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Use of NICE appraised medicines in the NHS in England – Experimental Statistics

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Executive Summary

The National Institute for Health and Clinical Excellence (NICE) Technology Appraisal process assesses the clinical and cost effectiveness of new and existing medicines and treatments, and provides guidance on their use by the NHS. As part of the Pharmaceutical Price Regulation Scheme (PPRS) agreement, which became effective on 1 January 2009, the Department of Health (DH) and the Association of the British Pharmaceutical Industry (ABPI) agreed to publish information on variation in the use in the NHS of selected medicines recommended by NICE.

The Metrics Working Group (MWG) was established between DH, the pharmaceutical industry and NICE to define metrics, data sources, publication channels and governance mechanisms for this work.

The NHS Information Centre was asked to produce a bulletin looking at the variation in use of these medicines in relation to the expected number of eligible patients as estimated by NICE. Data on the number of patients being treated is not available and so predicted use (using the expected number of eligible patients, the average dose and average length of treatment) was compared with observed use. Data on observed use in 2008 was taken from the primary care prescribing data (ePACT), and secondary care data (Hospital Pharmacy Audit Index). Data from the Prescribing Cost Analysis database was also used to look at long term trends in terms of cost.

A range of 26 medicines positively appraised by NICE was selected by the MWG, covering 13 technology appraisals. In some cases the estimated numbers of eligible patients were small, so this data is presented at national level only due to concern as to the robustness of the estimates at a low level and to avoid any danger of disclosure.

This is an experimental publication and is the first of a planned annual series. It includes some SHA level information and, for medicines predominantly used in primary care, (anonymised) PCT level information to show variability. Feedback is requested from users to help inform how best to estimate uptake to allow meaningful interpretation of any variation across local NHS organisations in future.

Out of the 12 appraisals where a comparison could be made, observed use by the NHS in England was higher than the predicted use for 7 and lower for 5.

The appraisals where observed use exceeded the predicted use in 2008 are:

- Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's Disease
- Ezetimibe for the treatment of primary (heterozygous-familial and non-familial) hypercholesterolaemia
- Entecavir for the treatment of chronic hepatitis B
- Zaleplon, zolpidem and zopiclone for the short-term management of insomnia
- Varenicline for Smoking Cessation

- Hormonal therapies for the adjuvant treatment of early oestrogen-receptor-positive breast cancer
- Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women, plus Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women

The appraisals where observed use is lower than predicted use in 2008 are:

- Omalizumab for severe persistent allergic asthma
- Natalizumab for the treatment of adults with highly active relapsing-remitting multiple sclerosis
- Drotrecogin alfa (activated) for severe sepsis
- Riluzole (Rilutek) for the treatment of Motor Neurone Disease
- Orlistat, sibutramine and rimonabant for the treatment of obesity in adults

In one case observed use was lower than predicted use for 2008, but is rising and is likely to exceed the predicted level in 2009. For two medicines, safety warnings issued since the publication of NICE guidance, have resulted in drug withdrawal and more restricted use, respectively. For one of the medicines considered it was not possible to convert the predicted number of patients into a predicted volume of drug, so no meaningful assessment of the use could be made.

In interpreting these figures it is important to note that predicted and observed use may differ for a variety of reasons and should not be assumed to definitely indicate either 'under' or 'over' prescribing. Also, assumptions about the average length of treatment are central to producing predictions of use and there are difficulties in producing robust estimates of expected numbers of patients at a sub-national level. Further work is necessary to develop these.

Introduction

The 2009 Pharmaceutical Price Regulation Scheme (PPRS), an agreement between the Department of Health (DH) and the Association of the British Pharmaceutical Industry (ABPI), aims to ensure the NHS has access to good quality branded medicines at reasonable prices, and promotes a healthy, competitive pharmaceutical industry. The 2009 PPRS included the commitment to publish uptake comparison metrics for National Institute for Health and Clinical Excellence (NICE) positively appraised medicines at a national and international level.¹

To this end:

- The Metrics Working Group was established between the Department of Health, Industry and National Institute for Health and Clinical Excellence to define metrics, data sources, publication channels and governance mechanisms
- The Department of Health has committed to the annual publication of strategic health authority, primary care trust (PCT) and network-level metrics for the uptake of medicines positively appraised by NICE
- The metrics will be published through suitable channels on an on-going basis
- The Industry and the Department of Health to define a set of measures to allow comparison of usage of NICE positively appraised medicines in the UK with major EU economies²

The Metrics Working Group, with representatives from the pharmaceutical industry, DH, NICE, the Office of Health Economics and the NHS Information Centre has been analysing data to develop metrics. This experimental report is the first of planned annual publications on the uptake, by the NHS in England, of NICE positively appraised medicines. It is published by the NHS Information Centre on behalf of the Metrics Working Group, using a methodology agreed by the Group.

This report follows a previous exercise to measure variation in medicines uptake between areas in England, which was published jointly by the DH and ABPI in January 2007³. The

¹ *The Pharmaceutical Price Regulation Scheme 2009*, December 2008 (available at: http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/DH_091825)

² Further to Recommendation 6 in *Improving Access to Medicines for NHS Patients: a report for the Secretary of State for Health by Professor Mike Richards CBE*, November 2008 (available at: http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_089927), Professor Richards has been asked to lead further work to investigate the extent and causes of international variations in drug usage. This work will encompass delivery of, but is broader in scope than, the PPRS commitment to develop comparative international data on the usage of new medicines.

³ *Medicines uptake in England. A quantitative analysis of variation*, January 2007 (available at: http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_065198)

Department of Health has also reviewed the variation between cancer networks in England in the uptake of cancer medicines, the most recent publication of these data being in May 2009⁴.

Experimental Status

This information is released under 'experimental' status. This is a concept used for statistics in certain defined circumstances, largely to develop (with user input) new datasets which already have considerable immediate value to users, but are not fully developed and do not yet meet the quality standards of National Statistics. It is important that users understand that cautions apply to the interpretation of this data. More details are given within the report.

There is an expectation that these metrics are developed further, taking account of informed feedback from users. Please use the associated feedback form, which includes questions and requests general comments and suggestions.

⁴ *Uptake of NICE approved cancer drugs*, Professor Mike Richards CBE, Department of Health (available at http://www.dh.gov.uk/en/Publicationsandstatistics/Lettersandcirculars/Dearcolleagueletters/DH_098856)

Method

Ideally the measurement of uptake of new medicines would identify all patients who are eligible to receive the treatment for a specified indication and compare that with the number of patients who are actually receiving the treatment. The use of such a measurement at a specified time and for populations at a specified level (for example: Primary Care Trust (PCT), Strategic Health Authority (SHA) or Cancer Network) would provide an assessment of the extent of any variation between areas in the uptake of medicines, but not why that variation exists.

However, current information systems do not enable identification of either which patients are eligible to receive or are receiving a medicine for a specific indication.

For this report, estimates of the number of eligible patients were derived from the NICE costing templates for the selected technology appraisals. The NICE Technology Appraisal process assesses the clinical and cost effectiveness of new and existing drugs and treatments and provides guidance on their use by the NHS in England and Wales. This bulletin only considers England. NICE provides various costing tools to support the implementation of all guidance published since January 2005. Costing templates are intended for planning purposes and provide users with the ability to estimate the local cost impact of implementing guidance based on their population. These figures are estimates only and are not to be taken as the NICE view of desirable, or maximum or minimum figures.

NICE encourages users of the costing templates to modify the assumptions used in these templates to more accurately reflect local circumstances. However, for the purpose of this report the general assumptions in the templates have been used to provide an estimate of uptake at a local level. Local practice or circumstances may differ from the national estimates and could be a reason for variation.

Although it is not possible to identify the number of patients receiving a medicine for a specific condition it is possible to measure usage of a medicine. For this report, data on drug utilisation was collected. Usage of medicines in primary care is measured with a high level of accuracy, as dispensed prescriptions are collected locally and processed nationally by the NHS Business Services Authority. Some medicines may be supplied directly to patients, for example by smoking cessation clinics, and are therefore not recorded centrally. Usage of medicines in secondary care and through other channels such as use in ambulances is not collected nationally by the NHS. Issues from hospital pharmacy departments are collected by IMSHealth but the coverage is not as comprehensive as primary care – it is estimated that the hospitals in the sample cover 97% of NHS acute hospital beds in England.

Instances where a medicine has multiple indications are complex as it is not always possible to measure use of a medicine for a specific condition. This is possible for some medicines, such as bisphosphonates which are used for osteoporosis and Paget's disease, where different formulations are licensed for different conditions. However such medicines have largely not been included in this first report. Future editions will seek to address the analysis of variation in uptake of medicines which have more than one indicated use.

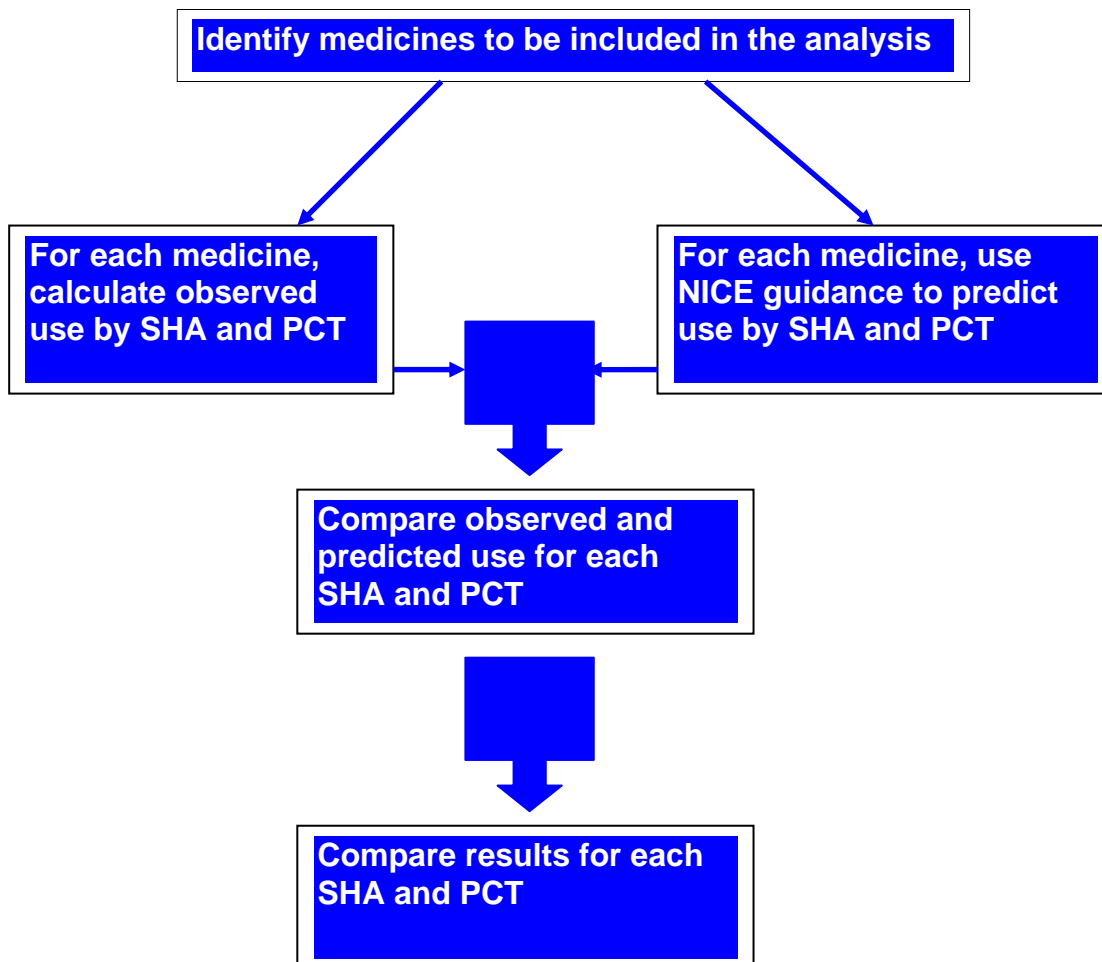
Variation in the use of medicines between SHAs and PCTs may be due to a number of factors including:

- Natural variation in populations
- The national model used for estimation of eligible patients or assumptions of the average length of treatment being inappropriate or inaccurate (for example, due to changes in clinical opinion after the guidance was issued)
- Variation in presentation to the NHS by the relevant populations
- Variation in prescribing at the local level
- Variation in the use of alternative products or procedures
- Differences in the extent to which local utilisation information is available

It should be noted that a detailed examination of the reasons for variation for individual technologies is beyond the scope of this report.

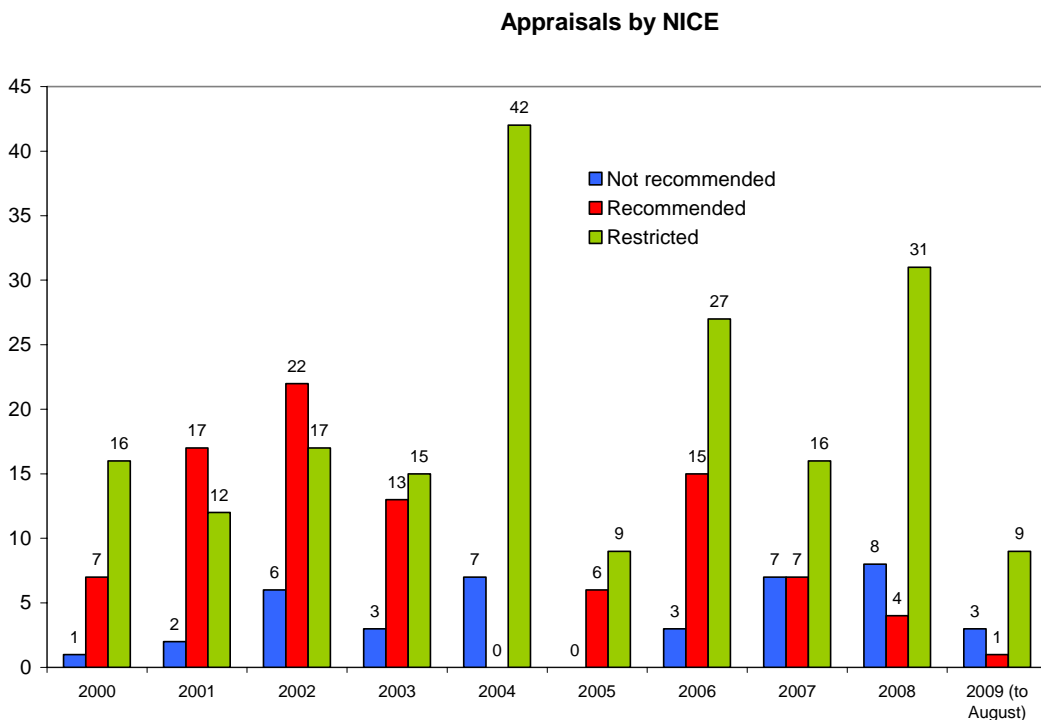
The steps taken to develop the comparators in this report are shown in the diagram below. Details for each medicine considered can be found later in the report.

Diagram: Outline process for development of the metrics



Selection of medicines for inclusion

The medicines considered were those receiving a restricted or recommended appraisal outcome. The chart below shows the outcome of NICE technology appraisals for medicines from 2000 to 2009. One appraisal may assess one or more medicines, and contain several different recommendations, depending in which patient group it is intended to be used.



Of the potential medicines that could be included in the analysis, a sample was selected using the following criteria:

- the set should include some used mainly in primary care and some used mainly in secondary care:
- medicines where NICE estimates of eligible patients are feasible
- medicines appraised prior to 2008 (as the level of uptake of more recently appraised medicines may not have yet reached a stable level)

Some medicines were excluded for one or more of the following reasons:

- the technology appraisal was for a specific age group,
- a significant proportion of use is supplied via the “homecare” route, as this information is not consistently collected
- where it is known that the data on use is likely to be incomplete
- where multiple indications make the estimation of eligible patients more complex.

Twenty six medicines positively appraised by NICE were selected, covering 13 clinical areas. These are shown in the list below. A list of other NICE reviewed medicines considered by the Metrics Working Group appears in the appendix.

Technology	NICE Technology Appraisal	Technology Appraisal Name	% cost from primary care in 2008
Donepezil Galantamine Rivastigmine	111	Donepezil, galantamine, rivastigmine (review) and memantine for the treatment of Alzheimer's Disease	68.8
Ezetimibe	132	Ezetimibe for the treatment of primary (heterozygous-familial and non-familial) hypercholesterolaemia	98.8
Omalizumab	133	Omalizumab for severe persistent allergic asthma	0.0
Natalizumab	127	Natalizumab for the treatment of adults with highly active relapsing-remitting multiple sclerosis	0.0
Entecavir	153	Entecavir for the treatment of chronic hepatitis B	43.4
Drotrecogin alfa (activated)	84	Drotrecogin alfa (activated) for severe sepsis	0.0
Riluzole	20	Guidance on the use of Riluzole (Rilutek) for the treatment of Motor Neurone Disease	71.0
Zaleplon Zolpidem Zopiclone	77	Guidance on the use of zaleplon, zolpidem and zopiclone for the short-term management of insomnia	93.5
Varenicline	123	Varenicline for Smoking Cessation	99.5
Trastuzumab	34 and 107	Guidance on the use of trastuzumab for the treatment of advanced breast cancer Trastuzumab for the adjuvant treatment of early-stage HER2-positive breast cancer	0.0
Anastrozole Exemestane Letrozole	112	Hormonal therapies for the adjuvant treatment of early oestrogen-receptor-positive breast cancer	95.1

Alendronate	160 and 161	Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women	93.0
Etidronate			
Risedronate			
Raloxifene			
Strontium Ranelate			
Teriparatide			
Orlistat	22	Use of Orlistat for the treatment of Obesity in adults	98.8
Rimonabant	144	Rimonabant for the treatment of overweight and obese adults	
Sibutramine	31	Guidance on the use of sibutramine for the treatment of obesity in adults	

Methodology

Brief details of the methodology are given in the bulletin. Further details can be provided on request. For each technology selected, the following method was used to compare expected with observed use:

- NICE provided estimates of the expected number of eligible patients. For some conditions the number of patients was a “whole person equivalent”, i.e. it took into account the proportion of patients who discontinued use of the medicine.
- The average length of treatment was determined based on the World Health Organisation Defined Daily Dose (where available) and the advice on suitable doses from the British National Formulary (BNF). Where there was no definitive information available we consulted with NICE as to a suitable estimate.
- The length of treatment (in days) was multiplied by the estimated number of eligible patients to produce an predicted number of days’ treatment
- The observed utilisation for 2008 was converted to Defined Daily Doses (DDDs). This way of standardising physical amounts of medicine to a standard measure was devised by the World Health Organisation. In simple terms, it converts drug use to the number of days of treatment. The drug utilisation figures came from prescription information supplied by NHS Prescription Services and the hospital data from IMSHealth. In some cases a specific formulation was excluded or the DDD modified because certain formulations were not appropriate to the appraisal being considered. Details are given for each technology.

- The ratio between the predicted number of days of treatment and the observed number was calculated. A value greater than one indicates a higher level of use of the medicine than anticipated.

This process was carried out at national level for all technologies except trastuzumab where it was not possible to determine the quantity which would constitute one day of treatment. The process was repeated at named SHA level, unless the estimated number of patients at SHA level was too low (below 250 patients). This was based on a concern as to the robustness of the estimates at a low level and to avoid any danger of disclosure. The data on use of medicines in hospitals is not available at lower than SHA level (see the section of Data Sources and Limitations).

Where a technology was predominantly used in primary care (this was defined as 93% or more of the costs occurring in primary care) the number of observed Defined Daily Doses per registered patient was calculated and a chart included illustrating the variation. We also produced a chart showing the number of Defined Daily Doses per expected number of patients based on the NICE costing estimates. Although the development of better estimates of eligible patients, particularly at PCT level, is an important future development, these charts have been included to illustrate variation and to stimulate discussion as to the best way forward.

Information for each of the selected drugs or technologies is presented as below:

- Overview – overview of drug(s) and main indications under consideration
- Relevant guidance - list of applicable NICE guidance
- Expected Eligible Patients– brief description of how this has been calculated, showing the assumptions used by NICE in their calculations. The expected number of eligible patients for a year is multiplied by an assumed average duration of treatment.
- Observed uptake – source of data used
- Results –
 - comparison of national (England) and SHA (where appropriate) predicted vs observed uptake expressed as DDDs for 2008
 - DDDs per registered patient and DDDs per expected patient by anonymised PCT (where possible)
 - national trends in expenditure over time

Data sources and limitations

Observed use of medicines

The word 'medicines' is generally used in this report. However, some NICE guidance uses the word 'drug' in the title.

The data used to measure uptake of the appraised medicines was obtained from three sources.

1. Prescription Cost Analysis database (PCA)
2. Prescription and Cost system (ePACT)
3. Hospital Pharmacy Audit Index

Prescription Cost Analysis database (PCA)

The PCA database is maintained by the NHS Information Centre using data provided by NHS Prescription Services (NHS RxS). It includes all prescriptions dispensed in the community i.e. by community pharmacists and appliance contractors, dispensing doctors, and prescriptions submitted by prescribing doctors for items personally administered in England. Also included are prescriptions written in Wales, Scotland, Northern Ireland and the Isle of Man but dispensed in England. The data do not cover medicines dispensed in hospitals, including mental health trusts, or private prescriptions. Prescribers are GPs, hospital doctors, dentists and non medical prescribers such as nurses and pharmacists. The data is only at an England level and is not broken down into SHA or PCT level. The advantage of this source is that it contains quarterly data back to 1991.

Prescription and Cost system (ePACT)

There are two ePACT systems maintained by NHS Prescription Services and made available over the NHS network. The first covers prescriptions prescribed by GPs, nurses, pharmacists and others in England and dispensed in the community in the UK (i.e. by community pharmacists and appliance contractors, dispensing doctors, and prescriptions submitted by prescribing doctors for items personally administered). For data at PCT level, prescriptions written by a prescriber located in a particular PCT but dispensed outside that PCT will be included in the PCT in which the prescriber is based. Prescriptions written in England but dispensed outside England are included. Prescriptions written in hospitals /clinics that are dispensed in the community, prescriptions dispensed in hospitals, dental prescribing and private prescriptions are not included. The second system is similar but includes only prescriptions written by hospital prescribers which are dispensed in the community, i.e. by community pharmacies or appliance contractors. Such prescriptions are often known as FP10HP prescriptions although the form from which this name comes no longer exists. The data is attributed to the organisation (usually a hospital) that employs the prescriber. Since patients may come from a much wider area than the immediate locality, it would be inappropriate to analyse this data by PCT. The data in ePACT is broken down by SHA (and PCT for the primary care data) for each of the last 60 months. As data for a new month is added the oldest month is removed.

Hospital Pharmacy Audit Index (HPAI)

The HPAI is a database containing hospital dispensing information provided by IMSHealth, a commercial company supplying information and analysis to the Department of Health and Industry. The HPAI is based on information collected and processed by IMSHealth from the majority of NHS hospitals in England. It is estimated to cover 97% of NHS acute beds in England. National figures are grossed up to give England level estimates on the basis of bed numbers. However figures for SHAs are not adjusted in any way and will be an under estimate if trusts do not contribute data. In 2008, there were non-contributing trusts in London, West Midlands, North West, South Central and South West SHAs. The NHS IC does not hold HPAI data at PCT level and it would be difficult to associate hospital use with a PCT. Patients from one PCT frequently attend hospitals in another PCT and so using the geographical location of the hospital to determine the appropriate PCT is likely to be misleading. The NHS Information Centre holds data from July 2000.

