

## **NATIONAL PRESCRIBING INDICATORS 2012–2013**

**Endorsed by the All Wales Medicines Strategy Group December 2011**

### **INTRODUCTION**

In October 2003, the All Wales Medicines Strategy Group (AWMSG) agreed that prescribing indicators were useful tools to promote rational prescribing. The indicators are intended to balance quality and cost with respect to prescribing recommendations<sup>1</sup>.

This guidance represents the view of AWMSG, which was arrived at after careful consideration of the available evidence. Implementation of the national indicators does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer<sup>2</sup>.

### **BACKGROUND**

National prescribing indicators agreed by AWMSG and the Welsh Government should be:

- Evidence-based.
- Clear, easily understood and applicable at practice level.

The associated targets should address efficiency as well as quality.

The national prescribing indicators will not be included within the Quality and Outcomes Framework (QoF) of the General Medical Services (GMS) contract for 2012–2013<sup>3</sup>.

### **METHOD USED TO REVIEW AND UPDATE NATIONAL PRESCRIBING INDICATORS**

An indicator working group of the All Wales Prescribing Advisory Group (AWPAG) was set up to review the 2011–2012 prescribing indicators to ensure they were still valid and reflected best practice. Additionally, the Antimicrobial Stewardship Forum had input into the antibiotic indicator review. Recommendations from this complete review used the following principles for setting national prescribing indicators previously agreed by AWMSG<sup>4</sup>:

- Targets should be challenging but achievable, and based on encouraging all health boards to achieve prescribing rates in the best quartile. The target is therefore not an absolute value, and can be achieved if there is movement towards the upper or lower quartile, depending on the indicator.
- Targets should be set based on the prescribing data for general practices for the quarter ending 31 December 2011.

Although quality and productivity indicators introduced in 2011 as part of the QoF are not applicable for 2012–2013, it is recommended that targets for the national prescribing indicators are set based on the same criteria:

- The maximum percentage should normally be set at the 75th centile of achievement nationally for the quarter ending 31 December 2011. This is consistent with 2011–2012 in establishing targets, and requires that this is set using all of the practices in Wales.
- It is proposed that the “specific therapeutic group age–sex related prescribing units” (STAR-PU) measurement is used for certain indicators instead of the prescribing unit (PU) weighting, in order to benchmark with the “Quality, innovation, productivity and prevention” (QIPP) comparators in England. However, indicators measured by PU in previous years will continue to be monitored for comparative trend analysis.

The supporting evidence and measurement units for the statin and insulin national indicators are adapted from the National Prescribing Centre (NPC) document “Key therapeutic topics”, which supports the English QIPP prescribing comparators for 2012–2013<sup>5</sup>.

### NATIONAL INDICATORS AND LOCAL COMPARATORS FOR 2012–2013

Table 1 details the national indicators for 2012–2013, with the evidence and supporting prescribing messages within the text that follows. Progress against the indicators for 2011–2012 (based on June 2011 data) is contained within Appendix 1. A paper on the proposed local comparators for 2012–2013 is in development, and will be discussed at the AWPAG meeting in January 2012. AWPAG is developing aligned indicators for hospital prescribing for the “hypnotics and anxiolytics”, “non-steroidal anti inflammatory drugs”, “antimicrobial” and “insulin” indicators.

**Table 1. National prescribing indicators 2012–2013**

Indicator	Unit	Target
Lipid modifying drugs	Items of LAC statins as a percentage of all statin, ezetimibe and simvastatin/ezetimibe combination prescribing	Maintain performance levels within the upper quartile, or show an increase towards the quartile above.
Dosulepin	DDD per 1,000 PUs	Maintain performance levels within the lower quartile, or show a reduction towards the quartile below
Hypnotics and anxiolytics	ADQ per STAR-PU (measured as a combined entity)	Maintain performance levels within the lower quartile, or show a reduction towards the quartile below.
Non-Steroidal Anti-inflammatory Drugs (NSAIDs)	ADQ per STAR-PU	Maintain performance levels within the lower quartile, or show a reduction towards the quartile below
	Ibuprofen and naproxen as a percentage of NSAID items	Maintain performance levels within the upper quartile, or show an increase towards the quartile above

