried out in 2015) of UK Armed Forces personnel prescribed mefloquine for deployment on Op HERRICK (Afghanistan) (**Annex A**).

Key Points

The MOD introduced a new policy on prescribing antimalarial drugs on 12 September 2016. This new policy was produced following the House of Commons Defence Committee inquiry into use of mefloquine in the UK Armed Forces.

The findings of the mefloquine audit in 2015 (Annex A) helped inform elements of the policy, in particular improvement in the collection of coded data.



Source: Defence Medical Information Capability Programme (DMICP) data warehouse.

[1]Please note this number is a minimum. Risk assessments and offers of alternative antimalarial drugs may have been done however the information was not coded into the central data warehouse and therefore was not available for this analysis.

Responsible statistician: Head of Health Tel: 030 67984423 Email: DefStrat-Stat-Health-Hd@mod.uk
Further information/mailing list: DefStrat-Stat-Health-PQ-FOI@mod.uk
Press office: 020 721 83253

Background quality report
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/614525/20170516_Background_Quality_Report.pdf

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Introduction

Malaria is an acute febrile illness. If malaria is not prevented it can be fatal, specifically if the strain *Plasmodium falciparum* is contracted. The Government has a duty of care to provide members of the Armed Forces with effective methods of chemoprophylaxis. Chemoprophylaxis refers to the taking of medication to prevent disease rather than treat it. Mefloquine is one of the main chemoprophylaxis drugs that are available for prescription in UK to prevent malaria. Others include doxycycline; chloroquine; proguanil; and atovaquone (when combined with proguanil it is marketed as Malarone).

Taking antimalarial chemoprophylaxis when visiting an area where there is a malaria risk is part of a suite of preventive actions which include bite avoidance, covering up with long clothing, wearing insect repellent and sleeping under mosquito nets etc. For members of the UK Armed Forces who are prescribed antimalarial drugs, information relating to the consultation is entered in the patient's electronic health record. All clinical information can be entered as free text in the record or as coded data. Only coded data can be exploited in the electronic health record data warehouse (DMICP). This bulletin focuses on coded data, and information provided by clinicians following a review three months after the new policy was introduced. To routinely search for information entered as free text requires the manual review of the patient record; thus any information entered as free text has not been included in this statistic.

A number of individuals including former Service personnel and their families, members of the public and MPs have campaigned to prevent the use of mefloquine in the UK Armed Forces due to the reported neuropsychological adverse reactions of the drug.

Following coverage in national media in 2015, MOD carried out an audit of UK Armed Forces personnel prescribed mefloquine for deployment on Op HERRICK (Afghanistan) between 1 April 2007 and 31 December 2014. The aim of the audit was to assess whether the rationale for prescribing mefloquine was documented within the patient's electronic medical record (Annex A).

In 2015 the House of Commons Defence Committee (HCDC) conducted an inquiry into the use of mefloquine (Lariam) in the UK Armed Forces. The information gathered from the audit was used to support the Government's response. The HCDC published its report into the use of mefloquine by the Armed Forces in May 2016, and made a number of recommendations concerning the future prescribing of the drug[1]. Amongst these were recommendations that:

- the MOD cease conducting risk assessments based solely on patients' records and prescribe Lariam, if at all, only after detailed face-to-face individual risk assessments

[1] https://www.publications.parliament.uk/pa/cm201516/cmselect/cmdfence/567/567.pdf

Introduction (Cont.)

- Records of face-to-face assessments should be recorded in individual's medical notes

- In addition to the need for a face-to-face interview…MOD ensures that each individual, when made aware of the risks of Lariam, must be offered the option of receiving an alternative anti-malarial drug.

In response to the inquiry and these recommendations, the MOD amended its policy on preventing malaria in military personnel which was implemented on 12 September 2016. In addition the Government response to the HCDC report was published in September 2016[2].

The HCDC stated that they would monitor the MOD's policy in relation to malaria protection by requesting six monthly updates on the MOD's use of mefloquine. Publication of this Official Statistic is to meet this requirement, to support the MOD's commitment to release information where possible and ensure that the public has equal access to the information.

In order to assess the impact of the revised anti-malarial policy, a new method of data capture through electronic templates was introduced. This allowed better recording of the processes undertaken when prescribing antimalarial drugs at MOD medical facilities. The new process enabled the collection of coded data on risk assessments for antimalarial drugs and confirmation that an alternative drug had been offered in place of mefloquine. Previously, to identify whether a risk assessment had taken place, a manual review of the record was required. This new process has enabled MOD to provide assurances that the policy is being followed. In addition, the new process also acted as a guide to clinicians to ensure the appropriate prescribing of mefloquine.