Note: IMS Health revise figures as new data becomes available and issue data for two years at a time so figures may be different when extracted on a different occasion. The system is based on the number of packs which are issued. These are priced using the Drug Tariff or standard price lists. The cost does not necessarily reflect what hospitals actually paid.

Defined Daily Doses

This bulletin uses Net Ingredient Cost (the basic price as shown in the Drug Tariff) and Defined Daily Doses (DDDs) (a system of measuring volume of drug use maintained by the World Health Organisation). The definition of a DDD is

“The assumed average maintenance dose per day for a drug used for its main indication in adults”

Where a medicine is used at different doses for children, adults and the elderly the DDD is necessarily a compromise. Similarly if the adult dose varies widely the DDD has to be a compromise, usually the average value given. Despite its problems the DDD is widely used to compare drug utilisation. In some cases we have modified how we measure certain drugs as the DDD has been set in terms of the use of a drug which is not the use we are considering, e.g. the use of risedronic acid for Paget’s disease rather than for osteoporosis. Such cases will be noted in the Observed Uptake section.

When use of a drug or group of drugs outside primary care is significant then we cannot produce figures at lower than SHA level and community use is aggregated to SHA level. If hospital use (either through the “FP10HP” route or from the hospital pharmacy) is not significant then figures are provided at PCT level.

Some drugs are not supplied to patients via a prescription. Other routes include Patient Group Directions (where a range of health professionals can supply directly to the patient) or through Contraception and Sexual Health Clinics or Smoking Cessation Clinics. Such provision is not recorded centrally and will not appear in our prescribing figures. Similarly hospitals use schemes where the drug is delivered to the patient in their own home, this service is known as homecare. In some hospitals this is organised by the pharmacy and the use is recorded in the HPAI. In others the use is not recorded in the pharmacy system and will not appear in HPAI. The observed DDDs are therefore subject to uncertainty.

NICE Costing Templates

As explained in the Methods section, these were used to estimate the expected number of eligible patients for appraisals published after 2005. For earlier appraisals the NICE costing methodology has been applied retrospectively.

The assumptions used within the costing templates are based on a range of data sources including:

- Background documents to the guidance
- Experts advising the bodies producing the guidance
- Previous uptake of similar drugs or technologies
- Preference studies (although rarely available). They can be particularly helpful when risks associated with treatment may affect patient or clinician preference
- Data on comorbid conditions that might exclude patients from treatment. If no specific data exists then NICE apply estimates of conditions in the whole population to the sub-group
- Areas that have already implemented the recommended practice ahead of the guidance being issued (perhaps even contributing to the evidence base on which the recommendation is based) may provide useful information about impact

When predicting uptake it is important not to rely only on one source and data is validated by triangulation against other sources wherever possible. Similarly, clinical opinion is usually gathered from a number of clinicians rather than relying on one person. Assumptions are subject to further scrutiny when the costing tools are consulted upon.

The assumptions, and the main source upon which they are based, are listed for each drug considered in this report. These assumptions have been applied to population figures for each SHA to estimate the eligible population for the treatment. SHA population figures were calculated using the lists of GPs in practices affiliated to each primary care organisation (PCO), extracted from the ADS2008 (see: <http://www.ic.nhs.uk/statistics-and-data-collections/population-and-geography/population/attribution-dataset-gp-registered-populations-2008>)

and reconciled to ONS mid 2007 estimates for local authorities (minus special populations). NICE have also applied this process to produce expected numbers at PCT level.

Finally, costing templates assume what is the optimum level of implementation once the guidance is fully implemented. The time taken to reach optimum levels of implementation could vary depending on how swiftly clinicians react to the guidance, and whether the guidance applies only to new patients or to those on existing medicines who are unlikely to be switched unless a reason for switching arises.

Where newer medicines are licensed and appraised for the same patient group or where there are subsequent changes to a product licence (for example products withdrawn because of safety concerns), this will not have been reflected in the original cost estimates.

Technologies

Alzheimer's disease - donepezil, galantamine and rivastigmine

Overview

Acetylcholinesterase inhibiting drugs are used in the treatment of Alzheimer's disease, specifically for mild to moderate disease. Rivastigmine is also licensed for mild to moderate dementia associated with Parkinson's disease

Relevant guidance

NICE Technology Appraisal 111 Alzheimer's disease - donepezil, galantamine, rivastigmine (review) and memantine www.nice.org.uk/TA111/

- *The three acetylcholinesterase inhibitors donepezil, galantamine and rivastigmine are recommended as options in the management of patients with Alzheimer's disease of moderate severity only. Memantine is not recommended as a treatment option for patients with moderately severe to severe Alzheimer's disease except as part of well designed clinical studies.*
- *When the decision has been made to prescribe an acetylcholinesterase inhibitor, it is recommended that therapy should be initiated with a drug with the lowest acquisition cost (taking into account required daily dose and the price per dose once shared care has started).*

This guidance was issued in November 2006 and was amended in September 2007 following the outcome of a judicial review in August 2007. The amendments clarified the steps healthcare professionals should take when assessing whether Alzheimer's disease is of moderate severity and highlights that clinicians should be mindful of the need to secure equality of access to treatment.

This guidance includes a review of NICE technology appraisal guidance 19 on the use of donepezil, galantamine and rivastigmine for the treatment of mild to moderately severe Alzheimer's disease issued in January 2001. The original guidance recommended that donepezil, rivastigmine and galantamine should be made available for those people with mild and moderate Alzheimer's disease.

Expected Number of Eligible Patients

The following assumptions were used in the calculation of the expected number of eligible patients. The assumptions are taken from data on existing practice, research and the views of experts in the field used in the NICE costing template (for further detail see <http://guidance.nice.org.uk/TA111/CostReport/xls/English>).

Assumption	Evidence / Source
<p>Prevalence rates:</p> <p>Males & Females aged 40-64 = 27.54 per 100,000</p> <p>Males aged 65+ = 2515.83 per 100,000</p> <p>Females aged 65+ = 5083.81 per 100,000</p>	<p>Rates per 100,000 for males and females over 65 are based on the assessment report (Table 1 available from http://www.nice.org.uk/page.aspx?o=245910).</p> <p>Rates for people under 65 are based on published research: Harvey RJ, Skelton-Robinson M and Rossor MN (2003) The prevalence and causes of dementia in people under the age of 65 years. <i>Journal of Neurology Neurosurgery and Psychiatry</i> 74: 1206–9.</p>
<p>Proportion of patients with moderate stage = 40%</p>	<p>Estimate of proportion that have moderate AD (as defined as scoring between 10 and 20 on the 'Mini mental state examination') based on expert opinion.</p> <p>The subtotal of patients with mild and moderate AD is therefore 70% which is in line with figures reported in the assessment report.</p>
<p>Proportion of patients prescribed an initial 6 month course of treatment each year = 13.8%</p>	<p>Estimate of patients initiated on therapy is based on the assumption that at the time of calculation twice as many patients with moderate disease are identified and commence treatment than patients with mild disease. This has then been adjusted to reflect annual spend which indicates that 13.8% of patients commence treatment each year. Clinical opinion on this assumption was then sought and confirmed that it seemed reasonable.</p>
<p>Proportion of patients continuing treatment for a further 2.5 years = 69%</p>	<p>The % and number of patients continuing treatment is based on audit data from Memory Clinics. This is considerably higher than that in trial patients and may be due to patients remaining on treatment inappropriately or a better response in the general population.</p>

This estimated level of uptake relates to prescribing for people with moderate Alzheimer's disease only. It does not include the use of these medicines for patients with other forms for dementia. When the revised guidance was issued patients who were receiving these medicines for mild Alzheimer's disease were allowed to continue on therapy until it was considered appropriate to stop. This may result in observed use being greater than predicted use.

Observed uptake

These medicines are used both within primary and secondary care and so data was taken from the two versions of ePACT and the HPAI database. The ePACT system does not have DDD figures for the transdermal form of rivastigmine and so this was calculated separately. Data from the PCA and HPAI databases was used for the cost graph to give figures over a longer period.

Since memantine is not positively appraised it was not included.

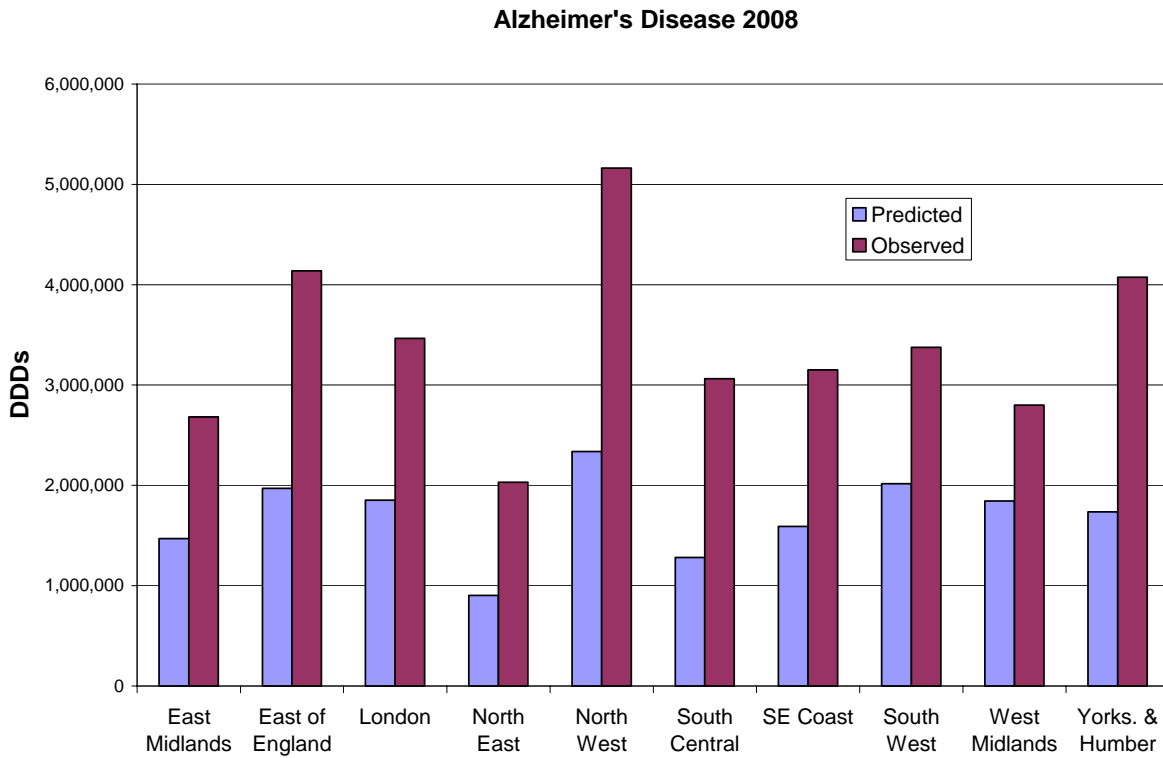
Results

The NICE costing report expected the equivalent of 46.6 thousand patients (allowing for those who discontinued treatment) would be treated each year leading to an estimate of 16,999 thousand daily doses annually, assuming each patient receives 365 doses per year. The observed use was 34,017 thousand defined daily doses, a ratio of 2.0 to 1.

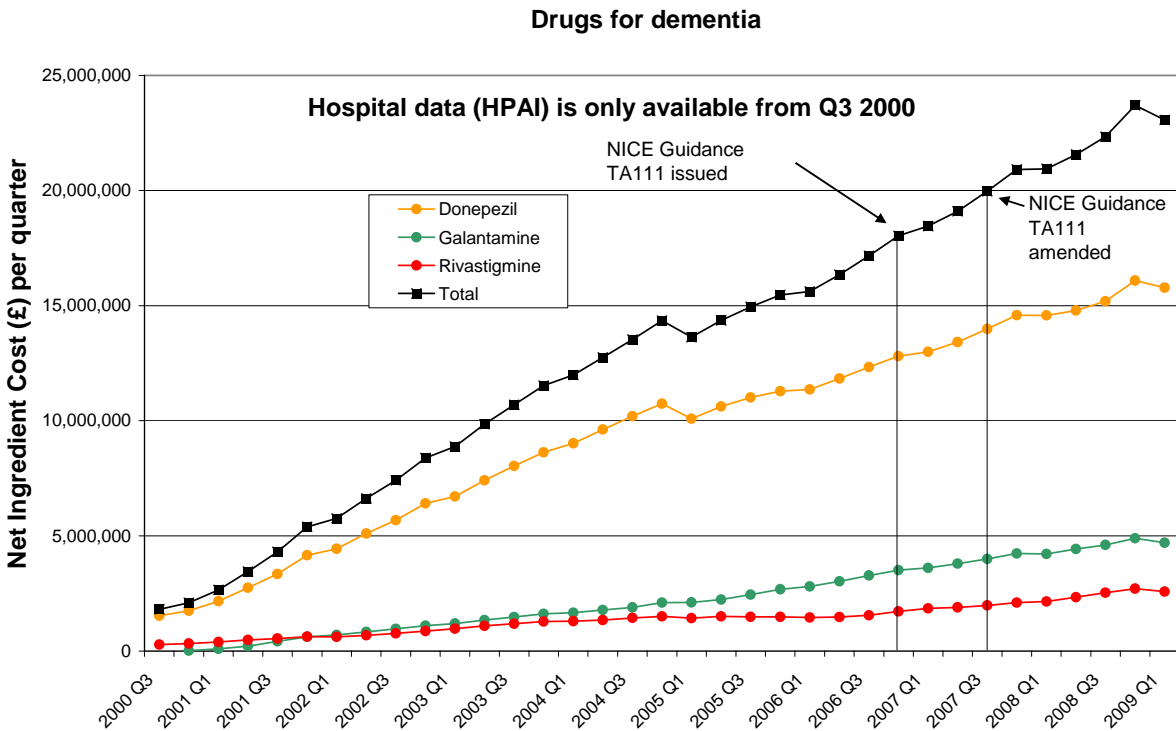
The table below compares data at SHA level.

SHA	Expected eligible patients (from NICE) in thousands	Predicted DDDs in thousands	Observed DDDs in thousands	Ratio
East Midlands	4	1,470	2,683	1.8
East of England	5	1,969	4,138	2.1
London	5	1,852	3,466	1.9
North East	2	904	2,029	2.2
North West	6	2,338	5,164	2.2
South Central	4	1,280	3,061	2.4
South East Coast	4	1,590	3,149	2.0
South West	6	2,017	3,376	1.7
West Midlands	5	1,843	2,800	1.5
Yorkshire and the Humber	5	1,736	4,074	2.3

The chart below compares predicted and observed use, measured by DDDs, in 2008 by SHA.



The graph below shows the expenditure in England for these medicines by quarter. It includes data for both hospital and community use.



Hypercholesterolemia – ezetimibe

Overview

Ezetimibe is licensed as an adjunct to dietary manipulation in patients with primary hypercholesterolaemia in combination with a statin or alone (if a statin is inappropriate), in patients with homozygous familial hypercholesterolaemia in combination with a statin, and in patients with homozygous familial sitosterolaemia (phytosterolaemia). If ezetimibe is used in combination with a statin, there is an increased risk of rhabdomyolysis.

Relevant guidance

NICE Technology Appraisal 132 Ezetimibe for the treatment of primary (heterozygous-familial and non-familial) hypercholesterolaemia www.nice.org.uk/TA132

- *Ezetimibe is recommended as a possible treatment for adults with primary (heterozygous-familial and non-familial) hypercholesterolaemia in the following circumstances.*
- *Ezetimibe can be taken on its own by a person who would normally be given a statin to treat their condition but can't because the person has a condition or takes another medicine that interferes with how the statin works, or because the statin is likely to cause side effects.*
- *Ezetimibe can be taken at the same time as a person's usual statin rather than changing to a new statin when cholesterol levels are not low enough despite increasing the dose of the statin, or if a person is unable to try higher doses of the statin because it is likely to cause side effects.*
- *When a person has side effects from using a statin, this is described as 'intolerance'. Side effects include muscle pain, severe stomach problems or when tests indicate that the liver is not functioning normally.*
- *A decision on whether a person's cholesterol level is low enough should be based on an individual risk assessment.*
- *If it is decided that a person should take their usual statin and ezetimibe together, then the least expensive form of ezetimibe should be prescribed.*

The guidance was published in November 2007 and it is recommended that it is read in conjunction with NICE guidance on the initiation of statin therapy (NICE technology appraisal guidance 94) and in the context of the following clinical guidelines also published by NICE:

- Type 2 Diabetes - newer agents (CG87)
- Secondary prevention in primary and secondary care for patients following a myocardial infarction (CG48)
- Cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease (CG67)
- Identification and management of familial hypercholesterolaemia (CG71)

Expected Number of Eligible Patients

The following assumptions were used in the calculation of the expected number of eligible patients. The assumptions are taken from data on existing practice, research and the views of experts in the field used in the NICE costing statement (for further detail see <http://guidance.nice.org.uk/TA132/CostReport/pdf/English>).

Assumption	Evidence / Source
<p>The prevalence of primary heterozygous-familial hypercholesterolaemia is assumed to be 0.2% with 15% likely to be diagnosed with the condition and all then needing treatment.</p> <p>The prevalence of primary heterozygous-non-familial hypercholesterolaemia is assumed to be 4% with 40% of these likely to be diagnosed and 75% then needing treatment.</p>	<p>Prevalence of primary heterozygous- familial hypercholesterolaemia and primary heterozygous-non-familial hypercholesterolaemia is taken from Thompson, G., Morrell, J., and Wilson, P. Dyslipidaemia in Clinical Practice, 2nd Edition. Oxford Informa Healthcare 2006. Estimated prevalence among European adults (1 in 500 adults).</p> <p>Estimates of percentage likely to be diagnosed and needing treatment are based on a consensus of clinical opinion.</p>
<p>Approximately 2% of eligible patients are unable to take statins because of contraindication or intolerance and would be appropriate for treatment with ezetimibe and 30% of those able to tolerate a statin would be considered for an alternative statin or ezetimibe.</p>	<p>HEART UK submission to NICE for NICE Health Technology Assessment of Ezetimibe. HEART UK 2006. 1-3% of patients are unable to tolerate statins due to gastrointestinal or muscular side effects.</p> <p>Yang, C. C., Jick, S. S., and Testa, M. A. Discontinuation and switching of therapy after initiation of lipid-lowering drugs: The effects of co-morbidities and patient characteristics. British Journal of Clinical Pharmacology 2003; 56 84-91. 30% of patients on statins switch from their initial therapy within the first year of treatment.</p>

More recent research which suggests that 30% of patients switch their therapy within the first year of treatment could imply that the original analysis could have under-estimated the number of people switching to ezetimibe in combination with a statin in subsequent years.

Observed uptake

The use of ezetimibe (both on its own and in combination with simvastatin) in hospitals is very low (less than £1 million in 2008 compared with a primary care spend of almost £78 million) and so has been ignored for this purpose. The data used here is taken from the two ePACT systems. For the cost graph, national data has been taken from the PCA and HPAI databases to show expenditure over a longer time.

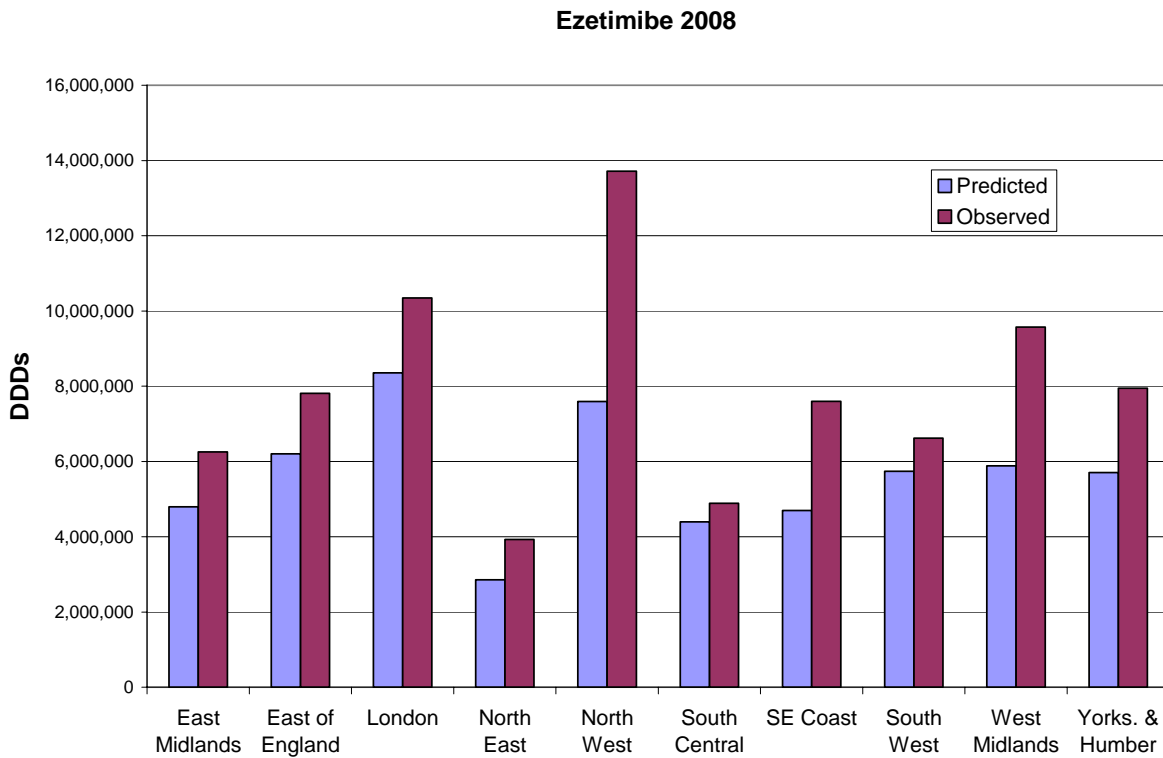
Results

The NICE costing model gives an estimate of 154.0 thousand patients per year. The medicine is likely to be taken continuously (365 doses per year) and so the model would predict usage of 56,224.2 thousand doses. The ePACT data gives 78,719.4 thousand DDDs in 2008 (for the combination product with simvastatin only the ezetimibe content was used in measuring the number of DDDs). This is a ratio of 1.4 to 1.