Indicator	Unit	Target
Antibiotics	Antibacterial items per STAR-PU	Maintain performance levels within the lower quartile, or show a reduction towards the quartile below
	Top nine antibacterials (penicillin V, flucloxacillin, amoxicillin, oxytetracycline, doxycycline, erythromycin, clarythromycin, trimethoprim and nitrofurantoin) as a percentage of total antibacterial items	Maintain performance levels within the upper quartile, or show an increase towards the quartile above
	Cephalosporins as a percentage of total antibacterial items	Maintain performance levels within the lower quartile, or show a reduction towards the quartile below
	Quinolones as a percentage of total antibacterial items	Maintain performance levels within the lower quartile, or show a reduction towards the quartile below
	Co-amoxiclav as a percentage of total antibacterial items	Maintain performance levels within the lower quartile, or show a reduction towards the quartile below
Opioid prescribing	Morphine as a percentage of strong opioid prescribing	Maintain performance levels within the upper quartile, or show an increase towards the quartile above
<b>Collaborative indicator for hospital and primary care prescribing</b>		
Insulin	Long-acting insulin analogues as a percentage of total long- and intermediate-acting insulin (excluding biphasics)	Maintain performance levels within the lower quartile, or show a decrease towards the quartile below.
ADQ = average daily quantity; DDD = defined daily dosage; LAC = low acquisition cost; NSAID = non-steroidal anti-inflammatory drug; PU = prescribing unit; STAR-PU = specific therapeutic group age–sex related prescribing units		

NB: The prescribing indicators highlighted in Table 1 constitute guidance **only**, and this document, either in isolation or as part of wider policy, is not associated with any financial incentive scheme, and does not offer any medical practice and/or practitioner any financial incentive to prescribe a specific named medicine. Implementation of the national indicators does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

## References

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## 1.0 COST EFFECTIVE USE OF LIPID MODIFYING DRUGS

**Purpose:** Ensure appropriate prescribing of lipid modifying drugs with the lowest acquisition cost (LAC).

**Unit of measure:** Items of LAC statins as a percentage of all statin, ezetimibe and simvastatin/ezetimibe combination prescribing.

**Target for 2012–2013:** Maintain performance levels within upper quartile, or show an increase towards the quartile above.

### Background and evidence

The use of LAC statins is promoted through the Department of Health “Better Care, Better Value” (BCBV) indicators<sup>1</sup>. The BCBV indicators are not targets, but are intended to provide useful comparative information for NHS organisations to decide where and how to improve performance. There are still substantial savings to be made by some NHS organisations through the use of LAC statins.

The patent on atorvastatin is expected to expire in May 2012; therefore atorvastatin will be included in the basket of LAC statins from April 2012. It is not possible to determine when the generic atorvastatin cost will be included in the drug tariff, or when the price will fall to a similar level as simvastatin and pravastatin, so prescribers should continue to be mindful of the comparative cost of atorvastatin. Until the cost of atorvastatin falls to a similar level, simvastatin and pravastatin should remain the agents of choice.

National Institute for Health and Clinical Excellence (NICE) guidance on lipid management in people without type 2 diabetes advises that simvastatin 40 mg daily should be prescribed for people for whom statins are indicated. If there are potential drug interactions or simvastatin 40 mg is contraindicated, a lower dose or alternative preparation, such as pravastatin, may be chosen<sup>2</sup>. It is important to note that NICE lipid guidance explicitly sets no targets that such patients are expected to achieve for either primary or secondary prevention.

**\*Note:** The Medicines and Healthcare products Regulatory Agency (MHRA) has advised that the black triangle (▼) refers to intensive monitoring of simvastatin only when used in children and adolescents (10–17 years of age), in line with the recently licensed paediatric dosing recommendation.

In patients requiring **secondary prevention**, who do not have acute coronary syndrome (ACS), NICE advises that prescribers should consider increasing the dose of simvastatin to 80 mg daily **only** in patients whose total cholesterol is greater than 4 mmol/L, **and** whose low-density lipoprotein (LDL) cholesterol is greater than 2 mmol/L<sup>2</sup>. If either is below that level, then increasing the dose of simvastatin is not recommended. It is important to note that these are lipid levels which should prompt prescribers to consider increasing the dose. They are **not** targets patients are expected to achieve.

NICE also advises that any decision to offer a higher intensity statin should not be automatic, but should take into account the patient's informed preference, including the benefits and risks of treatment<sup>2</sup>. This is consistent with advice from the MHRA given in the May 2010 edition of the Drug Safety Update<sup>3</sup>, which highlighted the increased risk of myopathy associated with simvastatin 80 mg daily, as found in the SEARCH study. The Medicines Resource Centre (MeReC) Rapid Review 1423 discusses the place in therapy of simvastatin 80 mg daily in the context of the MHRA advice, NICE guidance

and the current evidence base, including the risks of other statins at high doses<sup>4</sup>. SEARCH has now been published in full<sup>5</sup>. It found no significant reduction in major vascular events among people randomised to simvastatin 80 mg vs 20mg daily for secondary prevention. The higher dose was associated with an increased risk of muscle side effects, but myopathy was uncommon and rhabdomyolysis was rare. SEARCH is discussed further in MeReC Rapid Review 2138<sup>6</sup>.