Regular feedback from users allowed refinement and improvement of the process to ensure the clinicians followed the policy prior to the prescription of antimalarial drugs. This was an iterative process which progressively developed to deliver a more usable and efficient format for clinicians. As clinicians became more familiar with the policy and the new data capture process the centrally held data has improved; this is known as the diffusion of innovation.[3]

[2] https://www.publications.parliament.uk/pa/cm201617/cmselect/cmdfence/648/648.pdf

[3] Rogers, Everett (16 August 2003). Diffusions of Innovations. 5th Edition. Simon and Schuster.

Main Findings – Mefloquine Prescriptions 12 September 2016- 31 March 2017

Between 12 September and 31 March 2017 there were **8,367** antimalarial drug prescriptions given to UK Armed Forces personnel. Of these, **115** prescriptions were for mefloquine, accounting for **1%** of the antimalarial drug prescriptions during this period.

Please note, information presented in this Official Statistic focuses on coded data from the data warehouse and information supplied by clinicians in December 2016 having reviewed individual medical records.

Of the **115** prescriptions for mefloquine;

a. **102 (89%)** had a face to face risk assessment prior to, or at the time of prescription. The majority were identified from the coded data (99 prescriptions) and three prescriptions with no coded data but where the clinician responsible reviewed the record and confirmed a risk assessment had taken place.

b. **13 (11%)** did not have a record of either a coded data entry for a face to face risk assessment in the data warehouse or a face to face risk assessment confirmed by a clinician.

c. **82 (71%)** had an alternative antimalarial drug offered during the consultation but the patient declined it. This was identifiable from coded data available in the DMICP data warehouse for 79 patients. A further three patients did not have coded data in the data warehouse however the clinician responsible reviewed the record and confirmed an alternative drug was offered.

Limitations

There has been no review of individual medical records since December 2016, thus there may be additional text information entered in the patients' record relating to risk assessments or alternative drugs offered which can only be accessed by a clinician reviewing the individual medical record.

Methodology

This section provides a brief summary of the methodology and data sources; more detailed information is available in the background quality report for this bulletin.

Prescription data – mefloquine prescriptions 12 September 2016 to 31 March 2017

Data on prescriptions for mefloquine were extracted from the electronic patient record data warehouse (DMICP). Data were extracted as at 21 April 2017. The rollout of DMICP commenced during 2007 and comprises an integrated primary Health Record (iHR) for clinical use and a pseudo-anonymised central data warehouse. Prior to DMICP medical records were kept locally at each individual medical centre. By 2010 DMICP was fully available in the UK and the majority of Germany. Rollout to other overseas locations commenced in November 2011.

The information presented relates to the number of antimalarial drug prescriptions. Individuals may have received more than one prescription during the reporting period.

A patient was categorised as having received a face to face risk assessment prior to the prescription of mefloquine if codes were entered into DMICP on the day of the prescription or at some other point previously.

In December 2016 a three month review was carried out for records where a prescription of mefloquine was identified but there was no coded data relating to a risk assessment or alternative drug offered. When a clinician confirmed that a face to face risk assessment had been carried out or alternative drug offered then these records were categorised and included in the analysis.

The data on mefloquine presented was based on personnel who have been prescribed the drug; it does not reflect whether the individual has taken the drug.

The data presented was reviewed in line with Statistical Disclosure Control, JSP200 – Statistics. Following a risk assessment it was concluded that there was a low risk for disclosure of medical information and high demand from the public for the release of small numbers, hence the decision to present all the numbers without Statistical Disclosure Control processes in place.

Glossary

Adverse reactions – Also known as side effects, are unwanted symptoms caused by medical treatment[4].

Chemoprophylaxis – Taking of medication to prevent disease rather than treat it.

Contraindication[5] - A contraindication is a specific situation in which a drug, procedure, or surgery should not be used because it may be harmful to the person.

Epilepsy - A condition that affects the brain and causes repeated seizures[6].

Traumatic Brain Injury (TBI) - happens when a bump, blow, jolt, or other head injury causes damage to the brain[7].

Post Traumatic Stress Disorder (PTSD) - a type of anxiety disorder. It can occur after you have gone through an extreme emotional trauma that involved the threat of injury or death[8].