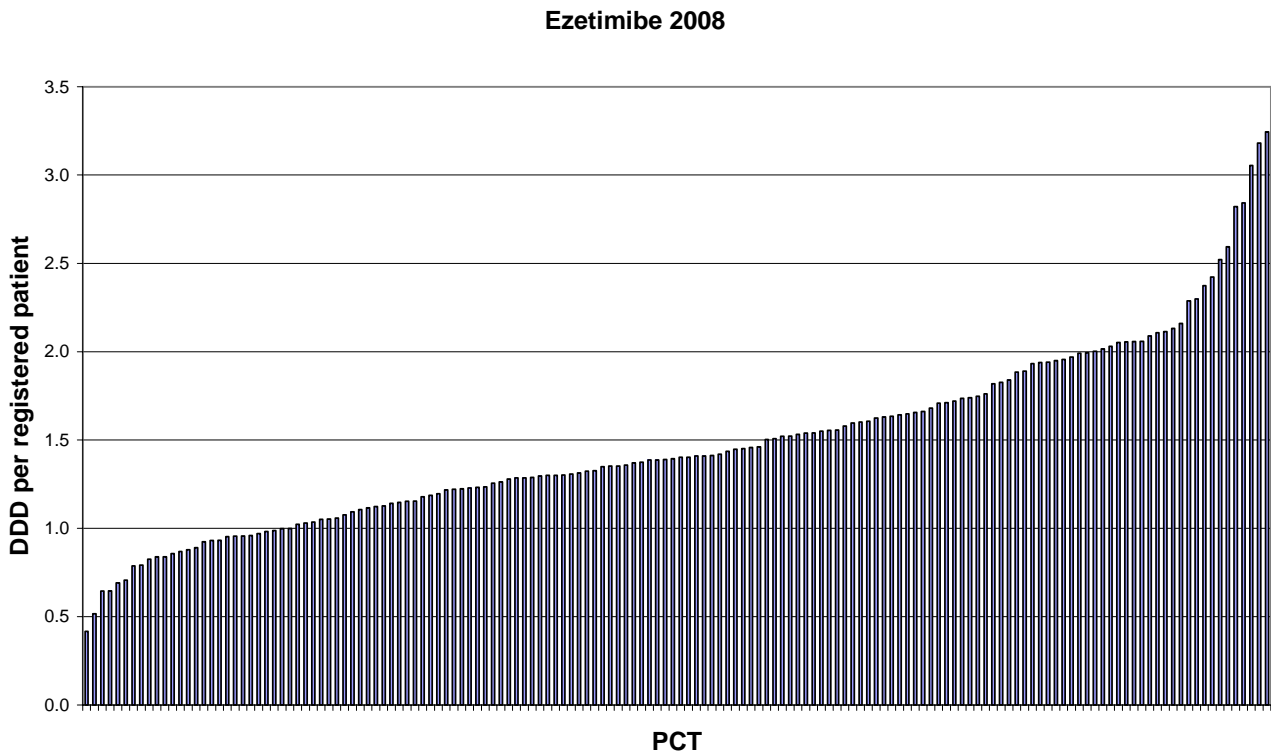
The table below shows data at SHA level.

SHA	Expected eligible patients (from NICE) in thousands	Predicted DDDs in thousands	Observed DDDs in thousands	Ratio
East Midlands	13	4,797	6,257	1.3
East of England	17	6,201	7,812	1.3
London	23	8,355	10,348	1.2
North East	8	2,855	3,924	1.4
North West	21	7,592	13,719	1.8
South Central	12	4,395	4,890	1.1
South East Coast	13	4,697	7,598	1.6
South West	16	5,741	6,621	1.2
West Midlands	16	5,885	9,574	1.6
Yorkshire and the Humber	16	5,706	7,948	1.4

The chart below compares predicted and observed use by DDD in 2008 by SHA.

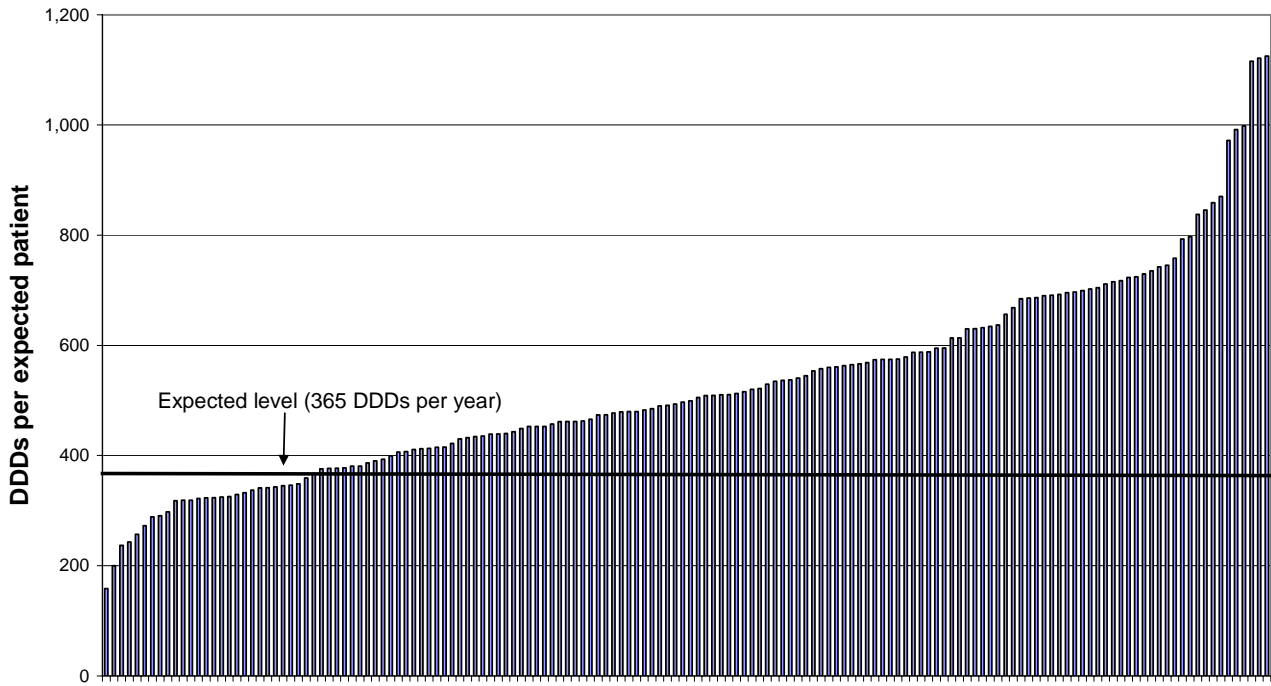


The chart below shows the use (measured as number of DDDs per registered patient) for 2008 by PCT



The figure below shows the number of DDDs per expected eligible patient (using the NICE costing model) by PCT for 2008. If observed use matched predicted use then we would expect 365 DDDs per expected patient. A line has been drawn on the graph to show this level.

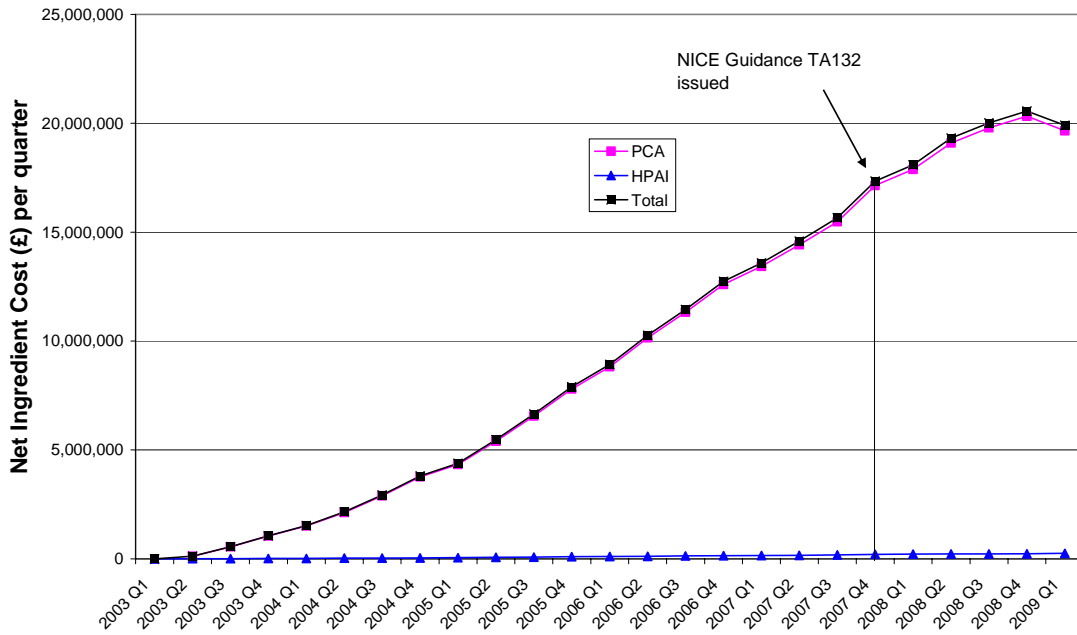
Ezetimibe 2008



Although the shape is very similar to the previous figure, the position on individual PCTs differs depending on which denominator is used.

The figure below shows the national (England) expenditure by quarter, using data from the PCA and HPAI databases.

Ezetimibe and simvastatin with ezetimibe



Asthma (uncontrolled) – omalizumab

Overview

Omalizumab is licensed for use as additional therapy in individuals with proven IgE-mediated sensitivity to inhaled allergens, whose severe persistent allergic asthma cannot be controlled adequately with high-dose inhaled corticosteroid together with a long-acting beta₂ agonist.

Relevant guidance

NICE Technology Appraisal 133 Omalizumab for severe persistent allergic asthma

<http://guidance.nice.org.uk/TA133>

- *Omalizumab is recommended as a possible treatment for adults and young people over 12 years with severe persistent allergic asthma when all of the following circumstances apply.*
- *When the person's asthma is still severe and unstable despite best efforts to control it with other asthma medicines taken as directed by their doctor.*
- *When the person has stopped smoking, if their doctor feels it is appropriate.*
- *When the person has allergic asthma. This should be confirmed by checking past symptoms and skin testing for allergies.*
- *When the person has had at least two asthma attacks within the past year that have needed admission to hospital, or when the person has had three or more severe asthma attacks within the past year, one of which has needed admission to hospital and the other two have needed additional treatment in an accident and emergency department.*
- *Omalizumab treatment should be given along with the person's current asthma medicines. It should be prescribed by a doctor who is experienced in asthma and allergy medicine at a specialist centre.*
- *If omalizumab does not control the asthma after 16 weeks, treatment should be stopped.*

This guidance was published in November 2007. NICE has also issued guidance on the use of inhaler devices and corticosteroids for the management of asthma. However this additional guidance is unlikely to impact on the uptake of omalizumab which is for patients whose condition is less stable.

Expected Number of Eligible Patients

The following assumptions were used in the calculation of the expected number of eligible patients. The assumptions are taken from data on existing practice, research and the views of experts in the field used in the NICE costing template (for further detail see <http://guidance.nice.org.uk/TA133/CostTemplate/xls/English>).

Assumption	Evidence / Source
Proportion of patients admitted to hospital on 2 or more occasions with asthma = 0.023%	The number of patients admitted to hospital two or more times for asthma in the past 12 months has been calculated using Hospital Episode Statistics (HES) data, by using an anonymous patient identifier to isolate those individuals that have been admitted to A&E on two occasions in the past year.
Proportion of patients admitted to hospital on one occasion and also attending A&E on 2 or more occasion = 24.5% NB: Clinical practice has changed since 1994, specifically increased use of inhaled corticosteroids, so the proportion stated here is likely to be an overestimate.	A national census of those attending UK accident and emergency departments with asthma. Partridge MR, Latouche D, Trako E et al. (1997) Journal of Accident and Emergency Medicine 14: 16-20. The census undertaken in 1994 reported that 24.5% of those attending A&E had attended A&E within the previous 3 months. These data have been used as a proxy to identify the proportion of patients that were admitted to hospital once and attended A&E on at least two occasions.
Proportion of patients with allergic asthma = 58%	ENFUMOSA Study Group. The ENFUMOSA cross-sectional European multicentre study of clinical phenotype of chronic severe asthma. Eur Respir J 2003; 23: 470-77.
Proportion of patients with immunoglobulin E (IgE) levels in the required range = 79.3%	The proportion of patients with immunoglobulin E (IgE) levels in the required range has been estimated using data supplied in the manufacturer's model.

Observed uptake

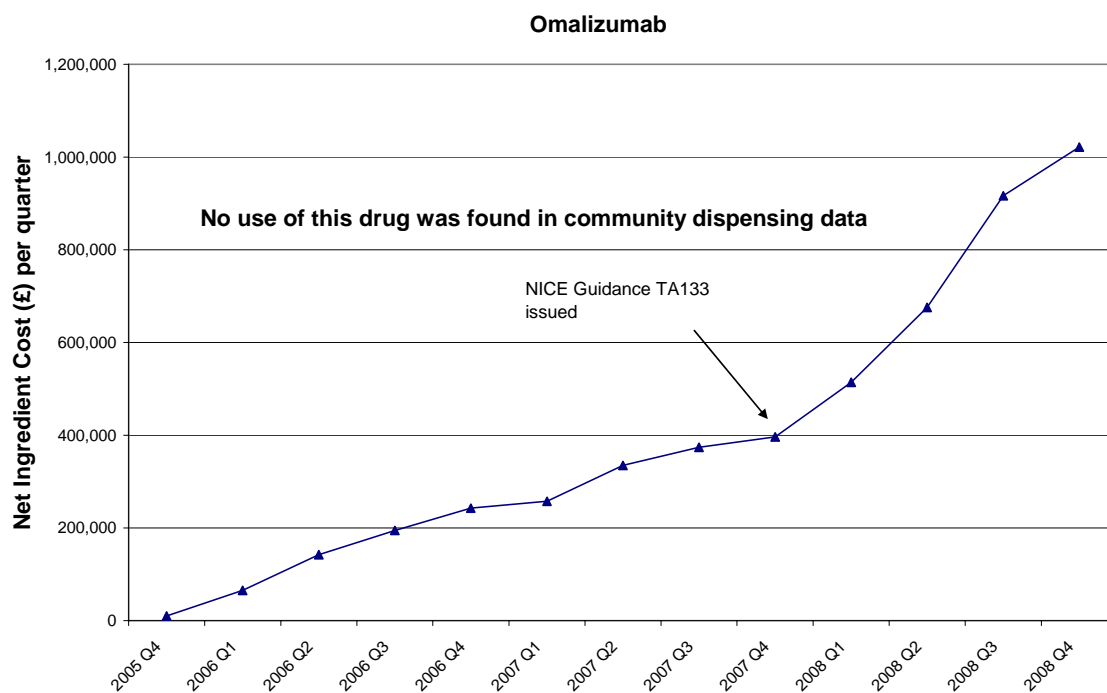
No primary care use of omalizumab was found so only HPAI data was used.

Results

The NICE costing template expected the annual equivalent of 1,172 patients (this figure allows for some patients discontinuing at 16 weeks) giving 427.8 thousand doses per year (assuming continuous use throughout the year). The observed use in 2008 was 114.5 thousand defined daily doses, a ratio of 0.3 to 1. Use was increasing over 2008 and if the use in the first quarter of 2009 continued throughout the year then the use in 2009 would be 160.6 thousand DDDs giving a ratio of 0.4 to 1.

The expected numbers of eligible patients in each SHA varied from 60 to 173 and so a sub-national analysis is not appropriate.

The graph below shows national (England) expenditure by quarter, since 2005.



Multiple sclerosis – natalizumab

Overview

Natalizumab is licensed for use in patients with highly active *relapsing-remitting multiple sclerosis* despite treatment with interferon beta or those with rapidly evolving severe relapsing-remitting multiple sclerosis. Treatment with natalizumab should be initiated and supervised by a specialist.

Relevant guidance

NICE Technology Appraisal 127 Natalizumab for the treatment of adults with highly active relapsing-remitting multiple sclerosis <http://www.nice.org.uk/TA127>

- *Natalizumab is recommended as an option for the treatment only of rapidly evolving severe relapsing-remitting multiple sclerosis (RES). RES is defined by two or more disabling relapses in 1 year, and one or more gadolinium-enhancing lesions on brain magnetic resonance imaging (MRI) or a significant increase in T2 lesion load compared with a previous MRI.*
- *People currently receiving natalizumab, but for whom treatment would not have been recommended according to section 1.1 of the guidance (above), should have the option to continue therapy until they and their clinicians consider it appropriate to stop.*

This guidance was published in August 2007. NICE has also published the following guidance:

- Multiple sclerosis: management of multiple sclerosis in primary and secondary care. NICE clinical guideline 8 (2003)
- Beta interferon and glatiramer acetate for the management of multiple sclerosis. NICE technology appraisal guidance 32 (2002).

Expected Number of Eligible Patients

The following assumptions were used in the calculation of the expected number of eligible patients. The assumptions are taken from data on existing practice, research and the views of experts in the field used in the NICE costing template (for further detail see <http://guidance.nice.org.uk/TA127/CostTemplate/xls/English>).

Assumption	Evidence / Source
Numbers of multiple sclerosis patients eligible for disease-modifying treatments = 9000	HSC 2002/004 Cost effective provision of disease modifying therapies for people with multiple sclerosis estimates an upper limit of 9000 patients in England and Wales eligible for disease modifying therapies, scaled for England only.

Proportion of patients assumed to have relapsing-remitting multiple sclerosis = 86%.	Palace J, Cooper C, MS risk-sharing scheme monitoring study uptake estimates 14% of multiple sclerosis patients eligible for disease modifying therapies have secondary progressive MS, the remainder have relapsing-remitting MS.
Proportion of patients with rapidly evolving relapsing-remitting multiple sclerosis = 22%	AFFIRM study
Proportion of patients assumed to be appropriate for treatment with natalizumab = 26%	Expert clinical opinion was sought as to the likely proportion of patients who would be switched to natalizumab.

Observed uptake

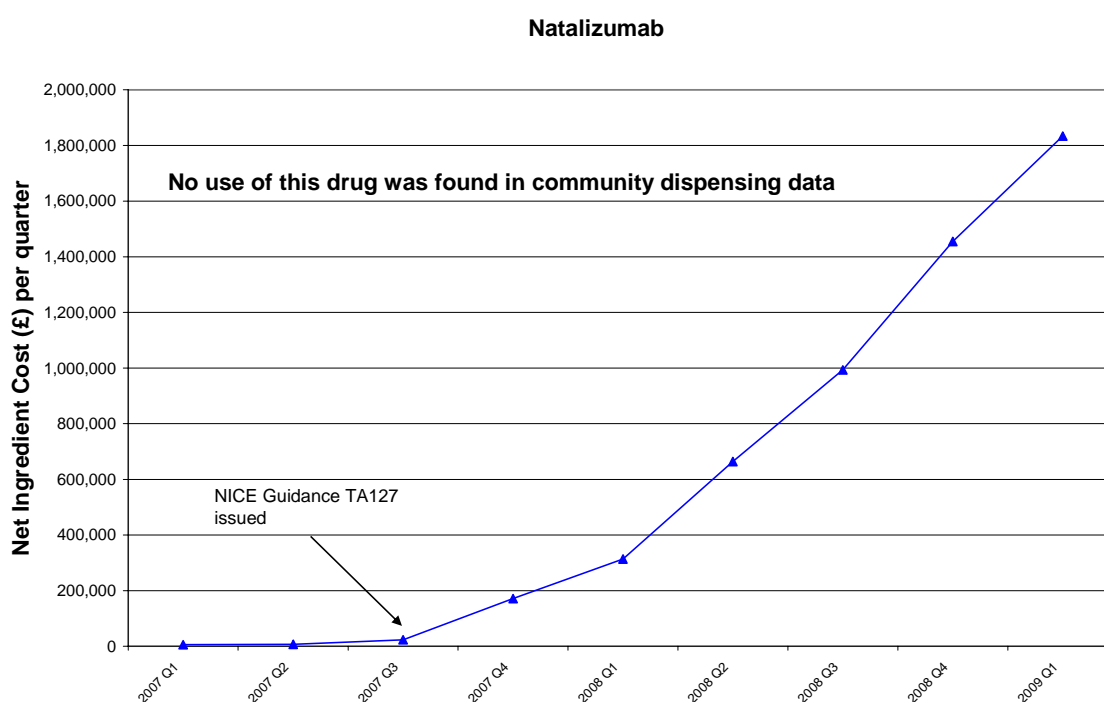
No use of this medicine was found in community data and so only HPAI data was used.

Results

The NICE costing template expected the annual equivalent of 419 patients giving a predicted use of 152.9 thousand doses per year. The observed use in 2008 was 91.0 thousand defined daily doses, a ratio of 0.6 to 1. Use was increasing over 2008 and if the use in the first quarter of 2009 continued throughout the year then the use in 2009 would be 194.7 thousand DDDs which would give a ratio of 1.3 to 1.

The expected number of eligible patients at SHA level ranged from 21 to 62 patients and so a sub-national analysis is not appropriate.

The graph below shows national (England) expenditure by quarter since 2007.



Hepatitis B – entecavir

Overview

Entecavir is indicated for chronic hepatitis B infection with compensated liver disease, evidence of viral replication, and histologically documented active liver inflammation or fibrosis.

Relevant guidance

NICE Technology Appraisal 153 Entecavir for the treatment of chronic hepatitis B
<http://www.nice.org.uk/TA153>

- *This guidance does not apply to people with chronic hepatitis B who also have hepatitis C, hepatitis D or HIV.*
- *Entecavir, within its marketing authorisation, is recommended as an option for the treatment of people with chronic HBeAg-positive or HBeAg-negative hepatitis B in whom antiviral treatment is indicated.*

This guidance was published in August 2008. NICE has also published the following guidance:

- Adefovir dipivoxil and peginterferon alfa-2a for the treatment of chronic hepatitis B. NICE technology appraisal guidance 96 (2006)
- Telbivudine for the treatment of chronic hepatitis B. NICE technology appraisal guidance 154 (2008)
- Tenofovir disoproxil fumarate for the treatment of hepatitis B. NICE technology appraisal guidance 173 (2009)

Expected Number of Eligible Patients

The following assumptions were used in the calculation of the expected number of eligible patients. The assumptions are taken from data on existing practice, research and the views of experts in the field used in the NICE costing statement (for further detail see <http://guidance.nice.org.uk/TA153/CostReport/pdf/English>).

Assumption	Evidence / Source
Number of people in England with chronic hepatitis B = 300,000	<p>Pendleton S, Wilson-Webb P (2007) Rising curve: chronic hepatitis B infection in the UK. http://www.hepb.org.uk/information/resources/rising_curve_chronic_hepatitis_b_infection_in_the_uk</p> <p>This is a national estimate that has been apportioned in line with population. In practice it is likely that local variation exists in prevalence, particularly in areas with people migrating from countries with a high prevalence.</p>

Proportion diagnosed = 26%	National Institute for Health and Clinical Excellence (2006) Adefovir dipivoxil and peginterferon alfa-2a for the treatment of chronic hepatitis B. NICE technology appraisal guidance 96. Available from: www.nice.org.uk/TA096
Proportion receiving antiviral treatment = 5%	Based on clinical opinion
Proportion of those where appropriate treatment is lamivudine or adefovir dipivoxil = 75%	Based on clinical opinion
Proportion of those expected to switch to entecavir = 6.9%	Based on clinical opinion

The proportion meeting treatment criteria and expected to switch to entecavir is based on clinical opinion and could vary significantly between treatment centres based on clinician experience and preference. There is also anecdotal evidence that patients travel to London from surrounding areas for treatment.