A recent large meta-analysis has confirmed the results of earlier meta-analyses regarding the benefits of standard dose statin therapy on cardiovascular outcomes<sup>7</sup>. It also suggests additional benefits from more intensive statin therapy in selected high-risk populations. However, it did not fully explore the potential harms associated with more intensive statin therapy, or examine the cost effectiveness of this approach. This meta-analysis and its implications are discussed in MeReC Rapid Review 2127<sup>8</sup>.

NICE recommends that, **taking into account the patient's informed preference** as above, people with ACS should be offered treatment with a higher intensity statin<sup>2</sup>. NICE found that atorvastatin 80 mg and simvastatin 80 mg are both cost effective daily doses for ACS if more intensive statin treatment is required. However, NICE does not recommend lipid level targets in people with ACS. In addition, NICE does not give guidance about how long people with ACS should take a higher intensity statin; that is, at what point after their ACS event they should be treated in the same way as other patients that are taking statins for secondary prevention.

NICE guidance on lipid management in people with type 2 diabetes recommends simvastatin 40 mg daily as the usual choice and dose of statin, with an increase to 80 mg daily if the total cholesterol is more than 4 mmol/L, **and** the LDL cholesterol is more than 2 mmol/L<sup>9</sup>. In people with type 2 diabetes with existing or newly diagnosed cardiovascular disease, or increased albumin excretion, NICE advises the **consideration** of intensifying lipid-lowering treatment to achieve total cholesterol of less than 4 mmol/L **or** LDL cholesterol of less than 2 mmol/L. However, in line with good medical practice, such a decision should take into account the patient's informed preference, including the benefits and risks of treatment.

NICE guidance on management of familial hypercholesterolaemia (FH) includes using the maximum licensed or tolerated dose of statins, plus ezetimibe if necessary, to try to achieve at least 50% reduction in LDL cholesterol from baseline<sup>10</sup>. However, if a patient cannot tolerate or does not wish to take such intensive treatment, cohort studies show that the prognosis for patients with FH improved substantially when standard doses of 'less intensive' statins were introduced, to the point where their risk of cardiovascular events was reduced to that of the general population. There is no good outcome data to show that a more intensive regimen is better than a standard one (see MeReC Rapid Review 357<sup>11</sup>).

A MeReC bulletin on lipid-modifying treatment is also available<sup>12</sup>. This:

- addresses the similarities and differences between NICE guidance for people with and without type 2 diabetes;
- provides clarification on NICE recommendations regarding thresholds for intensifying treatment;
- discusses the evidence-base for high intensity statins and ezetimibe, the reliability of single cholesterol measurements, and the side effects of statins.

More information on statins and other lipid-modifying drugs can be found within the NPC e-learning materials on lipids<sup>13</sup>.

A prescribing comparator is available in England to support the same QIPP topic<sup>14</sup>.

Table 2 shows the absolute and percentage reductions in LDL cholesterol concentration according to the statin and the licensed daily dose used<sup>15</sup>.

**Table 2. The absolute and percentage reductions in LDL cholesterol concentration according to the statin and the daily dose used.**

Drug	Dose				
	5 mg	10 mg	20 mg	40 mg	80 mg
<b>Atorvastatin</b>	1.51 (1.28–1.74) 31%	1.79 (1.62–1.97) 37%	2.07 (1.90–2.25) 43%	2.36 (2.12–2.59) 49%	2.64 (2.31–2.96) 55%
<b>Fluvastatin</b>	0.46 (0.18–0.75) 10%	0.74 (0.55–0.93) 15%	1.02 (0.90–1.13) 21%	1.3 (1.19–1.41) 27%	1.58 (1.40–1.76) 33%
<b>Pravastatin</b>	0.73 (0.54–0.92) 15%	0.95 (0.83–1.07) 20%	1.17 (1.10–1.23) 24%	1.38 (1.31–1.46) 29%	1.6 (1.46–1.74) 33%
<b>Rosuvastatin</b>	1.84 (1.74–1.94) 38%	2.08 (1.98–2.18) 43%	2.32 (2.20–2.44) 48%	2.56 (2.42–2.70) 53%	2.8 (2.63–2.97) 58%
<b>Simvastatin</b>	1.08 (0.93–1.22) 23%	1.31 (1.22–1.40) 27%	1.54 (1.46–1.63) 32%	1.78 (1.66–1.90) 37%	2.01 (1.83–2.19) 42%

From Table 3 it can be seen that simvastatin 40 mg daily reduces LDL cholesterol to the same extent as atorvastatin 10 mg daily<sup>16</sup>.