Cardiac conduction disorder - a rare inherited heart rhythm disturbance where the heart's electrical impulses are conducted very slowly[9].

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.

Febrile Illness – Fever; a fever is the body's way of reacting to something abnormal in the body. Fevers can be caused by a number of conditions including: infections, reactions to medications, reactions to blood transfusions, cancer, or autoimmune diseases, or in the case of malaria, a protozoan parasite called Plasmodium.

Intolerance - an inability to take a drug without adverse effects.

Joint Personnel Administration (JPA) – The MOD's personnel database containing information on demographics, job and pay details.

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 is used to prevent malaria where there is a high risk of chloroquine resistant malaria.

Operation HERRICK - Operation HERRICK is the name associated to all British operations in Afghanistan. Operation HERRICK also encompasses the whole of the Joint Operation Area in the region so personnel deployed to this operation do not have to be solely deployed within Afghanistan. Not all supporting operational posts are geographically located within Afghanistan.

[4] NHS, http://www.nhs.uk/chq/pages/997.aspx?categoryid=73&subcategoryid=108 , accessed 9 May 2017
[5] Medline Plus, Medical Encyclopedia, https://medlineplus.gov/ency/article/002314.htm, accessed 15 August 2016.
[6] Medline Plus, Medical Encyclopedia, https://medlineplus.gov/epilepsy.html , accessed 9 May 2017
[7] Medline Plus, Medical Encyclopedia, https://medlineplus.gov/traumaticbraininjury.html, accessed 9 May 2017
[8] Medline Plus, Medical Encyclopedia, https://medlineplus.gov/ency/article/000925.htm , accessed 9 May 2017
[9] British Heart Foundation, https://www.bhf.org.uk/heart-health/conditions/pccd , accessed 9 May 2017

Glossary (Cont.)

Operation HERRICK consists of the British contribution to the NATO-led International Security Assistance Force (ISAF) and support to the US-led Operation Enduring Freedom (OEF).

Pseudo-anonymisation - refers to a process that replaces clear identifiers (e.g. name, subject number) with alternative identifiers that bear no overt relationship to the true values. As a consequence, linkage back to the original data or to another de-identified copy from the same source can be achieved with, and only with, knowledge of the de-identification key or algorithm. This allows legitimate linking of data sets and other information but prevents inappropriate or unauthorised access to the identifiable records.

Yellow Card - national reporting system is used by the Medicines Healthcare Regulation Agency to monitor the safety of all health care products in the UK to ensure they are acceptably safe for patients. For more information on the Yellow Card System please see URL: https://yellowcard.mhra.gov.uk/downloadable-information/guidance-on-yellow-card-reporting/

Further Information

ACMP

The Advisory Committee on Malaria Prevention provides guidelines for health professionals on the prevention of malaria for travellers from the UK. More information can be found on the following link: https://www.gov.uk/government/collections/advisory-committee-on-malaria-prevention-acmp

Contact Us

Defence Statistics welcome feedback on our statistical products. If you have any comments or questions about this publication or about our statistics in general, you can contact us as follows:

Defence Statistics Health Telephone: 030 67984423

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

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Other contact points within Defence Statistics are:

Defence Expenditure Analysis	030 6793 4531	DefStrat-Econ-ESES-DEA-Hd@mod.uk
Price Indices	030 6793 2100	DefStrat-Econ-ESES-PI-Hd@mod.uk
Naval Service Manpower	023 9254 7426	DefStrat-Stat-Navy-Hd@mod.uk
Army Manpower	01264 886175	DefStrat-Stat-Army-Hd@mod.uk
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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,
Oak 0 West #6028
Abbey Wood North
Bristol
BS34 8JH

For general MOD enquiries, please call: 020 7218 9000

For Press Office, please call: 020 721 83253

Annex A – Op HERRICK Mefloquine Audit

Of the **131,000**[10] UK Armed Forces personnel deployed on Operation HERRICK between 01 April 2007 and 31 December 2014, **536 (0.4%)** had a record of being prescribed mefloquine in the data warehouse for deployment in Afghanistan[11] on Operation HERRICK. Additionally;

a. **40,477 (31%)** UK Armed Forces personnel were prescribed chloroquine and proguanil
b. **4,095 (3%)** UK Armed Forces personnel were prescribed doxycycline
c. **2,554 (2%)** UK Armed Forces personnel were prescribed atovaquone plus proguanil (Malarone)
d. **12,908 (10%)** UK Armed Forces personnel were prescribed chemoprophylaxis but we are unable to identify which chemoprophylaxis they were prescribed from the data warehouse

Please note personnel have been counted for each chemoprophylaxis drug prescribed, thus adding up the numbers will not equal the total number of personnel identified as having a prescription.