Observed uptake

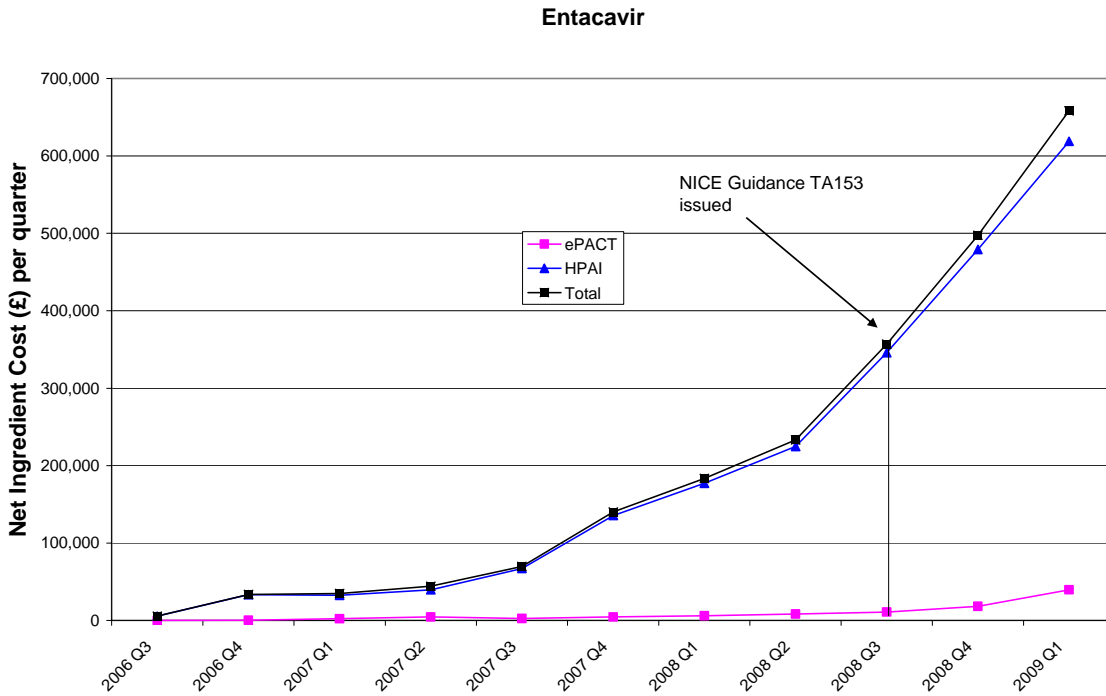
The figures were taken from the HPAI database and the two versions of ePACT although, in 2008, 93% of all use (by cost) was in hospitals.

Results

The NICE costing template expected the annual equivalent of 202 patients giving a predicted use of 73.7 thousand doses per year. The observed use in 2008 was 143.6 thousand defined daily doses, a ratio of 1.9 to 1.

The expected number of eligible patients at SHA level ranged from 10 to 30 patients and so a sub-national level analysis is not appropriate.

The graph below shows national (England) expenditure by quarter.



Sepsis (severe) – drotrecogin

Overview

Drotrecogin is indicated for adjunctive treatment of severe sepsis with multiple organ failure—start treatment within 24 hours (and no later than 48 hours) after onset of organ failure

Relevant guidance

NICE Technology Appraisal 84 Drotrecogin alpha (activated) for severe sepsis
<http://guidance.nice.org.uk/TA84>

- *Drotrecogin alfa (activated) is recommended for use in adult patients who have severe sepsis that has resulted in multiple organ failure (that is, two or more major organs have failed) and who are being provided with optimum intensive care support.*
- *The use of drotrecogin alfa (activated) should only be initiated and supervised by a specialist consultant with intensive care skills and experience in the care of patients with sepsis*

Since the NICE guidance on drotrecogin alpha (activated) was issued in September 2004, the European Medicines Evaluation Agency has recommended changes to the way that drotrecogin alpha (activated) should be used. These changes can be found on the European Medicines Agency (EMA) website at
<http://www.emea.europa.eu/humandocs/Humans/EPAR/xigris/XigrisM2.htm>

In summary, the EMA consider that drotrecogin alfa (activated) should only be used in high-risk patients, mainly in situations when therapy can be started within 24 hours of the onset of organ failure. In addition, it should only be used by experienced doctors in institutions skilled in the care of patients with severe sepsis. Drotrecogin alfa (activated) should not be used in patients with single organ dysfunction, especially if they have had recent surgery (within 30 days).

Expected Number of Eligible Patients

The following assumptions were used in the calculation of the expected number of eligible patients. The assumptions are taken from data on existing practice, research and the views of experts in the field used in the NICE guidance; section 6 'Implications for the NHS'. These were developed before the EMA guidance was published which is likely to reduce the use of this medicine.

Assumption	Evidence / Source
Admissions to critical care = 0.27808%	ICNARC data https://www.icnarc.org/
Admissions for patients with severe sepsis per day (within 24 hrs) = 27%	As per guidance and ICNARC data

Proportion of patients with multiple organ failure = 84%	As per guidance and ICNARC data
Proportion of patients eligible for treatment = 4%	Clinical opinion

Observed uptake

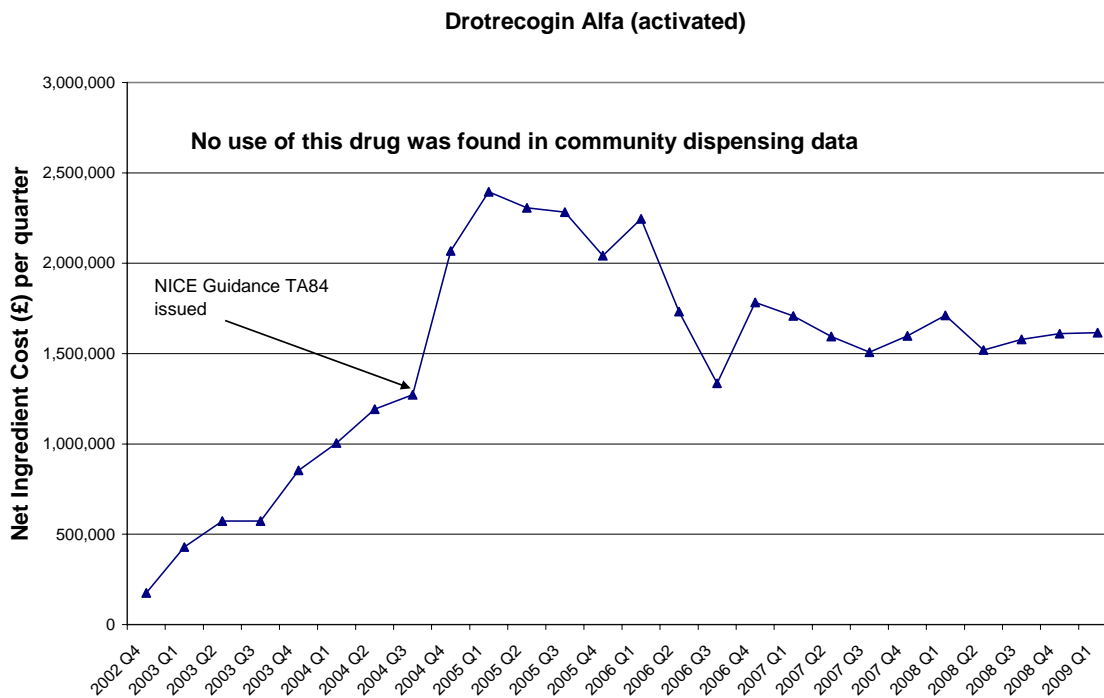
There was no evidence of use in the community so only the HPAI database was used.

Results

The NICE costing template expected the annual number of patients to be 4,362 eligible patients. However the guidance does not indicate for how long treatment would be expected to last. The patients involved are severely ill and may die within a short time of treatment being initiated. Patients who benefit from the treatment may receive it for up to 96 hours (EMA guidance). In consultation with NICE we agreed to assume that patients would receive the medicine for an average of two days giving a predicted use of 8.7 thousand doses per year. The observed use in 2008 was 5.3 thousand defined daily doses, a ratio of 0.6 to 1.

The expected number of eligible patients at SHA ranged from 221 to 650 patients and so a sub-national level analysis is not appropriate.

The graph below shows national (England) expenditure, by quarter.



Motor neurone disease – riluzole

Overview

Riluzole is indicated to extend life in patients with amyotrophic lateral sclerosis, initiated by specialists experienced in the management of motor neurone disease.

Relevant guidance

NICE Technology Appraisal 20 Riluzole (Rilutek) for the treatment of Motor Neurone Disease
<http://www.nice.org.uk/ta20>

- Riluzole is recommended for the treatment of individuals with the amyotrophic lateral sclerosis (ALS) form of Motor Neurone Disease (MND).
- Riluzole therapy should be initiated by a neurological specialist with expertise in the management of MND. Routine supervision of therapy should be managed by locally agreed shared care protocols undertaken by general practitioners.

Predicted uptake

The following assumptions were used in the calculation of the expected number of eligible patients. The assumptions are taken from data on existing practice, research and the views of experts in the field used in the NICE guidance; section 5 'Implications for the NHS'.

Assumption	Evidence / Source
Prevalence of amyotrophic lateral sclerosis = 4.35 per 100,000 (4-4.7)	As per NICE guidance http://guidance.nice.org.uk/TA20/Guidance/pdf/English
Annual incidence of new cases eligible for riluzole to be 2 per 100,000 (1.8-2.2)	As per NICE guidance http://guidance.nice.org.uk/TA20/Guidance/pdf/English

Observed uptake

Riluzole is used both in the community and in hospital. The HPAI database and the two versions of ePACT were the data sources used. The graph showing the costs over time use data from the PCA database as this has data for a longer period.

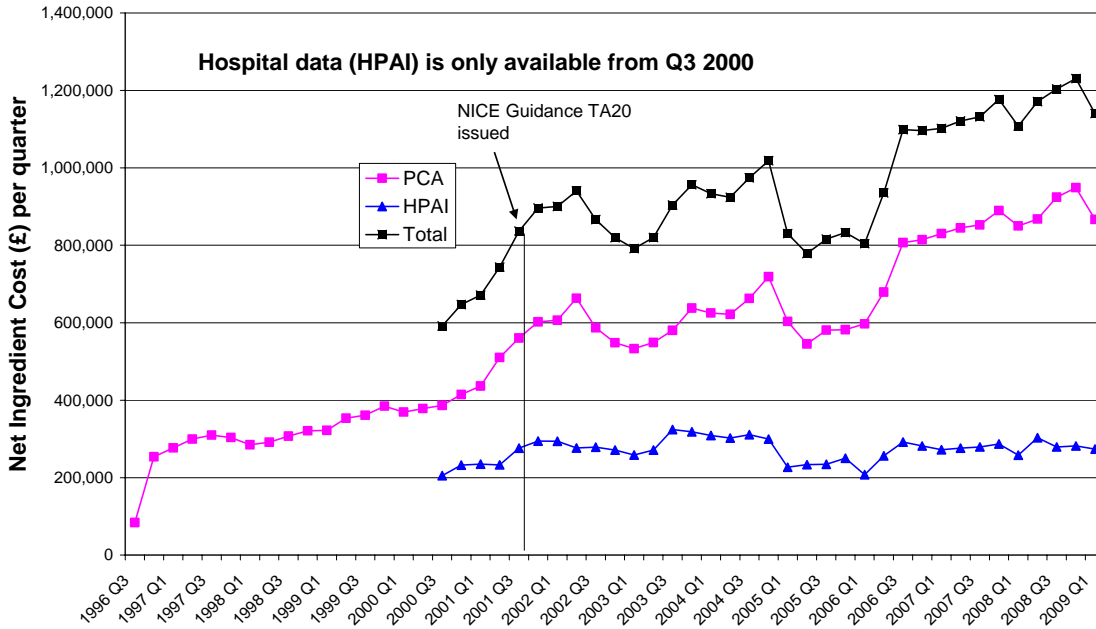
Results

The NICE costing template expected an annual number of 1,735 patients giving a predicted use of 633.3 thousand doses per year. The observed use in 2008 was 544.4 thousand defined daily doses, a ratio of 0.9 to 1.

The expected number of eligible patients at SHA level ranged from 88 to 258 and so a sub-national analysis is not appropriate.

The graph below shows the national (England) expenditure by quarter from 1996.

Riluzole



Insomnia - newer hypnotic drugs

Overview

Zaleplon, zolpidem and zopiclone are non-benzodiazepine hypnotics, but they act at the benzodiazepine receptor. Zolpidem and zopiclone have a short duration of action; zaleplon is very short acting. All three drugs are not licensed for long-term use; dependence has been reported in a small number of patients.

Relevant guidance

NICE Technology Appraisal 77 Zaleplon, zolpidem and zopiclone for the management of insomnia <http://www.nice.org.uk/ta77>

- *When, after due consideration of the use of nonpharmacological measures, hypnotic drug therapy is considered appropriate for the management of severe insomnia interfering with normal daily life, it is recommended that hypnotics should be prescribed for short periods of time only, in strict accordance with their licensed indications.*
- *It is recommended that, because of the lack of compelling evidence to distinguish between zaleplon, zolpidem, zopiclone or the shorter-acting benzodiazepine hypnotics, the drug with the lowest purchase cost (taking into account daily required dose and product price per dose) should be prescribed.*
- *It is recommended that switching from one of these hypnotics to another should only occur if a patient experiences adverse effects considered to be directly related to a specific agent. These are the only circumstances in which the drugs with the higher acquisition costs are recommended.*
- *Patients who have not responded to one of these hypnotic drugs should not be prescribed any of the others.*

Expected Number of Eligible Patients

The following assumptions were used in the calculation of the expected number of eligible patients.

Assumption	Evidence / Source
Proportion of population presenting to services for treatment = 1.4%	Disease Analyser data, 2006

The relative quantities of hypnotics that are prescribed in the context of long- or short-term treatment are unknown. National prescriptions data is not linked to patient information, so it is not possible to know whether one or more prescriptions have been issued for the same person over a period of time.

Observed uptake

Hospital use of these medicines is low but has been included with data from the two ePACT systems. The cost graph uses national PCA data to show expenditure over a longer period.

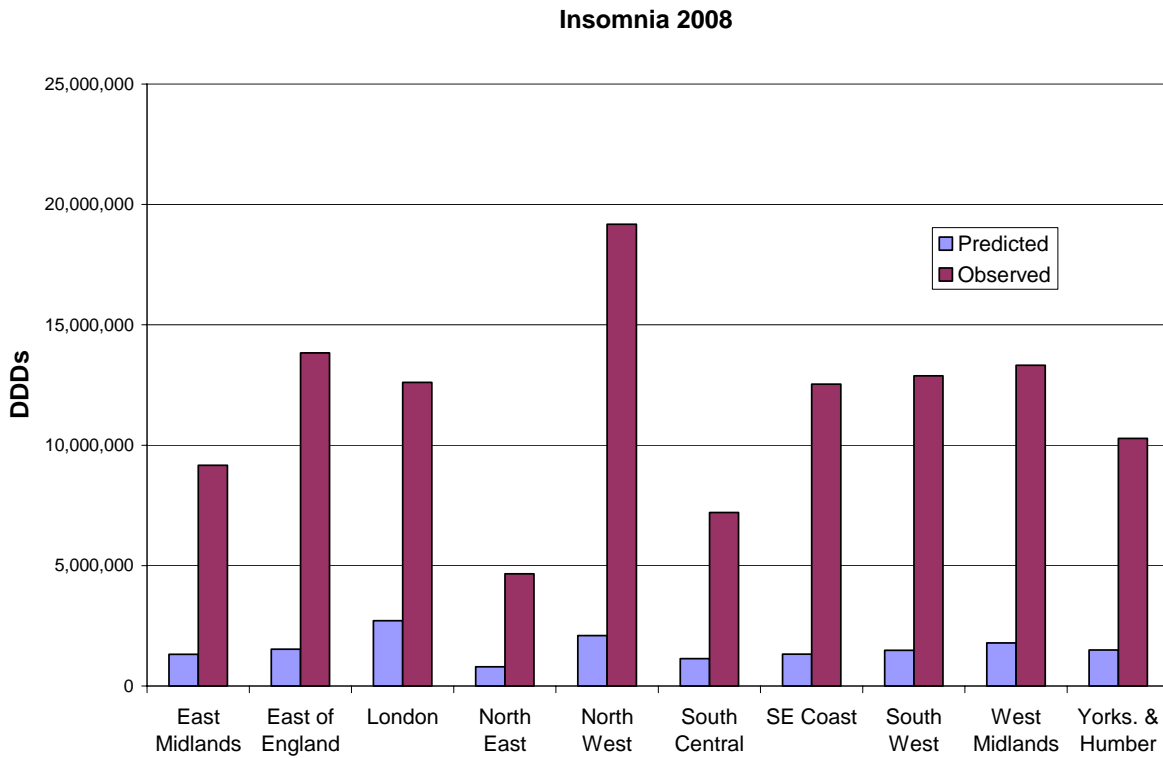
Results

The NICE costing template expected an annual number of 558.4 thousand patients. The recommended period of use is no more than 28 days. If we assume that all patients receive 28 days' treatment then this gives a predicted use of 15,634.4 thousand doses per year. The observed use in 2008 was 115,854.8 thousand defined daily doses, a ratio of 7.4 to 1. Temazepam, an alternative hypnotic, has been classified as a Controlled Drug, which may have led to increased prescribing of these medicines.

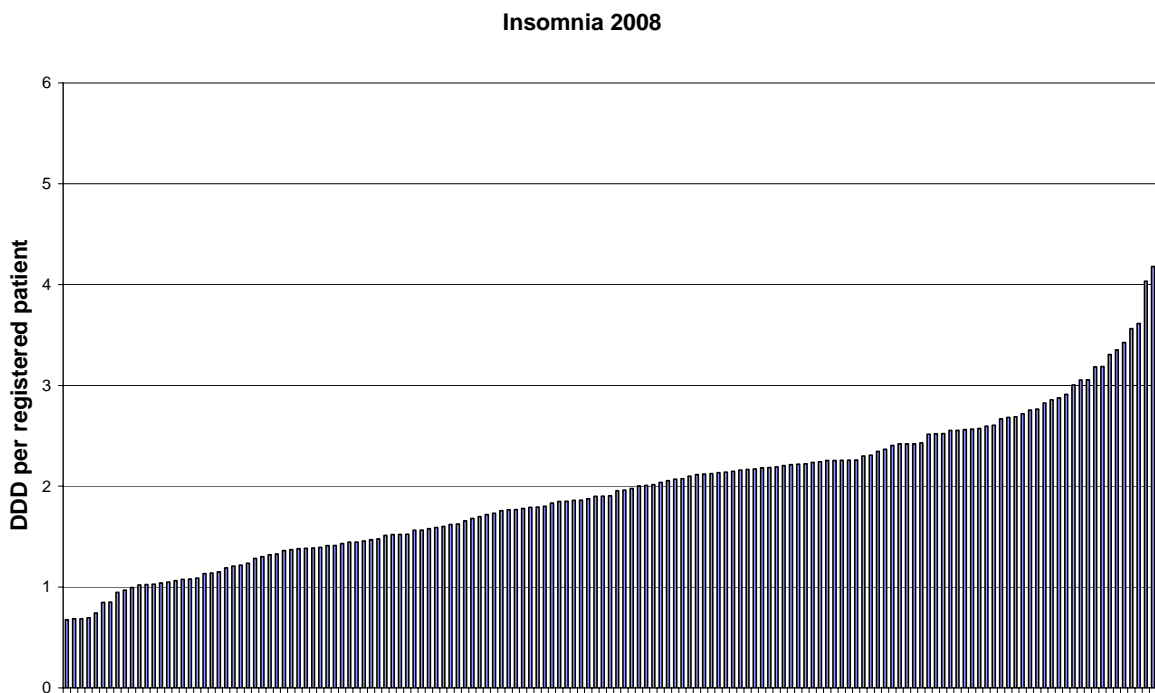
The table below shows data at SHA level.

SHA	Expected eligible patients (from NICE) in thousands	Predicted DDDs in thousands	Observed DDDs in thousands	Ratio
East Midlands	47	1,310	9,167	7.0
East of England	55	1,528	13,834	9.1
London	97	2,708	12,606	4.7
North East	28	794	4,655	5.9
North West	75	2,090	19,180	9.2
South Central	41	1,135	7,210	6.4
South East Coast	47	1,321	12,533	9.5
South West	53	1,486	12,886	8.7
West Midlands	64	1,787	13,319	7.5
Yorkshire and the Humber	53	1,490	10,286	6.9

The chart below compares predicted and observed use, measured by DDDs, in 2008 by SHA.

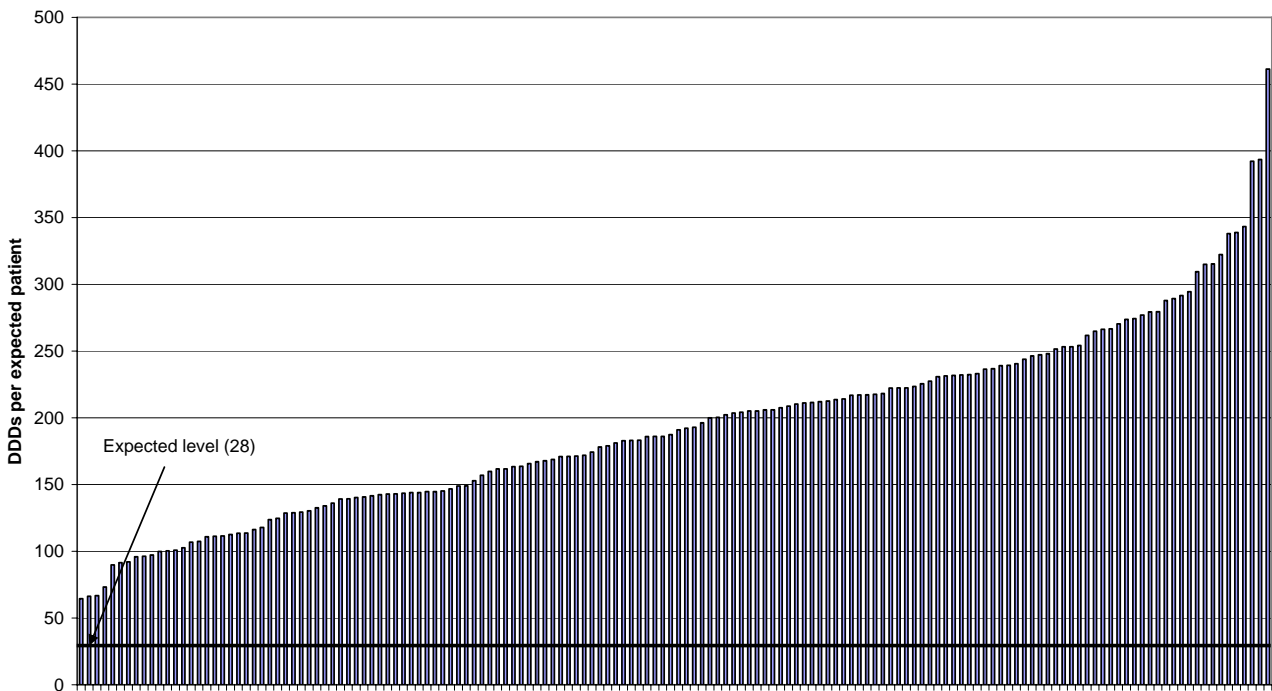


The chart below shows the number of DDDs per registered patient by PCT for 2008, using only data from the primary care ePACT system. Such use accounts for over 93% of the national cost.