**Table 3. The percentage reductions in LDL cholesterol concentration and the cost for 28 days, according to the statin and daily dose used.**

Drug	Strength (daily dose)	Reductions in serum LDL cholesterol	Cost for 28 days*
Simvastatin	40 mg	37%	£1.13
Pravastatin	40 mg	29%	£1.90
Fluvastatin	80 mg	33%	£19.20
Atorvastatin	10 mg	37%	£13.00
Rosuvastatin	5 mg	38%	£18.03

\*November 2011 drug tariff costs (based on BNF dose range for hypercholesterolaemia)<sup>16</sup>.

In June 2011, simvastatin and pravastatin accounted for 72% of statin prescribing in primary care as an average across NHS Wales, which is the same as the 72% achieved in March 2010<sup>17</sup>. The performance of the localities ranged between 59% and 77%. Benchmarking with England shows that out of 151 primary care trusts, the mean achievement was 74%, with performance ranging between 61% and 85%<sup>18</sup>. This demonstrates that greater efficiencies could be made in Wales.

NICE guidance on the use of ezetimibe is given in TA132<sup>19</sup>, which is referred to in clinical guidelines on lipid management and type 2 diabetes<sup>9</sup>. Ezetimibe is recommended as an option by NICE, **only** for the treatment of adults with primary (heterozygous-familial or non-familial) hypercholesterolaemia, and **then only** in the following circumstances:

- where statins are contraindicated or not tolerated;
- in conjunction with a statin where serum total or LDL cholesterol is not appropriately controlled by initial statin therapy (after appropriate dose titration or because dose titration is limited by intolerance), **and** when consideration is being given to changing the initial statin therapy to an alternative statin.

The NICE ezetimibe implementation costing statement estimates that this guidance could result in approximately 900 patients receiving ezetimibe monotherapy, and 11,000 patients receiving ezetimibe and simvastatin combination therapy<sup>19,20</sup>. This amounts to approximately £4 million per year. Within the last 12 months, the cost to NHS Wales for ezetimibe monotherapy has amounted to £5 million, with the combination product costing an additional £0.3 million per annum<sup>17</sup>.

## References

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## 2.0 IMPLEMENTATION OF NICE GUIDANCE: THE USE OF DOSULEPIN

**Purpose:** Reduce inappropriate prescribing of dosulepin in line with NICE clinical guideline 90 (CG90)<sup>1</sup>.

**Unit of measure:** Defined daily dosage (DDD) of dosulepin per 1,000 PUs.

**Target for 2012–2013:** Maintain performance levels within the lower quartile, or decrease towards the quartile below.

### Background and evidence

Dosulepin is a tricyclic antidepressant, historically used where an anti-anxiety or sedative effect is required. Dosulepin has a small margin of safety between the maximum therapeutic dose and a potentially fatal dose<sup>2</sup>.

The MHRA Drug Safety Update of December 2007 reported that dosulepin continued to be prescribed widely, and accounted for about 10% of the antidepressant market in England<sup>2</sup>. At this time, up to 200 people in England and Wales committed suicide or took a potentially fatal overdose of dosulepin in one year. About 20% of fatal dosulepin overdoses are associated with accidental death<sup>2</sup>.

The updated NICE clinical guideline 90 “Depression: the treatment and management of depression in adults” strengthens the previous advice, stating “*do not switch to, or start, dosulepin because evidence supporting its tolerability relative to other antidepressants is outweighed by the increased cardiac risk and toxicity in overdose*”<sup>1</sup>.

Although only one locality is prescribing within the lower quartile (73 DDD per 1,000 PUs), most practices are moving towards the target as of June 2011 (see Appendix 1)<sup>3</sup>.

### Notes for prescribers and advisors

- Encourage Yellow Card reporting.

### References

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### 3.0 HYPNOTICS AND ANXIOLYTICS

**Purpose:** Reduce inappropriate prescribing of hypnotics and anxiolytics.

**Unit of measure:** Average daily quantity (ADQ) per STAR-PU of hypnotics and anxiolytics, measured as a combined entity.

**Target for 2012–2013:** Maintain performance levels within the lower quartile, or reduction towards the quartile below.