54% of UK Armed Forces personnel deployed in Afghanistan on Operation HERRICK did not have a record of being prescribed a chemoprophylaxis drug in the data warehouse. It is a possibility that this population includes personnel who may not have required a prescription for a chemoprophylaxis drug as they deployed outside of the risk season, and personnel who were prescribed a chemoprophylaxis drug in theatre for which a record was entered in their medical record as free text. The electronic health record (DMICP) was being rolled out across the UK fixed base between 2007 and 2010 and was not available in the deployed locations until after this time. It is possible that some of these personnel were issued prescriptions which were recorded on legacy patient record systems.

Audit Results

When reviewing the patient notes, doctors were asked to gather three pieces of information: (1) to identify the reason for the prescription; (2) to identify any past medical history of the patient prior to the prescription being issued; and (3) the consequences during or after the mefloquine prescription period.

Of the **536** UK Armed Forces personnel deployed in Afghanistan[c] on Operation HERRICK with a record of being prescribed mefloquine in the data warehouse, in the time available for the audit, 448 had their electronic medical record reviewed. For these 448 personnel there were 486 prescriptions for mefloquine, a summary of the audit findings are presented in Table 1.

Of the **486** prescriptions of mefloquine that were reviewed:

a. **221 (45%)** had a clear reason documented for choosing mefloquine and no contraindication. The reasons for prescribing mefloquine included patient intolerant to alternative antimalarial drugs; deploying to high risk areas with chloroquine resistant malaria and other antimalarial drugs would have had an adverse drug interaction with another therapy.
b. **239 (55%)** had insufficient information recorded to make a judgment on the reason for prescribing mefloquine; no contraindication was recorded. In the majority it was documented that the decision to prescribe mefloquine was made by a doctor.

[10] Number represents anyone deployed on Op HERRICK to all locations, not only Afghanistan.
[11] Please note, personnel can be prescribed Mefloquine for deployment on Op HERRICK for locations other than Afghanistan, these figures are not included in this publication.

Op HERRICK Audit (Cont.)

c. There were **40** prescriptions with 'other reason' for prescribing mefloquine; eight of these were prescribed due to patient choice.

d. **26 (5%)** had a contraindication to mefloquine documented. In these cases the prescription was deemed inappropriate by the reviewing clinician. Please note that for two of these prescriptions there were two documented contraindications (see Table 1 where the total number of contraindications was reported as 28).

e. A total of **11 (2.5%)** personnel prescribed mefloquine suffered adverse reactions (also known as side effects) subsequently reported using the Yellow Card system[12]. One of these patients required the drug to be withdrawn. The remaining personnel may have only presented with adverse reactions after completion of the drug therapy and therefore the drug could not been withdrawn. The individual may also have chosen to cease taking the drug of their own accord if they were experiencing adverse reactions.

f. A total of **eight (1.8%)** personnel prescribed mefloquine required the drug to be withdrawn. This includes one patient who also had adverse reactions reported through the Yellow Card system.

Adverse reactions to any drug can be experienced by some personnel; the MOD will continue to keep their policies and procedures under review to ensure that the anti-malarial being prescribed can be tolerated by the individual patient.

Table 1: Op HERRICK UK Armed Forces Mefloquine Prescription Audit Questions, Number

01 April 2007 - 31 December 2014

Number of Prescriptions Audited	**486**
Reason for Prescription (one or more responses may have been recorded for each prescription)	
Intolerance to alternative antimalarials (Chloroquine and Proguanil; Doxycycline; Atovaquone plus Proguanil)	143
Serial/Concurrent high risk deployment or regional activity with Mefloquine as the preferred drug	41
Activity before or after Afghanistan deployment in high risk area (e.g. Kenya exercise)	90
Adverse drug interaction with other therapy (i.e. a medical contraindication to other anti-malarials	42
Other Reason	40
Reason unclear from medical record	213
Audit Reason for Prescription not captured	16
Past Medical History prior to prescription (none, one or more responses may have been recorded for each prescription)	
Prior side effects from other anti-malarial	98
Contradications	28
- Prior side effects from Mefloquine	7
- History of mental ill health, including stress disorder and PTSD	16
- History of traumatic brain injury (TBI)	3
- History of epilepsy	2
- Cardiac conduction disorder	0
Consequences during or after mefloquine prescription period	
Was a Yellow Card raised	11
Was Mefloquine discontinued as a result of side effects	8