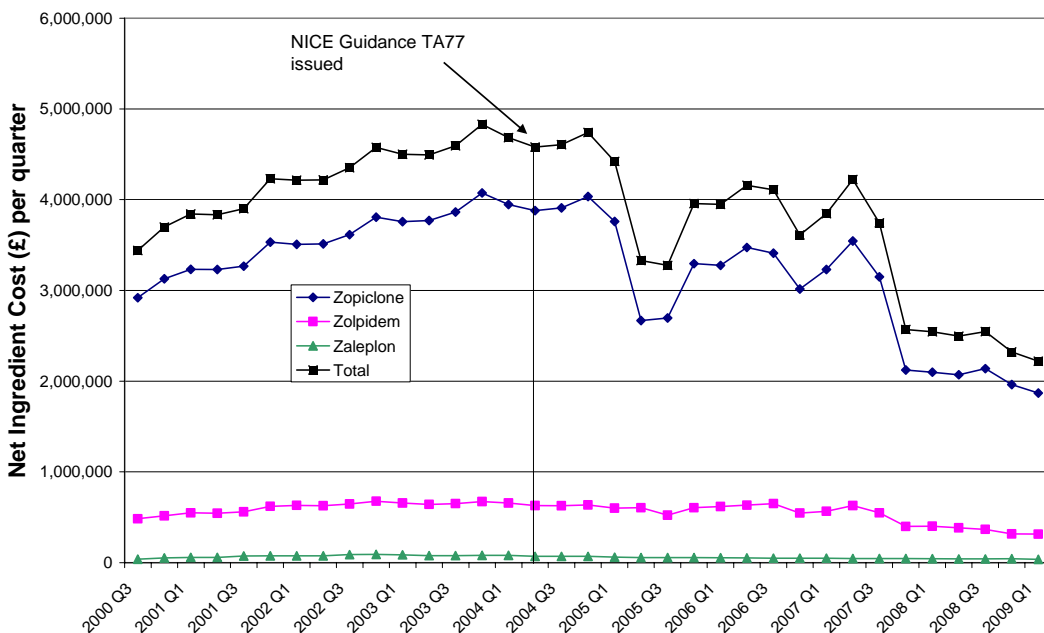
The chart below shows the number of DDDs per expected patient (using the NICE costing model) by PCT for 2008. If observed use matched expected use then we would anticipate 28 DDDs per expected patient. A line has been drawn on the graph to show this level.

Insomnia 2008



The graph below shows the national (England) expenditure by quarter. The cost of zopiclone (and hence the overall cost since zopiclone is the most commonly prescribed) has fallen following the availability of generic formulations.

Zolpidem, zopiclone and zaleplon



Smoking cessation - varenicline

Overview

Varenicline is a selective nicotine receptor partial agonist used as an aid for smoking cessation.

Relevant guidance

NICE Technology Appraisal 123 Varenicline for smoking cessation

<http://www.nice.org.uk/ta123>

- *Varenicline is recommended within its licensed indications as an option for smokers who have expressed a desire to quit smoking.*
- *Varenicline should normally be prescribed only as part of a programme of behavioural support*

Since the NICE guidance on varenicline was issued in July 2007, the EMEA and MHRA have also issued statements to prescribers to increase awareness of cases of suicidal ideation and suicide attempts reported in patients using this drug.

Expected Number of Eligible Patients

The following assumptions were used in the calculation of the expected number of eligible patients. The assumptions are taken from data on existing practice, research and the views of experts in the field used in the NICE costing template (for further detail see <http://guidance.nice.org.uk/TA123/CostTemplate/xls/English>).

Assumption	Evidence / Source
Number of smokers setting a quit date by age band – actual rates provided, National average = 6.3% of smokers	Information interpolated from 'Statistics on NHS stop smoking services in England, April 2005 to March 2006' annual bulletin
Estimated number of smokers setting a quit date receiving pharmacological interventions = 65%	Current prescribing practice derived from 'Prescription cost analysis' 2006
Proportion prescribed varenicline = 16%	Varenicline Single Technology Appraisal submission 17th January 2007 - Pfizer UK Ltd

There is considerable regional variation in the rates of smokers and the reported proportion that attempt to quit. The warnings from the EMEA and MHRA may have made prescribers more cautious about the use of this drug and this is not taken into account by the estimates which are based only on evidence available at the time of the appraisal.

Observed uptake

Use of varenicline in hospitals is extremely low (less than £24,000 in 2008 compared with community spend of over £24 million) and so only community data has been used, taken

from the two versions of ePACT. The starter pack contains both 500 mcg tablets (11 of them) and 1 mg tablets (14 of them). In order to convert this to daily doses we have regarded this as 14 days treatment following the BNF advice of 500 mcg for 3 days, 500 mcg twice daily for 4 days and 1 mg twice daily thereafter. For all other formulations we have used the WHO DDD of 2 mg although this may underestimate the number of days of treatment.

Note that this medicine may be supplied via Smoking Cessation Clinics and such use would not appear in our data.

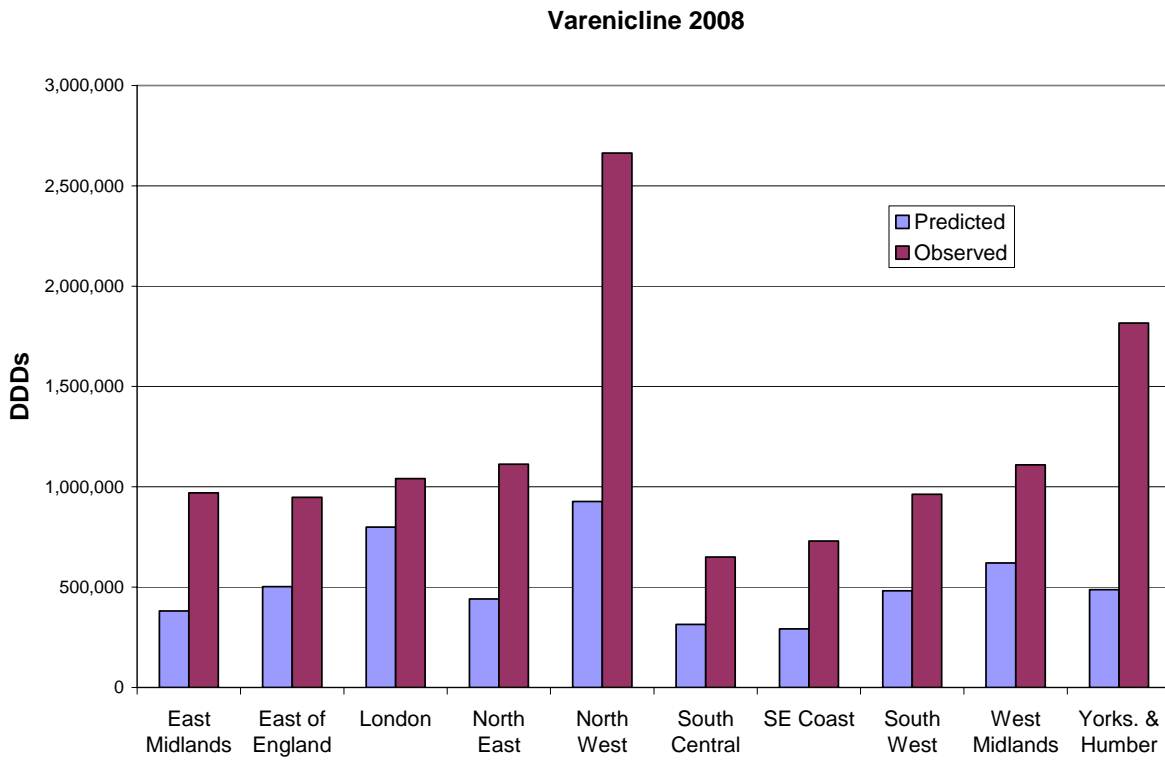
Results

The NICE costing template expected an annual number of 62.4 thousand patients 2008. The BNF recommends a 12 week treatment course. This gives a predicted use of 5,245.2 thousand doses per year. The observed use in 2008 was 12,028.5 thousand defined daily doses (see note above on how these were calculated), a ratio of 2.3 to 1.

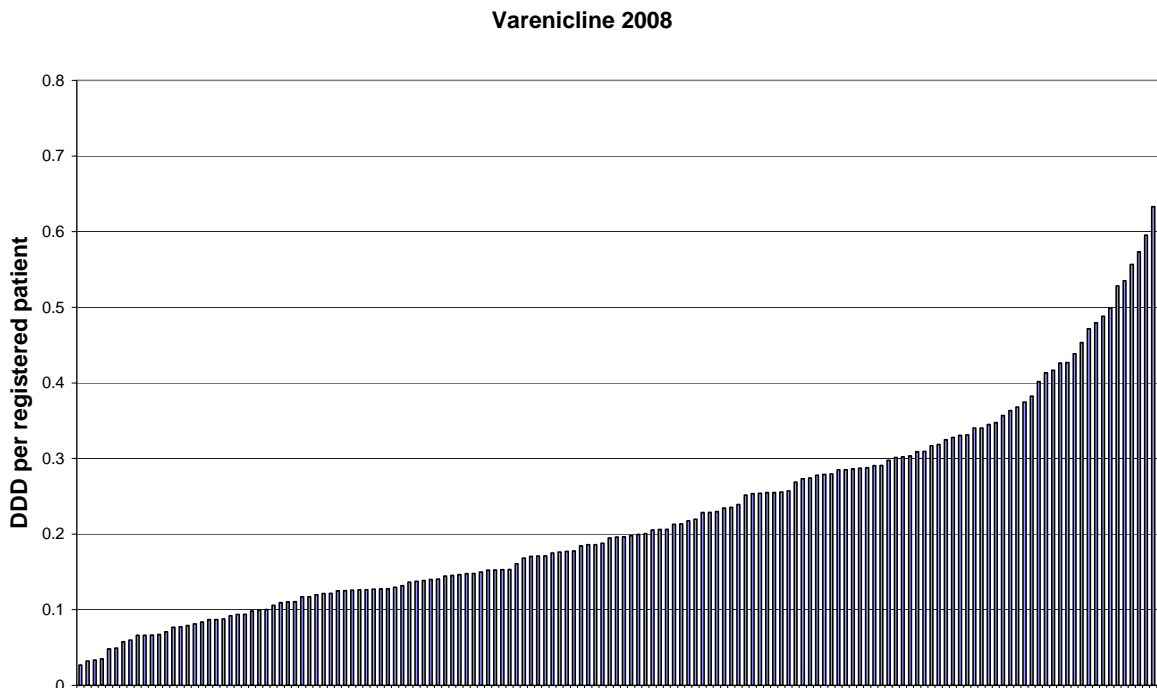
The table below shows the data at SHA level.

SHA	Expected eligible patients (from NICE) in thousands	Predicted DDDs in thousands	Observed DDDs in thousands	Ratio
East Midlands	5	381	970	2.5
East of England	6	502	947	1.9
London	10	800	1,041	1.3
North East	5	441	1,113	2.5
North West	11	927	2,663	2.9
South Central	4	314	651	2.1
South East Coast	3	292	729	2.5
South West	6	481	962	2.0
West Midlands	7	620	1,110	1.8
Yorkshire and the Humber	6	487	1,816	3.7

The chart below compares predicted and observed use, measured by DDDs, in 2008 by SHA.

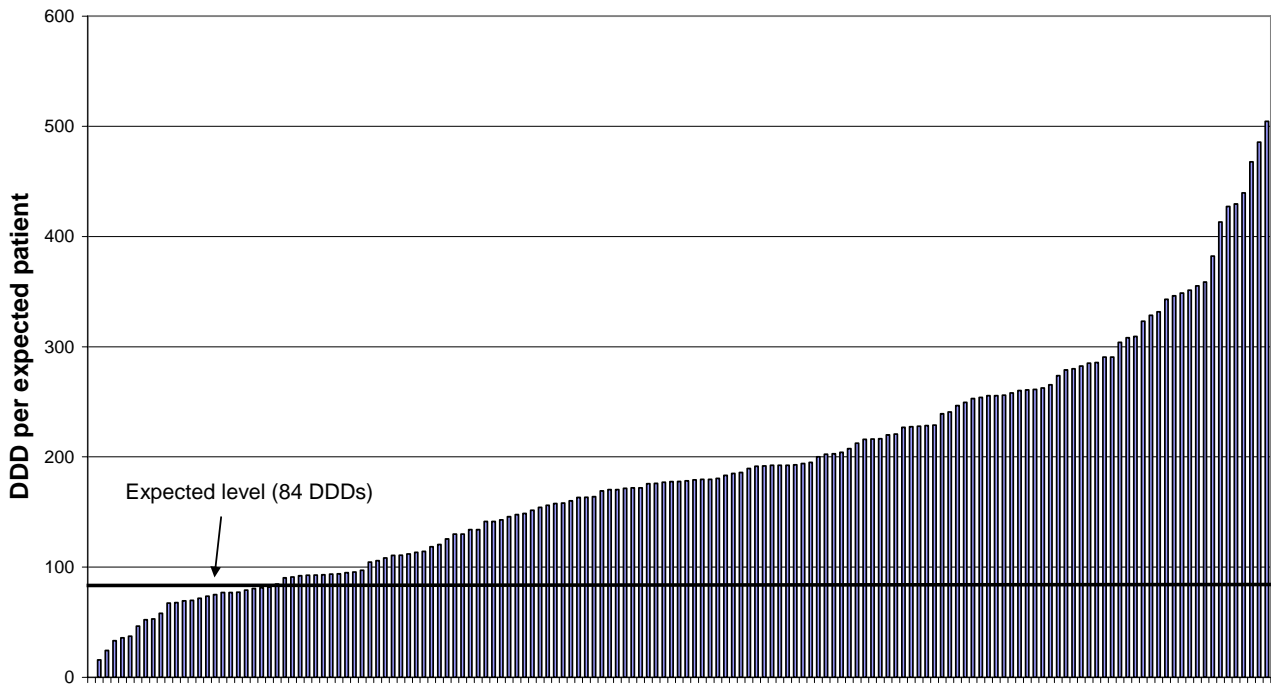


The graph below shows the number of DDDs per registered patient by PCT for 2008. The data has been taken from the primary care ePACT system. Such use accounts for over 99% of use by cost.



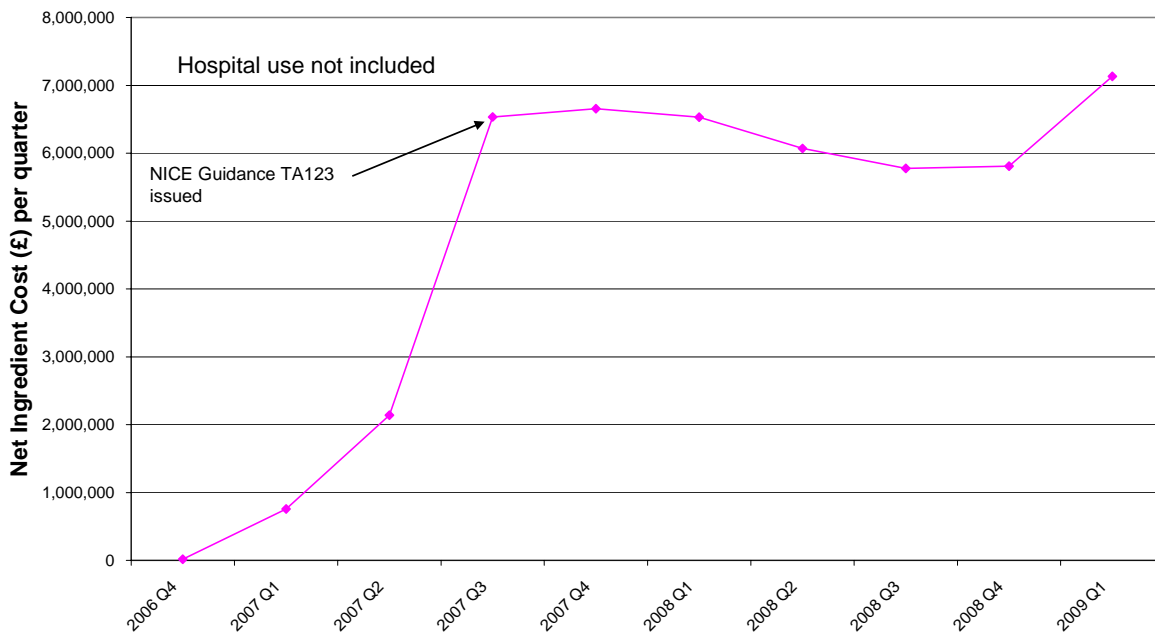
The chart below shows the number of defined daily doses per expected eligible patient by PCT, for 2008.

Varenicline 2008



The graph below shows the national (England) expenditure per quarter. Hospital use is very low, so has not been included.

Varenicline



Breast cancer (early and advanced) – trastuzumab

Overview

Trastuzumab is licensed for the treatment of early breast cancer which overexpresses human epidermal growth factor receptor-2 (HER2).

Trastuzumab is also licensed, in combination with paclitaxel or docetaxel, for metastatic breast cancer in patients with HER2-positive tumours who have not received chemotherapy for metastatic breast cancer and in whom anthracycline treatment is inappropriate.

Trastuzumab is also licensed, in combination with an aromatase inhibitor, for metastatic breast cancer in postmenopausal patients with hormone-receptor positive HER2-positive tumours not previously treated with trastuzumab.

Trastuzumab is also licensed as monotherapy for metastatic breast cancer in patients with tumours that overexpress HER2 who have received at least 2 chemotherapy regimens including, where appropriate, an anthracycline and a taxane; women with oestrogen-receptor-positive breast cancer should also have received hormonal therapy.

Relevant guidance

NICE Technology Appraisal 34 The clinical effectiveness and cost effectiveness of trastuzumab for breast cancer <http://www.nice.org.uk/ta34>

- *Trastuzumab in combination with paclitaxel is recommended as an option for people with tumours expressing human epidermal growth factor receptor 2 (HER2) scored at levels of 3+ who have not received chemotherapy for metastatic breast cancer and in whom anthracycline treatment is inappropriate.*
- *Trastuzumab monotherapy is recommended as an option for people with tumours expressing HER2 scored at levels of 3+ who have received at least two chemotherapy regimens for metastatic breast cancer. Prior chemotherapy must have included at least an anthracycline and a taxane where these treatments are appropriate. It should also have included hormonal therapy in suitable oestrogen receptor positive patients.*

NICE Technology Appraisal 107 Trastuzumab for the adjuvant treatment of early-stage HER2-positive breast cancer <http://www.nice.org.uk/ta107>

- *Trastuzumab, given at 3-week intervals for 1 year or until disease recurrence (whichever is the shorter period), is recommended as a treatment option for women with early-stage HER2-positive breast cancer following surgery, chemotherapy (neoadjuvant or adjuvant) and radiotherapy (if applicable).*

The recommendations in TA107 were updated as part of the NICE clinical guideline 80 - Early and locally advanced breast cancer. This guidance was issued in February 2009, so may not be reflected in the data available.

Expected Number of Eligible Patients

The following assumptions were used in the calculation of the expected number of eligible patients. The assumptions are taken from data on existing practice, research and the views of experts in the field used in the NICE costing template (for further detail see <http://guidance.nice.org.uk/TA107/CostTemplate/xls/English>).

Assumption	Evidence / Source
New diagnoses of breast cancer	Data from Cancer Research UK for total new cases in England in 2006. This was split across SHAs based on a split of incidence by Government Regional Office which are coterminous with SHAs, with the exception of South East. The South East GRO covers both South East SHA and South Central SHA and the cases have been split pro rata to population.
Proportion likely to have early breast cancer suitable for adjuvant treatment following surgery and chemotherapy and radiotherapy = 70%	Data from the audit of the cancer screening programme. This represents cancers detected as part of the screening programme, which is the majority of cancers, especially early stage breast cancers.
% estimated to be confirmed as HER2+ = 22%	Based on submission by manufacture Roche.
% unsuitable for treatment due to risk of adverse events = 20%	% unsuitable for treatment due to adverse events is difficult to estimate. In their original submission, Roche estimated this to be 10%. However, other information received indicates that this is an underestimation. Concerns over cardiotoxicity associated with the adjuvant treatment could increase the number excluded due to poor baseline cardiac assessment.
Advanced = new diagnoses X 6.41% X 22%	Based on manufacturer's submission and estimates of impact for the NHS, 6.41% is the estimate of cases that receive treatment for metastatic disease and 22% is the estimate of patients that are confirmed as HER2+.

Observed uptake

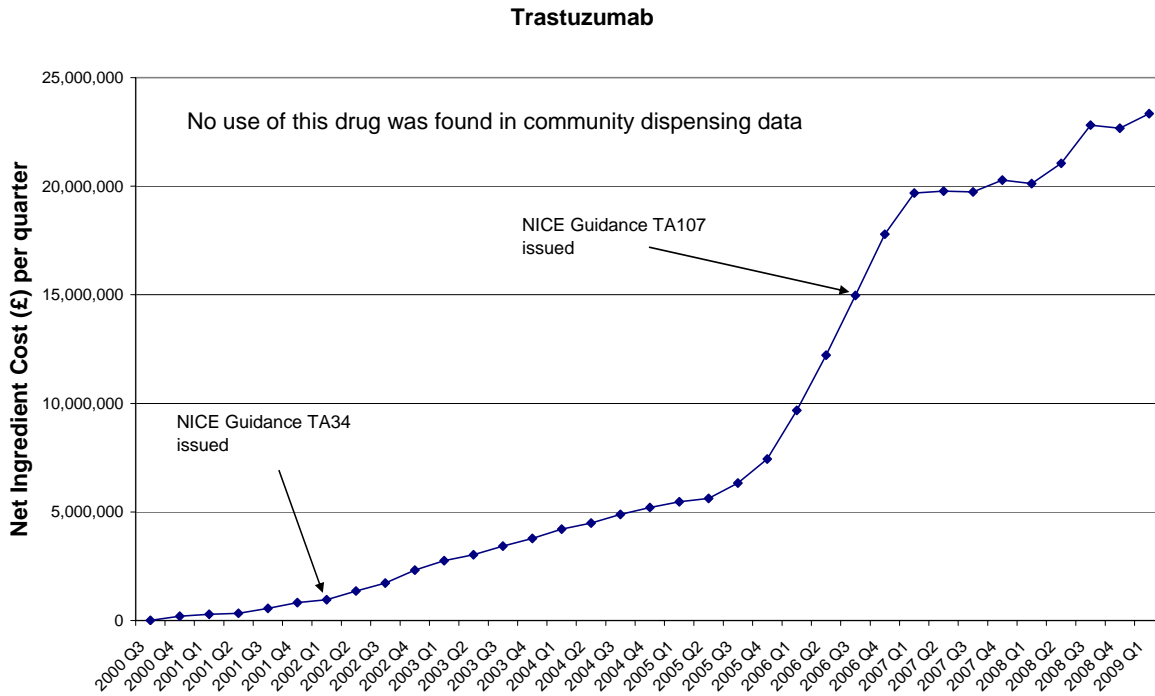
No use of trastuzumab outside secondary care was found, and so only HPAI data has been used.

Results

The NICE costing template expected an annual number of 5,218 patients. However we have found no way to convert this figure to a predicted number of doses. The 2009 edition of the

WHO table of DDDs does not define a DDD for this medicine and the BNF gives no guidance on dosage.

The graph below shows the national (England) expenditure per quarter.



Breast cancer (early) - hormonal treatments (anastrozole, exemestane, letrozole)

Overview

Anastrozole is indicated for the adjuvant treatment of oestrogen-receptor-positive early invasive breast cancer in postmenopausal women; adjuvant treatment of oestrogen-receptor-positive early breast cancer in postmenopausal women following 2–3 years of tamoxifen therapy; advanced breast cancer in postmenopausal women which is oestrogen-receptor-positive or responsive to tamoxifen.

Exemestane is indicated for the adjuvant treatment of oestrogen-receptor-positive early breast cancer in postmenopausal women following 2–3 years of tamoxifen therapy; advanced breast cancer in postmenopausal women in whom anti-oestrogen therapy has failed.

Letrozole is indicated for the adjuvant treatment of oestrogen-receptor-positive early breast cancer in postmenopausal women; advanced breast cancer in postmenopausal women (including those in whom other anti-oestrogen therapy has failed); early invasive breast cancer in postmenopausal women after standard adjuvant tamoxifen therapy; pre-operative treatment in postmenopausal women with localised hormone-receptor-positive breast cancer to allow subsequent breast conserving surgery.

Relevant guidance

NICE Technology Appraisal 112 Hormonal therapies for the adjuvant treatment of early oestrogen-receptor-positive breast cancer <http://www.nice.org.uk/ta112>

- *The aromatase inhibitors anastrozole, exemestane and letrozole, within their licensed indications, are recommended as options for the adjuvant treatment of early oestrogen-receptor-positive invasive breast cancer in postmenopausal women.*

Expected Number of Eligible Patients

The following assumptions were used in the calculation of the expected number of eligible patients. The assumptions are taken from data on existing practice, research and the views of experts in the field used in the NICE costing template (for further detail see <http://guidance.nice.org.uk/TA112/CostReport/xls/English>). This estimate is for the number of new patients who will become eligible in one year, however, treatment lasts for up to five years. Guidance was issued in November 2006, so in 2008 there should be two cohorts receiving treatment.

Assumption	Evidence / Source
New diagnoses of breast cancer rates per 100,000	National average for England by 5 year age bands used to estimate new diagnoses at PCT level.
Women aged 50 to 54: 262.3	
Women aged 55 to 59: 285.4	
Women aged 60 to 64: 332.3	
Women aged 65 to 69: 410.2	
Women aged 70 to 74: 319.9	

Women aged 75 to 79: 352.2 Women aged 80 to 84: 398.6 Women aged 85 & over: 409.7	
% of patients with stage I and II early breast cancer = 80%	The 'NHS Breast Screening Programme and association of breast surgery at BASO audit of screen detected breast cancers for the year of screening April 2004 to March 2005' states "Overall, 31% of invasive cancers were grade I, 49% were grade II, 18% were grade III and 2% were not assessable or unknown". http://www.cancerscreening.nhs.uk/breastscreen/publications/baso2004-2005.pdf
% of patients with oestrogen-receptor-positive tumours = 89%	The 'NHS Breast Screening Programme and association of breast surgery at BASO audit of screen detected breast cancers for the year of screening April 2004 to March 2005' states "Of invasive cancers with known ER status, 89% were ER positive and 11% were ER negative" (where ER is oestrogen receptor). http://www.cancerscreening.nhs.uk/breastscreen/publications/baso2004-2005.pdf
% of patients suitable for surgery = 89%	Estimated percentage of patients who are fit for surgery is taken from the assessment report.

This estimate is cumulative, as the treatment duration is five years.

Observed uptake

Use of these medicines is mainly in primary care, but HPAI and both ePACT systems were used to determine the observed use. For the graph the PCA database was used to give national figures over a longer time period.

Results

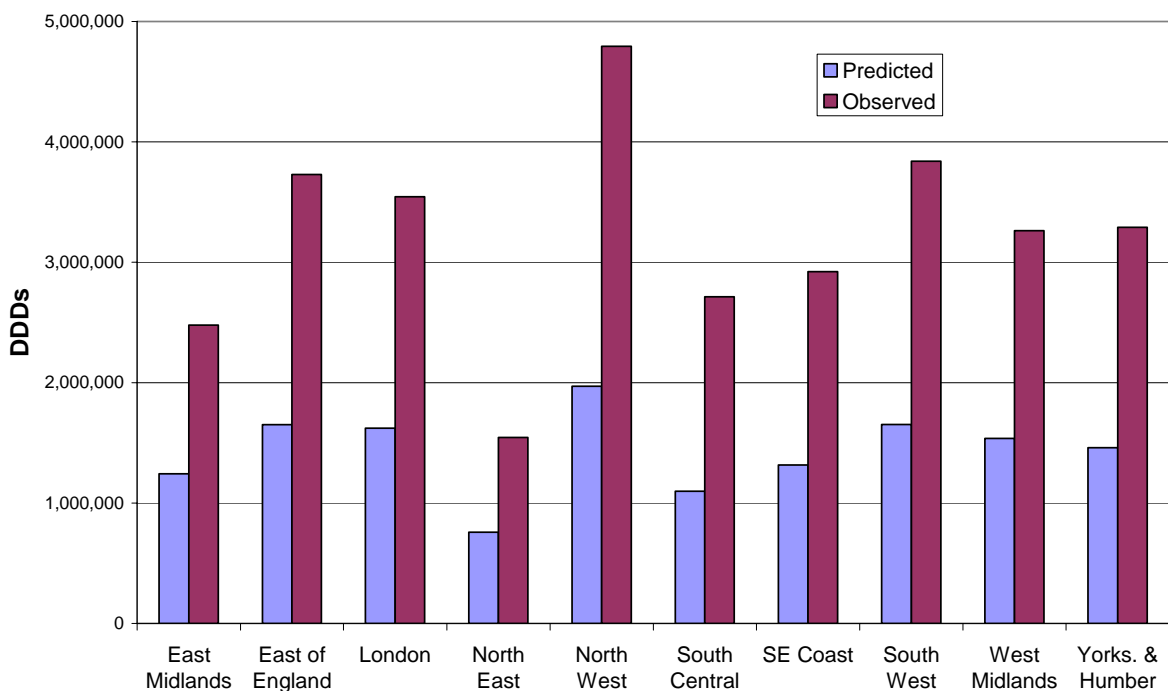
The NICE costing template expected an annual number of 19.6 thousand patients. By 2008 there should have been two cohorts receiving treatment. Assuming that treatment is continuous this would lead to a predicted use of 14,304.4 thousand doses in 2008. The observed use in 2008 was 32,145.6 thousand defined daily doses giving a ratio of 2.2 to 1.

The table below shows the data at SHA level.

SHA	Expected eligible patients (from NICE) in thousands	Predicted DDDs in thousands (assuming 2 cohorts treated in 2008)	Observed DDDs in thousands	Ratio
East Midlands	2	1,243	2,478	2.0
East of England	2	1,651	3,728	2.3
London	2	1,621	3,544	2.2
North East	1	758	1,545	2.0
North West	3	1,971	4,794	2.4
South Central	2	1,097	2,712	2.5
South East Coast	2	1,315	2,922	2.2
South West	2	1,652	3,840	2.3
West Midlands	2	1,537	3,261	2.1
Yorkshire and the Humber	2	1,459	3,291	2.3

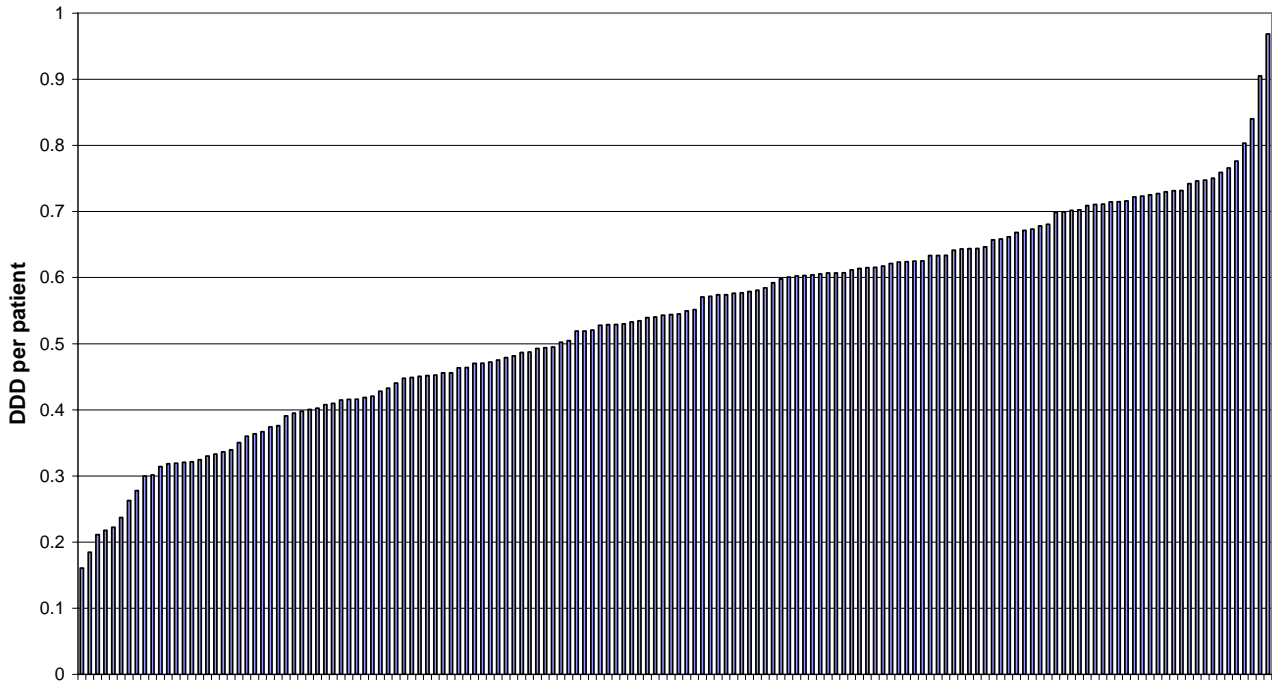
The chart below compares predicted and observed use, measured by DDDs, in 2008 by SHA.

Anastrozole, letrozole and exemestane 2008



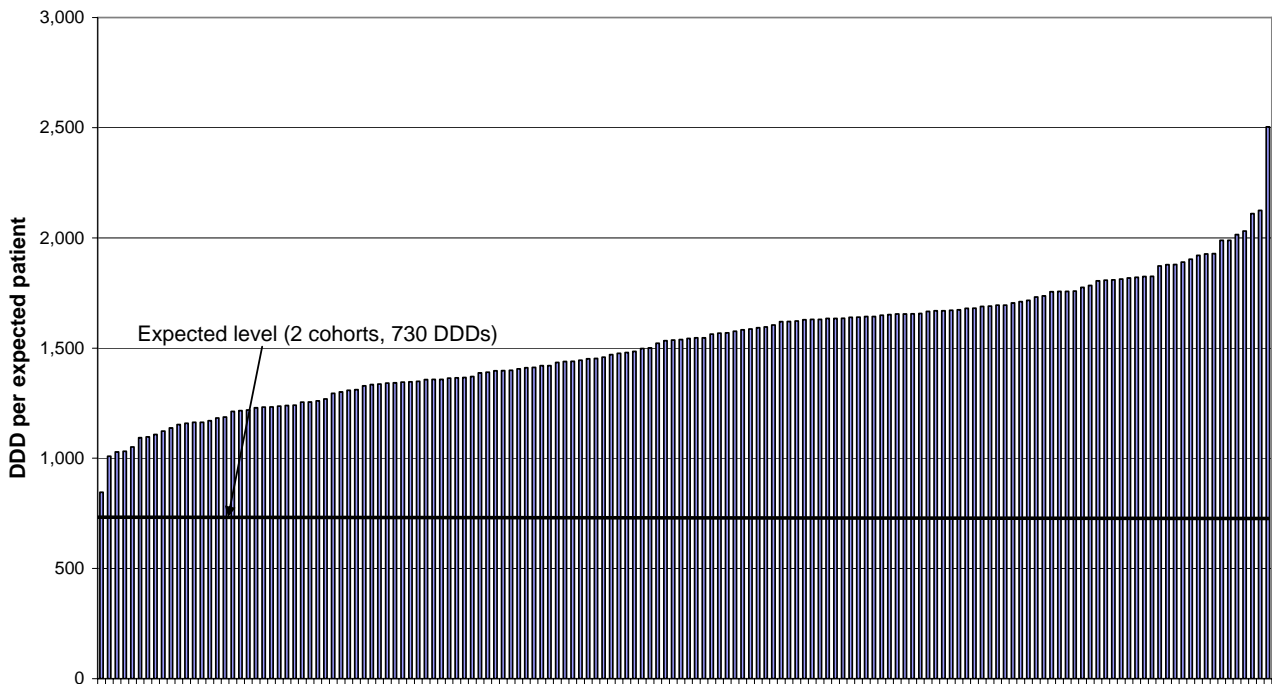
The chart below shows the number of DDDs per registered patient by PCT for 2008. Only data from the primary ePACT system has been used but this accounts for over 95% of use.

Anastrozole, exemestane and letrozole 2008



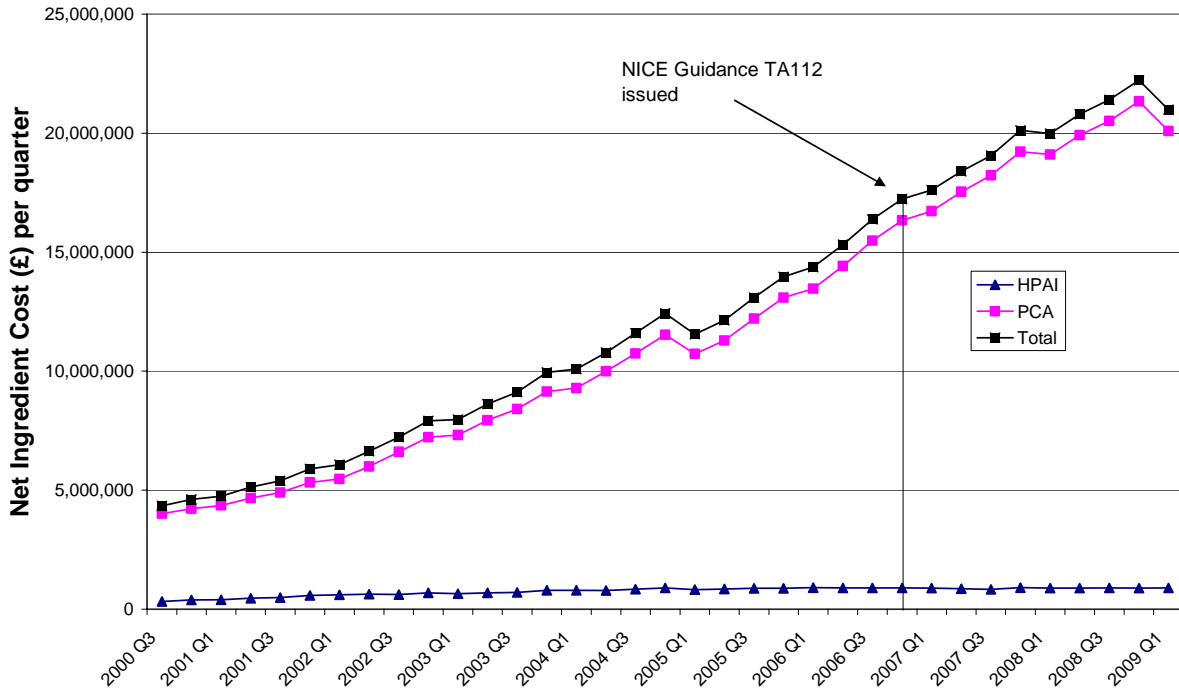
The chart below shows the number of defined daily doses per expected eligible patient by PCT for 2008.

Anastrozole, exemestane and letrozole 2008



The graph below shows the national (England) expenditure by quarter since 2000.

Anastrozole, Exemestane and Letrozole



Osteoporosis – alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide

Overview

Bisphosphonates are adsorbed onto hydroxyapatite crystals in bone, slowing both their rate of growth and dissolution, and therefore reducing the rate of bone turnover.

Bisphosphonates have an important role in the prophylaxis and treatment of osteoporosis and corticosteroid-induced osteoporosis; alendronic acid or risedronate sodium are considered the drugs of choice for these conditions, but disodium etidronate may be considered if these drugs are unsuitable or not tolerated.

Bisphosphonates are also used in the treatment of Paget's disease, hypercalcaemia of malignancy and in bone metastases in breast cancer. Disodium etidronate can impair bone mineralisation when used continuously or in high doses (such as in the treatment of Paget's disease).

Raloxifene is licensed for the treatment and prevention of postmenopausal osteoporosis; unlike hormone replacement therapy, raloxifene does not reduce menopausal vasomotor symptoms.

Strontium ranelate is indicated in the treatment of postmenopausal osteoporosis to reduce risk of vertebral and hip fractures

Teriparatide (a recombinant fragment of parathyroid hormone) is used for the treatment of postmenopausal osteoporosis, osteoporosis in men at increased risk of fracture, and corticosteroid-induced osteoporosis

Relevant guidance

NICE Technology Appraisal 160 Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women <http://www.nice.org.uk/ta160>

- *Whether or not a postmenopausal woman with osteoporosis is offered one of these drugs to prevent bone fractures will depend on her age, her bone density and how many risk factors for fracture and indicators of fragile bones she has.*
- *In principle, alendronate is recommended as a possible treatment for preventing bone fractures in postmenopausal women who have had osteoporosis diagnosed but have not had a fracture.*
- *If a woman can't take alendronate, risedronate and etidronate are recommended under certain circumstances as possible alternative treatments to prevent fractures.*
- *If a woman can't take alendronate or either risedronate or etidronate, then strontium ranelate is recommended under certain circumstances as a possible alternative treatment to prevent fractures.*

- *Raloxifene is not recommended as a treatment for preventing fractures in postmenopausal women with osteoporosis who have not had a fracture.*
- *The guidance says that women who are 75 or over may not need a bone scan to diagnose their osteoporosis.*

NICE Technology Appraisal 161 Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women <http://www.nice.org.uk/ta161>

- *Whether or not a postmenopausal woman who has had a bone fracture because of osteoporosis is offered treatment to prevent further fractures will depend on her age, her bone density and how many risk factors for fracture she has.*
- *Alendronate is recommended as a possible treatment for preventing bone fractures in postmenopausal women who have already had a fracture and have had osteoporosis diagnosed.*
- *If a woman can't take alendronate, risedronate and etidronate are recommended under certain circumstances as possible alternative treatments to prevent further fractures.*
- *If a woman can't take alendronate or either risedronate or etidronate, then strontium ranelate and raloxifene are recommended under certain circumstances as possible alternative treatments to prevent further fractures.*
- *If a woman can't take alendronate, or either risedronate or etidronate, or strontium ranelate, teriparatide is recommended under certain circumstances as a possible alternative treatment to prevent further fractures. Teriparatide is also recommended as a possible alternative treatment for a woman who has another fracture when she has been taking alendronate, risedronate or etidronate for 1 year (and her bone density has fallen).*
- *The guidance says that women who are 75 or over may not need a bone scan to diagnose their osteoporosis.*

NICE technology appraisal 161 (issued October 2008) replaces the previous technology appraisal (87) on this topic published in January 2005.

In February 2009 the High Court announced the outcome of a judicial review on the osteoporosis guidance, and NICE reiterated that the guidance remained in place.

Expected Number of Eligible Patients

The following assumptions were used in the calculation of the expected number of eligible patients. The assumptions are taken from data on existing practice, research and the views of experts in the field used in the NICE costing template. For further detail see <http://guidance.nice.org.uk/TA161/CostTemplate/xls/English>

NB: a joint template was published for TA160 & TA161.

Assumption	Evidence / Source
Prevalence osteoporosis Primary Secondary Women aged 50-54: 2% 2% Women aged 55-59: 3% 3% Women aged 60-64: 7% 7% Women aged 65-69: 12% 9% Women aged 70-74: 17% 14% Women aged 75-79: 21% 20% Women aged 80-84: 26% Women aged 85 & over: 31%	Clinical effectiveness and cost effectiveness of prevention and treatment of osteoporosis, produced by School of Health and Related Research (ScHaRR) University of Sheffield.
Proportion of post-menopausal women aged 50 years or older with osteoporosis eligible for treatment – 45.59% Postmenopausal women aged 50 years or older with osteoporosis and a clinically apparent osteoporotic fragility fracture eligible for treatment – 63.81%	See costing template for details on treatment assumptions http://guidance.nice.org.uk/TA160/CostTemplate/xls/English
Proportion of women eligible for treatment that are identified and present for treatment – 50%	Clinical opinion

This estimate is for patients with osteoporosis. The treatments are also used in Paget's disease (discussed below and actual usage adjusted) and for patients with bone metastases.

Observed uptake

Data from the HPAI and both ePACT systems was used. Some preparations of sodium risedronate were excluded as it was clear from the strength that they were intended for treatment of Paget's disease (typical daily dose 30 mg rather than the 5mg normally given for osteoporosis). Disodium etidronate is also used for Paget's disease and we excluded the 200 mg tablets and only considered the 400 mg tablets in a combined pack (where these tablets are only used for a small part of the 90 days treatment for which the pack is intended). This also meant devising a new DDD as the WHO figure is 400 mg, reflecting use for Paget's disease. We measured the use as if the tablets were used over the full 90 days, effectively giving a DDD of 62.2 mg. For teriparatide we used the BNF guidance that one pre-filled pen should provide treatment for 28 days.

For the combined products only the content of the drugs in the guidance was considered, i.e. any additional calcium or vitamin D content was excluded.

For the graph national PCA data was used with HPAI data. The preparations mentioned above were excluded.

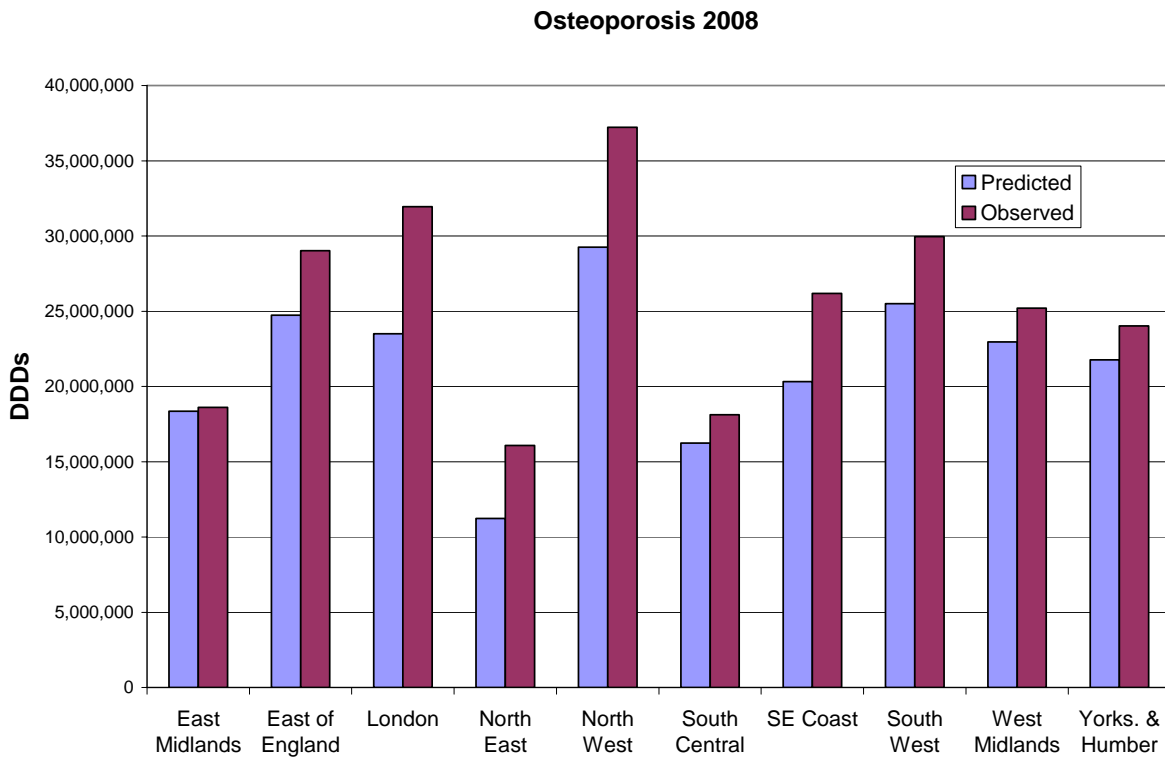
Results

The NICE costing template expected an annual number of 586.1 thousand patients. Assuming that treatment is continuous this would lead to a predicted use of 213,917.0 thousand doses per annum. The observed use in 2008 was 256,691.7 thousand defined daily doses giving a ratio of 1.2 to 1.