Source: DMICP Electronic patient record and data warehouse and Mefloquine audit questionnaire

[12] This national reporting system is used by the Medicines Healthcare Regulation Agency to monitor the safety of all health care products in the UK to ensure they are acceptably safe for patients. For more information on the Yellow Card System please see URL: https://yellowcard.mhra.gov.uk/downloadable-information/guidance-on-yellow-card-reporting/

Op HERRICK Audit (Cont.)

The results of the clinical audit highlighted the need to improve the policy for prescribing antimalarial drugs, and mefloquine in particular, and the need to improve how the prescribing clinician recorded the information in the patient's medical record. The lessons from the audit were used in the development of the new policy and when introducing the new process to ensure it enabled clinicians to prescribe in a safe and efficient manner.

Methodology

Data on prescriptions for mefloquine were extracted from the electronic patient record (DMICP) data warehouse. Data were extracted as at 18 August 2015.

To identify whether personnel were prescribed chemoprophylaxis for their deployment in Afghanistan on Op HERRICK, Defence Statistics sought advice from Permanent Joint Headquarters (PJHQ) with regards to how long prior to deployment they would be prescribed the drug. The time between prescription and deployment was indicated between 2 days and 6 weeks prior to deployment. This has been used to establish who has been prescribed antimalarial drugs for their specific deployment. Personnel who did not have a prescription for an antimalarial drug within 43 days prior to deployment (or whilst on deployment) have been excluded from the analysis.

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 mefloquine prior to their medical record being held in DMICP, therefore these records were not available centrally.
- If mefloquine prescriptions were recorded as free text only in the patient medical record they have not been included in the data.
- It may also have been possible to prescribe mefloquine to UK Armed Forces personnel through a Patient Specific Direction. In these cases the name of the drug prescribed was not recorded in the data warehouse therefore these have not been included in the data.
- In addition if mefloquine was prescribed by the NHS it has not been included in the numbers presented.
- The data on mefloquine presented is based on personnel who have been prescribed the drug; it does not ensure the individual has taken the drug.

Deployment

Deployment on Op HERRICK includes deployments to a number of locations. In order to audit a relevant cohort of people for prescription of mefloquine, MOD only considered personnel who were deployed on Op HERRICK in Afghanistan. Therefore there may be other locations on Op HERRICK where personnel were prescribed mefloquine which were not included in this publication.

Personnel prescribed mefloquine for a deployment were identified if they were prescribed the drug either up to 43 days prior to deployment or whilst on deployment.

Data on deployment was derived from the Joint Personnel Administration 'Move and Track' system which was introduced in April 2007.

Please note, DMICP and Move and Track are live systems, and thus figures may change as a result.

Methodology (Cont.)

Clinical Audit of Mefloquine Prescriptions

The mefloquine audit was conducted in June/July 2015. The audit represented a subset of UK Service personnel prescribed mefloquine between 01 April 2007 and 31 December 2014 (only those deployed on Op HERRICK who were identified as having been prescribed mefloquine). To conduct the same audit for all Service personnel prescribed mefloquine in this time period would be prohibitive within existing resources.

Defence Statistics identified the cohort of UK Service personnel who deployed on Op HERRICK to Afghanistan with a prescription for mefloquine and the current Defence Medical Service (DMS) medical practice of these patients from the pseudo-anonymised data warehouse. For those personnel who had left Service the last known DMS medical practice was identified.

Personal identifying numbers (Service numbers) and current practice details were provided to each of the Regional Clinical Directors (RCD) for personnel within their region. The RCD directed the relevant Senior Medical Officers (SMO) to undertake the audit of individual patient records at their practice.

The SMO recorded in the medical record of each patient that the audit had taken place both in the form of a unique read code and through free text in the notes. The audit information was collated by RCD's for their Region and passed back to DS in a pseudo-anonymised format in order to collate the overall results.

To ensure patient confidentiality was maintained throughout the audit the data were managed following a strict pseudo-anonymised process as directed in Joint Service Publication (JSP) 950.