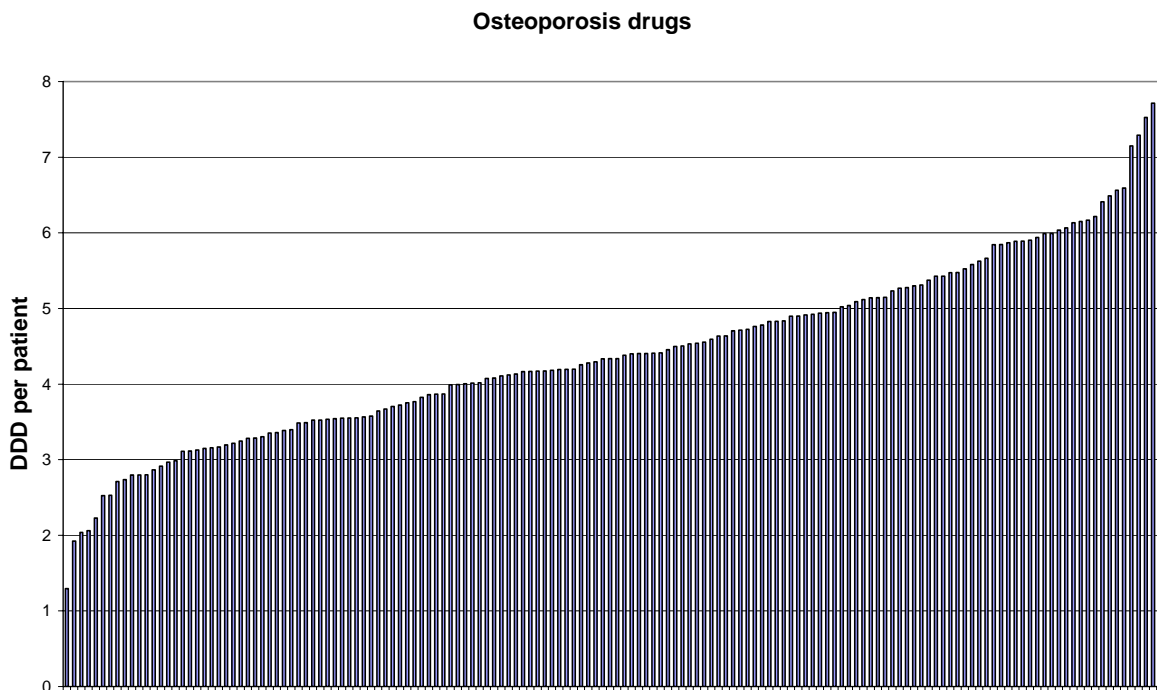
The table below shows data at SHA level.

SHA	Expected eligible patients (from NICE) in thousands	Estimated DDDs in thousands	Observed DDDs in thousands	Ratio
East Midlands	50	18,354	18,606	1.0
East of England	68	24,741	29,028	1.2
London	64	23,502	31,950	1.4
North East	31	11,235	16,079	1.4
North West	80	29,263	37,228	1.3
South Central	44	16,242	18,129	1.1
South East Coast	56	20,328	26,183	1.3
South West	70	25,511	29,955	1.2
West Midlands	63	22,966	25,207	1.1
Yorkshire and the Humber	60	21,775	24,027	1.1

The chart below compares predicted and observed use, measured by DDDs, in 2008 by SHA.

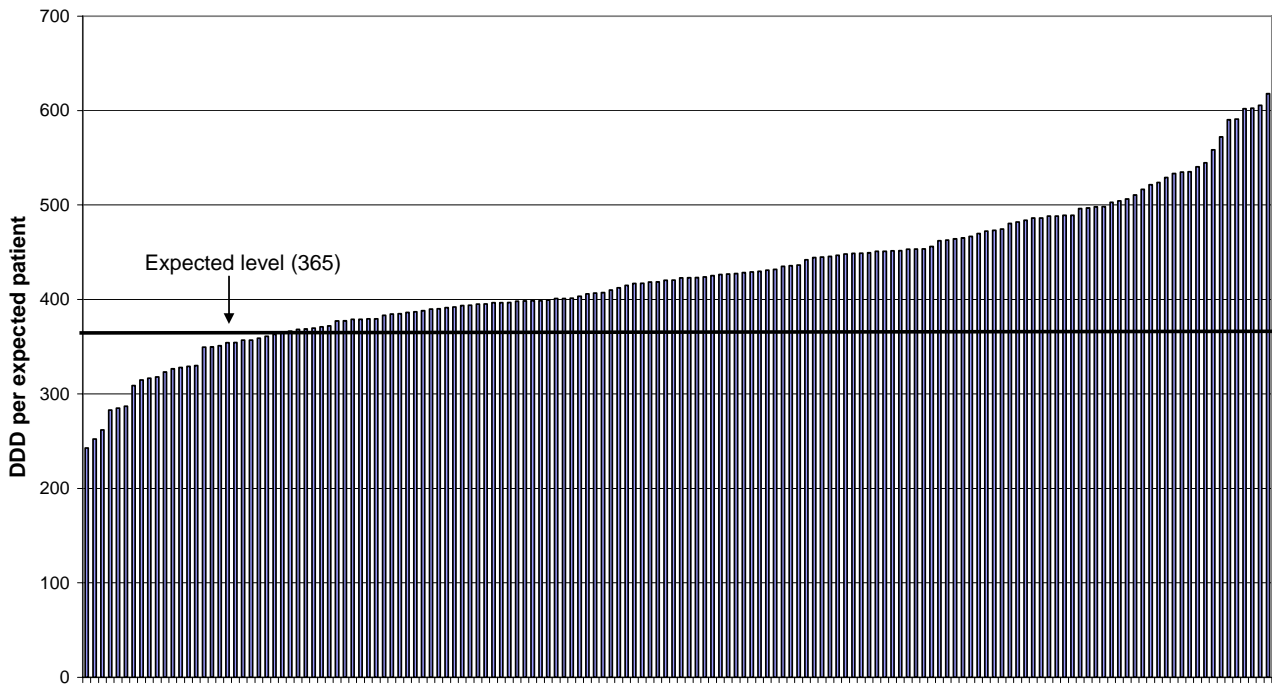


The chart below shows the number of DDDs per registered patient by PCT for 2008. Only data from the primary ePACT system has been used as this accounts for 93% of use.



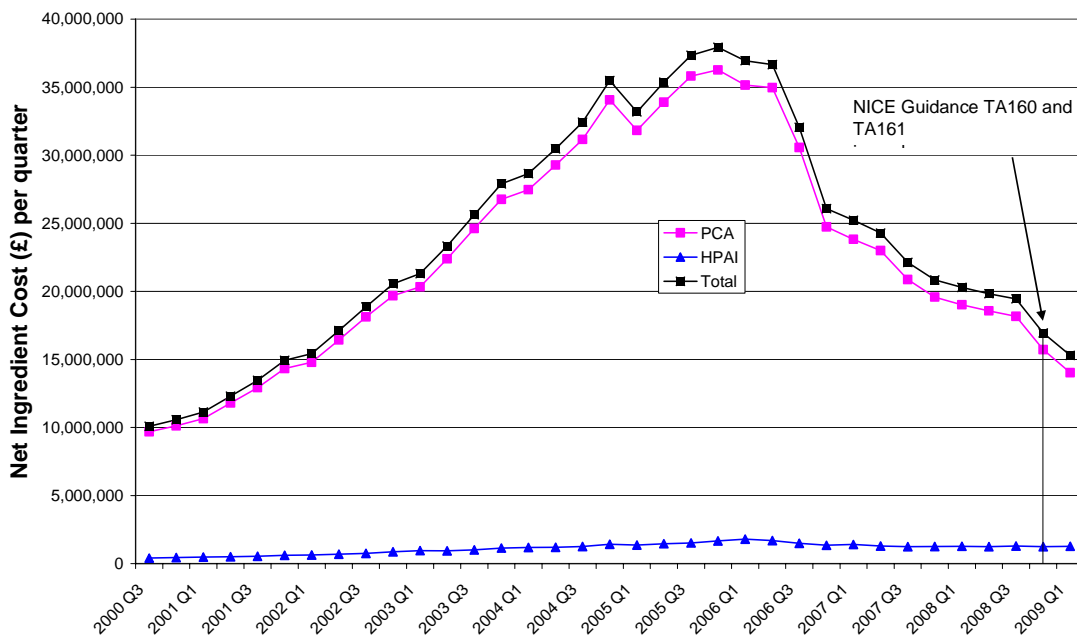
The chart below shows the number of defined daily doses per expected eligible patient by PCT for 2008.

Osteoporosis 2008



The graph below shows the national (England) expenditure by quarter. The fall in costs is associated with the availability of generic formulations.

Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide



Obesity – orlistat, sibutramine and rimonabant

Overview

Orlistat and sibutramine are licensed for the management of obesity. There is little evidence to guide selection between these drugs, but it may be appropriate to choose orlistat for those who have a high intake of fats whereas sibutramine may be chosen for those who cannot control their eating.

The marketing authorisation for rimonabant has been suspended following a review by the Committee for Medicinal Products for Human Use for the EMEA.

Combination therapy involving more than one anti-obesity drug is contra-indicated until further information about efficacy and long-term safety is available.

Relevant guidance

NICE Clinical Guideline 43 Obesity guidance on the prevention, identification, assessment and management of overweight and obesity in adults and children <http://www.nice.org.uk/cg43>

- *Drug treatment should be considered for patients who have not reached their target weight loss or have reached a plateau on dietary, activity and behavioural changes alone.*
- *Drug treatment is not generally recommended for children younger than 12 years.*
- *In children aged 12 years and older, treatment with orlistat or sibutramine is recommended only if physical comorbidities (such as orthopaedic problems or sleep apnoea) or severe psychological comorbidities are present.*

The NICE CG43 Obesity published in December 2006 replaced the original pieces of guidance regarding the use of these drugs: TA22 Obesity – orlistat (March 2001) and TA31 Obesity – sibutramine (October 2001).

Expected Number of Eligible Patients

The following assumptions were used in the calculation of the expected number of eligible patients. The assumptions are taken from data on existing practice, research and the views of experts in the field used in the NICE costing report (for further detail see <http://guidance.nice.org.uk/CG43/CostReport/pdf/English>).

Assumption	Evidence / Source
Number of children aged 12-16 and adults aged 16 and over that are overweight or obese.	Health Survey for England proportion of people that are overweight or obese, within different age bands
Number of children aged 12-16 that have co-morbidities or complex needs = 1.5%	Daniels SR (2006) The consequences of childhood overweight and obesity. The Future of Children 16: 47–67.

Number of overweight or obese children aged 12-16 with co-morbidities or complex needs that are considered for pharmacological treatment = 10%	Clinical opinion based on recommendations relating to children in the Clinical Guideline on prevention and treatment of obesity (CG43).
Percentage of overweight or obese adults initiated with pharmacological therapy = 1.41%	Data included in manufacturer's submission on total prescribing for drugs to treat obesity.

Observed uptake

Orlistat, sibutramine and rimonabant are used in hospitals as well as in the community and so data has been taken from the HPAI database as well as the two versions of ePACT. For the graph the HPAI and PCA databases were used to give data over a longer period.

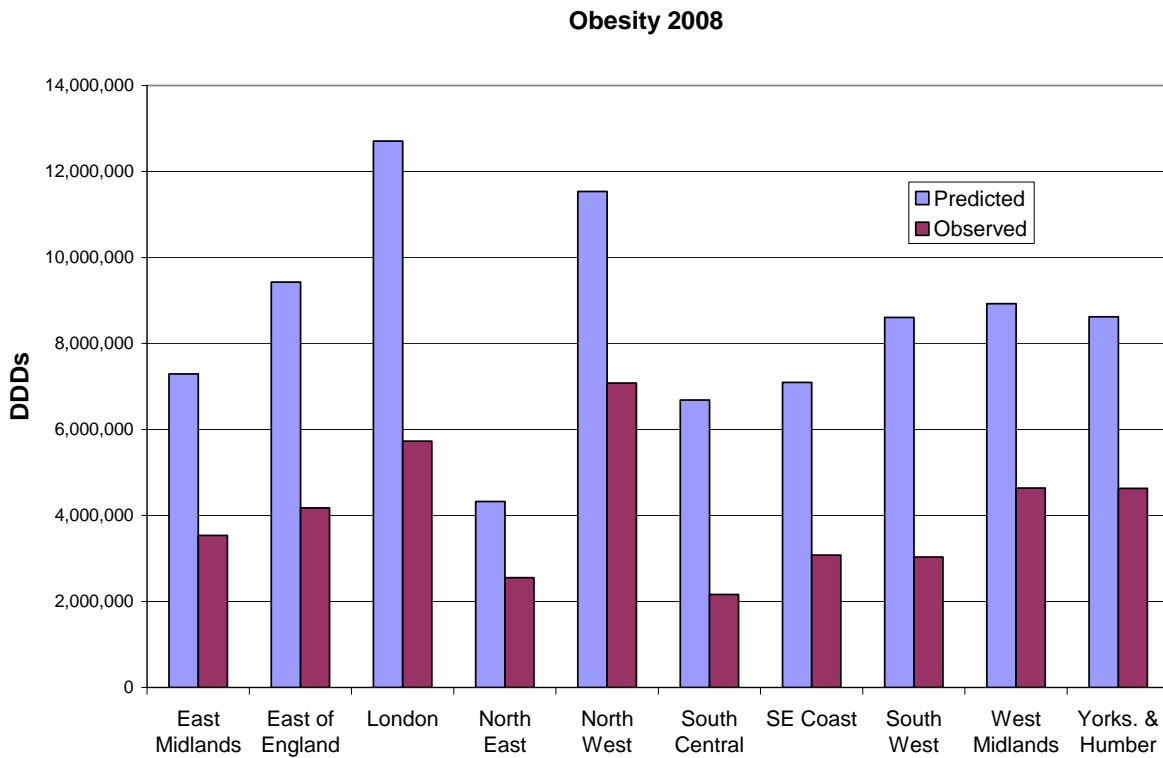
Results

The NICE costing template expected an annual number of 311.3 thousand patients. It is not clear for how long the guidance anticipates treatment to continue but we have used 9 months for our estimates. This would lead to a predicted use of 85,227.4 thousand doses per year. The observed use in 2008 was 40,676.9 thousand defined daily doses, a ratio of 0.5 to 1.

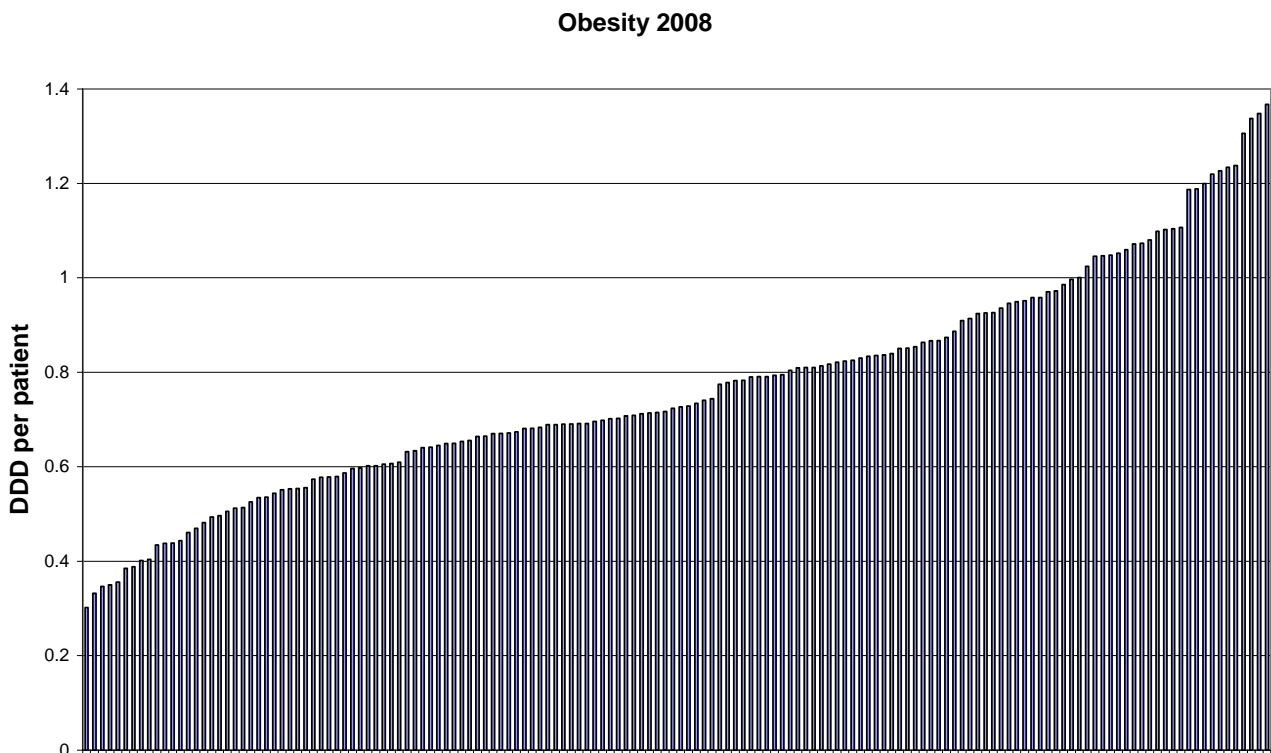
The table below shows data at SHA level.

SHA	Expected eligible patients (from NICE) in thousands	Predicted DDDs in thousands (assuming 9 months treatment)	Observed DDDs in thousands	Ratio
East Midlands	27	7,292	3,536	0.5
East of England	34	9,426	4,178	0.4
London	46	12,709	5,728	0.5
North East	16	4,327	2,556	0.6
North West	42	11,537	7,079	0.6
South Central	24	6,683	2,165	0.3
South East Coast	26	7,096	3,078	0.4
South West	31	8,608	3,034	0.4
West Midlands	33	8,929	4,637	0.5
Yorkshire and the Humber	31	8,621	4,629	0.5

The chart below compares predicted and observed use, measured by DDDs, in 2008 by SHA.

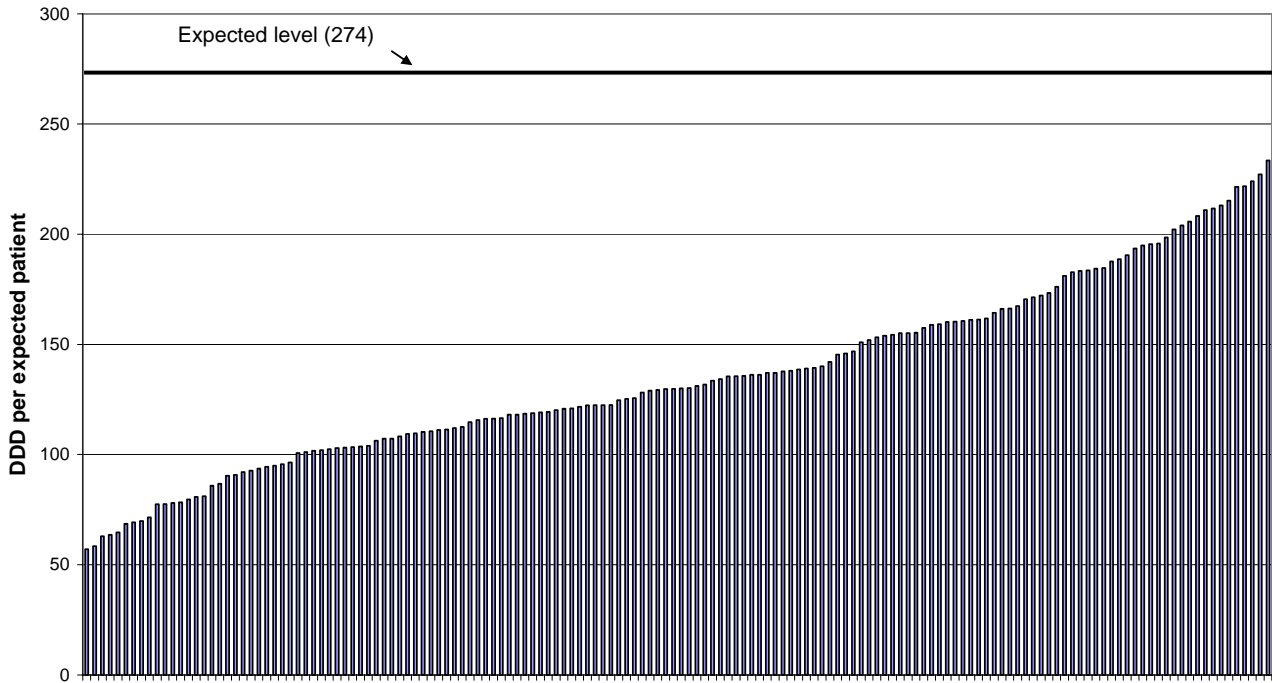


The chart below shows the number of DDDs per registered patient by PCT for 2008. Only data from the primary ePACT system has been used as this accounts for over 98% of use.



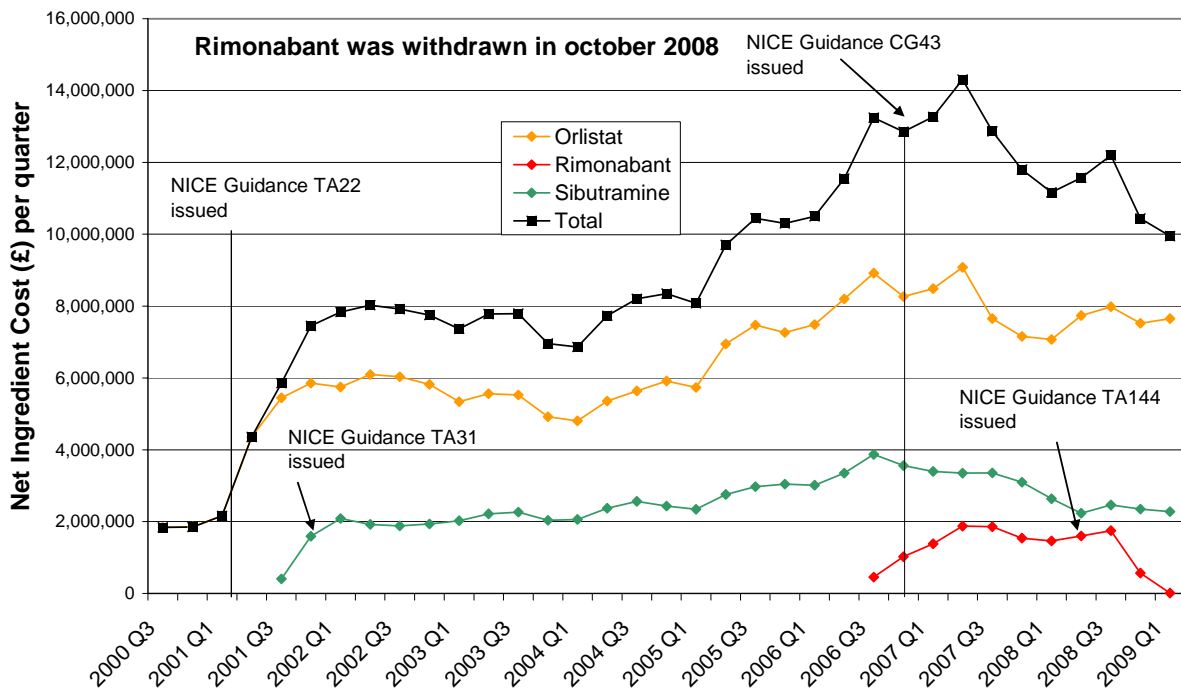
The chart below shows the number of DDDs per expected eligible patient by PCT for 2008.

Obesity 2008



The graph below shows national (England) expenditure by quarter.

Anti-obesity drugs



Future Developments

This is the first in a planned series of reports, and has experimental status. We hope to improve data collection and reporting in the future. We anticipate that improvements will also be informed by feedback from users.

The Metrics Working Group has recommended that the following issues should be considered for future reports:

- consideration of the methodology used in this report, with a view to:
 - developing ways to estimate the numbers of eligible patients, particularly at a local level
 - developing better estimates of the average duration of treatment
- the inclusion of newly appraised medicines
- the inclusion of medicines with multiple indications
- the use of Hospital Episode Statistics (HES) data to support the estimate of patient numbers for conditions managed predominantly in secondary care
- the use of drug utilisation data from other sources, such as clinical networks, the pharmaceutical industry or healthcare companies, to enhance the drug utilisation information currently available

If you wish to comment, please use the associated feedback form, which includes questions and requests general comments and suggestions.

Appendix

The table below lists all the technologies considered by the Metrics Working Group, excluding those in this report, with the reason they were not included.

HTA date	HTA number	HTA name	Drug	Recommendation	Reason for non-selection
09/2002	47	47: Guidance on the use of glycoprotein IIb/IIIa inhibitors in the treatment of acute coronary syndromes	Abciximab	Restricted	Multiple indications
08/2007	125	125: Adalimumab for the treatment of psoriatic arthritis	Adalimumab	Restricted	Multiple indications
10/2007	130	130: Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis	Adalimumab	Restricted	Multiple indications
05/2008	143	143: Adalimumab, etanercept and infliximab for ankylosing spondylitis	Adalimumab	Restricted	Multiple indications
06/2008	146	146: Adalimumab for the treatment of adults with psoriasis	Adalimumab	Restricted	Multiple indications
02/2006	96	96: Adefovir dipivoxil and peginterferon alfa-2a for the treatment of chronic hepatitis B	Adefovir dipivoxil	Recommended	Complex clinical area
10/2002	52	52: Guidance on the use of drugs for early thrombolysis in the treatment of acute myocardial infarction	Alteplase	Restricted	Multiple indications
06/2007	122	122: Alteplase for the treatment of acute ischaemic stroke	Alteplase	Recommended	Multiple indications
03/2006	98	98: Methylphenidate, atomoxetine and dexamfetamine for attention deficit hyperactivity disorder (ADHD) in children and adolescents	Atomoxetine	Recommended	Data not available by age group

HTA date	HTA number	HTA name	Drug	Recommendation	Reason for non-selection
01/2006	94	94: Statins for the prevention of cardiovascular events	Statins	Restricted	Limited potential to add value as other reviews available
09/2004	85	85: Immunosuppressive therapy for renal transplantation in adults	Basiliximab	Recommended	Data not available by age group
04/2006	99	99: Immunosuppressive therapy for renal transplantation in children and adolescents	Basiliximab	Recommended	Data not available by age group
11/2007	131	131: Inhaled corticosteroids for the treatment of chronic asthma in children under the age of 12 years	Beclometasone	Recommended	Data not available by age group
10/2007	129	129: Bortezomib monotherapy for relapsed multiple myeloma	Bortezomib	Restricted	Complex clinical area
11/2007	131	131: Inhaled corticosteroids for the treatment of chronic asthma in children under the age of 12 years	Budesonide	Recommended	Data not available by age group
01/2007	114	114: Methadone and buprenorphine for the management of opioid dependence	Buprenorphine	Recommended	Incomplete data
03/2002	39	39: Guidance on the use of nicotine replacement therapy (NRT) and bupropion for smoking cessation	Bupropion	Restricted	Incomplete data
05/2003	61	61: Guidance on the use of capecitabine and tegafur with uracil for metastatic colorectal cancer	Capecitabine	Recommended	Multiple indications
05/2003	62	62: Guidance on the use of capecitabine for the treatment of locally advanced or metastatic breast cancer	Capecitabine	Recommended	Multiple indications
04/2006	100	100: Capecitabine and oxaliplatin in the adjuvant treatment of stage III (Dukes' C) colon cancer	Capecitabine	Recommended	Multiple indications

HTA date	HTA number	HTA name	Drug	Recommendation	Reason for non-selection
07/2001	27	27: Guidance on the use of cyclo-oxygenase (Cox) II selective inhibitors, celecoxib, rofecoxib, meloxicam and etodolac for osteoarthritis and rheumatoid arthritis	Celecoxib	Restricted	Multiple indications, Subsequent safety concerns
06/2008	145	145: Cetuximab for the treatment of locally advanced squamous cell cancer of the head and neck	Cetuximab	Restricted	Too recent
01/2007	117	117: Cinacalcet for the treatment of secondary hyperparathyroidism in patients with end-stage renal disease on maintenance dialysis therapy	Cinacalcet	Restricted	Multiple indications
07/2004	80	80: Clopidogrel in the treatment of non-ST-segment-elevation acute coronary syndrome	Clopidogrel	Restricted	Multiple indications
05/2005	90	90: Clopidogrel and modified-release dipyridamole in the prevention of occlusive vascular events	Clopidogrel	Restricted	Multiple indications
06/2002	43	43: Guidance on the use of newer (atypical) antipsychotic drugs for the treatment of schizophrenia	Clozapine	Recommended	TA replaced
09/2008	157	157: Dabigatran etexilate for the prevention of venous thromboembolism after hip or knee replacement surgery in adults	Dabigatran etexilate	Recommended	Too recent
09/2004	85	85: Immunosuppressive therapy for renal transplantation in adults	Daclizumab	Recommended	Data not available by age group
04/2006	99	99: Immunosuppressive therapy for renal transplantation in children and adolescents	Daclizumab	Recommended	Data not available by age group

HTA date	HTA number	HTA name	Drug	Recommendation	Reason for non-selection
03/2006	98	98: Methylphenidate, atomoxetine and dexamfetamine for attention deficit hyperactivity disorder (ADHD) in children and adolescents	Dexamfetamine	Recommended	Data not available by age group
05/2005	90	90: Clopidogrel and modified-release dipyridamole in the prevention of occlusive vascular events	Dipyridamole (modified release)	Restricted	Multiple indications
06/2000	6	6: Guidance on the use of taxanes for breast cancer	Docetaxel	Restricted	Multiple indications
06/2001	26	26: Guidance on the use of docetaxel, paclitaxel, gemcitabine and vinorelbine for the treatment of non-small cell lung cancer	Docetaxel	Restricted	Multiple indications
09/2001	30	30: Guidance on the use of taxanes for the treatment of breast cancer	Docetaxel	Restricted	Multiple indications
06/2006	101	101: Docetaxel for the treatment of hormone-refractory metastatic prostate cancer	Docetaxel	Restricted	Multiple indications
09/2006	109	109: Docetaxel for the adjuvant treatment of early node-positive breast cancer	Docetaxel	Recommended	Multiple indications
07/2006	103	103: Etanercept and efalizumab for the treatment of adults with psoriasis	Efalizumab	Restricted	Withdrawn from market
05/2008	142	142: Epoetin alfa, epoetin beta and darbepoetin alfa for cancer treatment-induced anaemia	Epoetin alfa, epoetin beta and darbepoetin alfa	Restricted	Multiple indications
09/2002	47	47: Guidance on the use of glycoprotein IIb/IIIa inhibitors in the treatment of acute coronary syndromes	Eptifibatide	Restricted	Complex clinical area
11/2008	162	162: Erlotinib for the treatment of non-small cell lung cancer	Erlotinib	Restricted	Too recent

HTA date	HTA number	HTA name	Drug	Recommendation	Reason for non-selection
03/2002	35	35: Guidance on the use of etanercept for the treatment of juvenile idiopathic arthritis	Etanercept	Restricted	Multiple indications
03/2002	36	36: Guidance on the use of etanercept and infliximab for the treatment of rheumatoid arthritis	Etanercept	Restricted	Multiple indications
07/2006	103	103: Etanercept and efalizumab for the treatment of adults with psoriasis	Etanercept	Restricted	Multiple indications
07/2006	104	104: Etanercept and infliximab for the treatment of adults with psoriatic arthritis	Etanercept	Restricted	Multiple indications
10/2007	130	130: Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis	Etanercept	Restricted	Multiple indications
05/2008	143	143: Adalimumab, etanercept and infliximab for ankylosing spondylitis	Etanercept	Restricted	Multiple indications
07/2001	27	27: Guidance on the use of cyclo-oxygenase (Cox) II selective inhibitors, celecoxib, rofecoxib, meloxicam and etodolac for osteoarthritis and rheumatoid arthritis	Etodolac	Restricted	Subsequent safety concerns
11/2007	131	131: Inhaled corticosteroids for the treatment of chronic asthma in children under the age of 12 years	Fluticasone	Recommended	Data not available by age group
01/2006	94	94: Statins for the prevention of cardiovascular events	Fluvastatin	Restricted	Limited potential to add value as other studies have covered statins
03/2004	76	76: Newer drugs for epilepsy in adults	Gabapentin	Restricted	Data not available by age group
04/2004	79	79: Newer drugs for epilepsy in children	Gabapentin	Recommended	Data not available by age group
05/2001	25	25: Guidance on the use of gemcitabine for the treatment of pancreatic cancer	Gemcitabine	Restricted	Multiple indications

HTA date	HTA number	HTA name	Drug	Recommendation	Reason for non-selection
06/2001	26	26: Guidance on the use of docetaxel, paclitaxel, gemcitabine and vinorelbine for the treatment of non-small cell lung cancer	Gemcitabine	Recommended	Multiple indications
01/2007	116	116: Gemcitabine for the treatment of metastatic breast cancer	Gemcitabine	Restricted	Multiple indications
09/2002	47	47: Guidance on the use of glycoprotein IIb/IIIa inhibitors in the treatment of acute coronary syndromes	GP IIb/IIIa inhibitor	Restricted	Complex clinical area
10/2002	50	50: Guidance on the use of imatinib for chronic myeloid leukaemia	Imatinib	Restricted	Multiple indications
10/2003	70	70: Guidance on the use of imatinib for chronic myeloid leukaemia	Imatinib	Restricted	Multiple indications
10/2004	86	86: Imatinib for the treatment of unresectable and/or metastatic gastrointestinal stromal tumours	Imatinib	Restricted	Multiple indications
03/2002	36	36: Guidance on the use of etanercept and infliximab for the treatment of rheumatoid arthritis	Infliximab	Restricted	Multiple indications
07/2006	104	104: Etanercept and infliximab for the treatment of adults with psoriatic arthritis	Infliximab	Restricted	Multiple indications
10/2007	130	130: Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis	Infliximab	Restricted	Multiple indications
01/2008	134	134: Infliximab for the treatment of adults with psoriasis	Infliximab	Restricted	Multiple indications
12/2002	53	53: Guidance on the use of long-acting insulin analogues for the treatment of diabetes - insulin glargine	Insulin glargine	Restricted	Already known to exceed NICE estimates

HTA date	HTA number	HTA name	Drug	Recommendation	Reason for non-selection
08/2005	93	93: Irinotecan, oxaliplatin and raltitrexed for the treatment of advanced colorectal cancer	Irinotecan	Recommended	Multiple indications
03/2004	76	76: Newer drugs for epilepsy in adults	Lamotrigine	Restricted	Data not available by age group
04/2004	79	79: Newer drugs for epilepsy in children	Lamotrigine	Recommended	Data not available by age group
03/2004	76	76: Newer drugs for epilepsy in adults	Levetiracetam	Restricted	Data not available by age group
07/2001	27	27: Guidance on the use of cyclo-oxygenase (Cox) II selective inhibitors, celecoxib, rofecoxib, meloxicam and etodolac for osteoarthritis and rheumatoid arthritis	Meloxicam	Restricted	Subsequent safety concerns
01/2007	114	114: Methadone and buprenorphine for the management of opioid dependence	Methadone	Recommended	Incomplete data
03/2006	98	98: Methylphenidate, atomoxetine and dexamfetamine for attention deficit hyperactivity disorder (ADHD) in children and adolescents	Methylphenidate	Recommended	Data not available by age group
09/2004	85	85: Immunosuppressive therapy for renal transplantation in adults	Mycophenolate mofetil	Restricted	Data not available by age group
04/2006	99	99: Immunosuppressive therapy for renal transplantation in children and adolescents	Mycophenolate mofetil	Restricted	Data not available by age group
01/2007	115	115: Naltrexone for the management of opioid dependence	Naltrexone	Restricted	Incomplete data
03/2002	39	39: Guidance on the use of nicotine replacement therapy (NRT) and bupropion for smoking cessation	Nicotine replacement therapy	Restricted	Incomplete data

HTA date	HTA number	HTA name	Drug	Recommendation	Reason for non-selection
06/2002	43	43: Guidance on the use of newer (atypical) antipsychotic drugs for the treatment of schizophrenia	Olanzapine	Recommended	TA replaced
09/2003	66	66: Olanzapine and valproate semisodium in the treatment of acute mania associated with bipolar 1 disorder	Olanzapine	Recommended	Multiple indications
02/2003	58	58: Guidance on the use of zanamivir, oseltamivir and amantadine for the treatment of influenza	Oseltamivir	Restricted	Multiple indications
09/2003	67	67: Guidance on the use of oseltamivir and amantadine for the prophylaxis of influenza	Oseltamivir	Restricted	Multiple indications
09/2008	158	158: Oseltamivir, amantadine (review) and zanamivir for the prophylaxis of influenza	Oseltamivir	Restricted	Multiple indications
03/2002	33	33: Guidance on the use of irinotecan, oxaliplatin & raltitrexed for the treatment of advanced colorectal cancer	Oxaliplatin	Restricted	Multiple indications
08/2005	93	93: Irinotecan, oxaliplatin and raltitrexed for the treatment of advanced colorectal cancer	Oxaliplatin	Recommended	Multiple indications
04/2006	100	100: Capecitabine and oxaliplatin in the adjuvant treatment of stage III (Dukes' C) colon cancer	Oxaliplatin	Recommended	Multiple indications
03/2004	76	76: Newer drugs for epilepsy in adults	Oxcarbazepine	Restricted	Data not available by age group
04/2004	79	79: Newer drugs for epilepsy in children	Oxcarbazepine	Recommended	Data not available by age group
06/2001	26	26: Guidance on the use of docetaxel, paclitaxel, gemcitabine and vinorelbine for the treatment of non-small cell lung cancer	Paclitaxel	Recommended	Multiple indications

HTA date	HTA number	HTA name	Drug	Recommendation	Reason for non-selection
01/2003	55	55: Guidance on the use of paclitaxel in the treatment of ovarian cancer	Paclitaxel	Restricted	Multiple indications
05/2005	91	91: Paclitaxel, pegylated liposomal doxorubicin hydrochloride and topotecan for second-line or subsequent treatment of advanced ovarian cancer	Paclitaxel	Restricted	Multiple indications
02/2006	96	96: Adefovir dipivoxil and peginterferon alfa-2a for the treatment of chronic hepatitis B	Peginterferon alfa-2a	Recommended	Multiple indications
08/2006	106	106: Peginterferon alfa and ribavirin for the treatment of mild chronic hepatitis C	Peginterferon alfa-2a	Restricted	multiple indications
08/2006	106	106: Peginterferon alfa and ribavirin for the treatment of mild chronic hepatitis C	Peginterferon alfa-2b	Restricted	multiple indications
01/2004	75	75: Interferon alfa (pegylated and non-pegylated) and ribavirin for the treatment of chronic hepatitis C	Peginterferon alpha	Restricted	Multiple indications
05/2005	91	91: Paclitaxel, pegylated liposomal doxorubicin hydrochloride and topotecan for second-line or subsequent treatment of advanced ovarian cancer	Pegylated liposomal doxorubicin hydrochloride	Restricted	Complex clinical area
01/2008	135	135: Pemetrexed for the treatment of malignant pleural mesothelioma	Pemetrexed	Restricted	Too recent
08/2004	82	82: Tacrolimus and pimecrolimus for atopic eczema	Pimecrolimus	Restricted	Multiple indications
08/2003	63	63: Guidance on the use of glitazones for the treatment of type 2 diabetes	Pioglitazone	Restricted	
07/2000	7	7: Guidance on the use of proton pump inhibitors in the treatment of dyspepsia	Proton Pump Inhibitor	Restricted	Multiple indications
06/2002	43	43: Guidance on the use of newer (atypical) antipsychotic drugs for the treatment of schizophrenia	Quetiapine	Recommended	TA replaced

HTA date	HTA number	HTA name	Drug	Recommendation	Reason for non-selection
08/2008	155	155: Ranibizumab and pegaptanib for the treatment of age-related macular degeneration	Ranibizumab	Restricted	Incomplete data
10/2002	52	52: Guidance on the use of drugs for early thrombolysis in the treatment of acute myocardial infarction	Retepase	Recommended	Incomplete data
06/2002	43	43: Guidance on the use of newer (atypical) antipsychotic drugs for the treatment of schizophrenia	Risperidone	Recommended	TA replaced
03/2002	37	37: Guidance on the use of rituximab for recurrent or refractory Stage III or IV follicular non-Hodgkin's lymphoma	Rituximab	Restricted	Multiple indications
09/2003	65	65: Rituximab for aggressive non-Hodgkin's lymphoma	Rituximab	Restricted	Multiple indications
09/2006	110	110: Rituximab for the treatment of follicular lymphoma	Rituximab	Recommended	Multiple indications
08/2007	126	126: Rituximab for the treatment of rheumatoid arthritis	Rituximab	Restricted	Multiple indications
02/2008	137	137: Rituximab for the treatment of relapsed or refractory stage III and IV follicular non-Hodgkin's lymphoma	Rituximab	Recommended	Multiple indications
08/2003	63	63: Guidance on the use of glitazones for the treatment of type 2 diabetes	Rosiglitazone	Restricted	Recent safety concerns
06/2002	43	43: Guidance on the use of newer (atypical) antipsychotic drugs for the treatment of schizophrenia	Sertindole	Recommended	TA replaced
09/2004	85	85: Immunosuppressive therapy for renal transplantation in adults	Sirolimus	Restricted	Data not available by age group
04/2006	99	99: Immunosuppressive therapy for renal transplantation in children and adolescents	Sirolimus	Restricted	Data not available by age group

HTA date	HTA number	HTA name	Drug	Recommendation	Reason for non-selection
05/2002	42	42: Guidance on the use of human growth hormone (somatropin) in children with growth failure	Somatropin	Recommended	Multiple indications
08/2003	64	64: Human growth hormone (somatropin) in adults with growth hormone deficiency	Somatropin	Recommended	Multiple indications
10/2002	52	52: Guidance on the use of drugs for early thrombolysis in the treatment of acute myocardial infarction	Streptokinase	Restricted	Multiple indications
08/2004	82	82: Tacrolimus and pimecrolimus for atopic eczema	Tacrolimus	Recommended	Multiple indications
09/2004	85	85: Immunosuppressive therapy for renal transplantation in adults	Tacrolimus	Recommended	Data not available by age group
04/2006	99	99: Immunosuppressive therapy for renal transplantation in children and adolescents	Tacrolimus	Recommended	Data not available by age group
05/2003	61	61: Guidance on the use of capecitabine and tegafur with uracil for metastatic colorectal cancer	Tegafur with uracil	Recommended	Complex clinical area
04/2001	23	23: Guidance on the use of temozolomide for the treatment of recurrent malignant glioma (brain cancer)	Temozolomide	Restricted	Multiple indications
06/2007	121	121: Carmustine implants and temozolomide for the treatment of newly diagnosed high-grade glioma	Temozolomide	Restricted	Multiple indications
10/2002	52	52: Guidance on the use of drugs for early thrombolysis in the treatment of acute myocardial infarction	Tenecteplase	Recommended	Incomplete data sets
03/2004	76	76: Newer drugs for epilepsy in adults	Tiagabine	Restricted	Data not available by age group
04/2004	79	79: Newer drugs for epilepsy in children	Tiagabine	Recommended	Data not available by age group

HTA date	HTA number	HTA name	Drug	Recommendation	Reason for non-selection
09/2002	47	47: Guidance on the use of glycoprotein IIb/IIIa inhibitors in the treatment of acute coronary syndromes	Tirofiban	Recommended	Complex clinical area
03/2004	76	76: Newer drugs for epilepsy in adults	Topiramate	Restricted	Data not available by age group
04/2004	79	79: Newer drugs for epilepsy in children	Topiramate	Recommended	Data not available by age group
07/2001	28	28: Guidance on the use of topotecan for treatment of advanced ovarian cancer	Topotecan	Restricted	Multiple indications
05/2005	91	91: Paclitaxel, pegylated liposomal doxorubicin hydrochloride and topotecan for second-line or subsequent treatment of advanced ovarian cancer	Topotecan	Restricted	Multiple indications
09/2003	66	66: Olanzapine and valproate semisodium in the treatment of acute mania associated with bipolar 1 disorder	Valproate semisodium	Recommended	Multiple indications
09/2003	68	68: Guidance on the use of photodynamic therapy for age-related macular degeneration	Verteporfin	Restricted	Incomplete data sets
03/2004	76	76: Newer drugs for epilepsy in adults	Vigabatrin	Restricted	Data not available by age group
04/2004	79	79: Newer drugs for epilepsy in children	Vigabatrin	Restricted	Data not available by age group
06/2001	26	26: Guidance on the use of docetaxel, paclitaxel, gemcitabine and vinorelbine for the treatment of non-small cell lung cancer	Vinorelbine	Recommended	Multiple indications
12/2002	54	54: Guidance on the use of vinorelbine for the treatment of advanced breast cancer	Vinorelbine	Restricted	Multiple indications
02/2003	58	58: Guidance on the use of zanamivir, oseltamivir and amantadine for the treatment of influenza	Zanamivir	Restricted	Multiple indications

HTA date	HTA number	HTA name	Drug	Recommendation	Reason for non-selection
09/2008	158	158: Oseltamivir, amantadine (review) and zanamivir for the prophylaxis of influenza	Zanamivir	Restricted	Multiple indications

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