#### Background and evidence

There has been concern with regard to the high volume of anxiolytic and hypnotic prescribing within NHS Wales. Some prescribing may be inappropriate and contribute to the problem of physical and psychological dependence and/or may be responsible for masking underlying depression. In 1999, the Mental Health National Service Framework (NSF)<sup>1</sup> reinforced the Committee on Safety of Medicines (CSM)<sup>2</sup> advice, and recommended that benzodiazepines should be used for no more than two to four weeks for severe and disabling anxiety. It stated that by 2001 all health authorities should have systems in place to monitor and review prescribing rates of benzodiazepines within the local clinical audit programme. Key action point 33 in the revised Adult Mental Health NSF action plan for Wales states that “*healthcare organisations are to ensure that patients and service users are provided with effective treatment and care that conforms to the NICE technology appraisals and interventional procedures and the recommendations of AWMSG also based on nationally agreed best practice guidelines as defined in NSFs, NICE clinical guidelines, national plans and agreed national guidance on service delivery*”<sup>3</sup>. The performance target set was that by March 2007, local health boards/NHS trusts should have undertaken a systematic review of NICE guidelines and technology appraisals, and developed a local incremental implementation plan.

The substance misuse strategy of the Welsh Government “Working together to reduce harm” calls for the reduction of inappropriately prescribed benzodiazepines<sup>4</sup>.

The prescribing volume of hypnotics and anxiolytics in Wales has declined over recent years. In the financial year 2010/2011, the number of items dispensed was 1,603,548, compared with 1,631,893 the previous year: a reduction of 1.46% (total quantity of tablets reduced by 4.66% from 50,188,215 to 47,847,605 for the same period)<sup>5</sup>. The greatest reduction was for benzodiazepine hypnotic items (-4.6%), with a small increase in the number of items for “Z” drugs (0.23%)<sup>5</sup>. There is still a large variation in prescribing rates of these drugs across health boards, and also variation between GP practices within these health boards. When comparing hypnotic and anxiolytic prescribing in Wales to North-East England (the area of England most similar to Wales demographically), it was observed that Wales prescribes 46.2% more items/1,000 patients<sup>6</sup>.

Ensuring the appropriate prescribing of hypnotics and anxiolytics is also one of the Welsh Medicines Partnership’s (WMP) “Invest to Save” projects commissioned by the Welsh Government. In April 2011, an educational pack/prescribing toolkit was produced to aid health professionals in supporting the appropriate use of hypnotics and anxiolytics<sup>7</sup>. This pack is available on the AWMSG website.

#### Notes for prescribers and advisors

- Hypnotics and anxiolytics educational resource pack can be found [here](#).
- Ward level prescribing data is to be analysed and shared.

## References

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#### 4.0 NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs)

**Purpose:** Ensure that the cardiovascular and gastrointestinal (GI) risks from NSAIDs are minimised by appropriate choice and use.

**1. Unit of measure:** NSAID ADQ per 1,000 STAR-PU.

**Target for 2012–2013:** Maintain performance levels within the lower quartile, or reduction towards the quartile below.

**2. Unit of measure:** Ibuprofen and naproxen as a percentage of total NSAID items.

**Target for 2012–2013:** Maintain performance levels within the upper quartile, or show an increase towards the quartile above.

##### Background and evidence

There is overwhelming evidence to reduce prescribing of NSAIDs, especially for the elderly. Ensuring appropriate prescribing of NSAIDs is also one of WMP's "Invest to Save" projects commissioned by the Welsh Government. MHRA have issued five warnings to prescribers regarding the GI dangers of NSAIDs, culminating in the following warning issued in 2003<sup>1</sup>:

- *All NSAIDs, including ibuprofen and cyclo-oxygenase-2 (COX-2) selective inhibitors are associated with reports of serious GI toxicity. The elderly and those taking concomitant aspirin are high-risk groups.*
- *Detailed advice on the GI safety of NSAIDs (including aspirin and selective COX-2 inhibitors) has previously been provided. CSM continues to receive reports of serious and fatal GI reactions associated with NSAIDs.*

The risk of NSAID-induced renal failure in otherwise healthy patients has also been highlighted by the MHRA<sup>2</sup>. Furthermore, in October 2006 and December 2007, the MHRA issued warnings on the increased risk of thrombotic events associated with the long term use of NSAIDs<sup>3,4</sup>.

NPC provided prescribing advice based on the relative cardiovascular and GI adverse effects of NSAIDs in November 2007<sup>5</sup>. More recently, large observational studies have supported the finding that individual NSAIDs are associated with different safety profiles. Similarly, a meta-analysis published in 2011 concluded that naproxen appears least harmful in respect of cardiovascular toxicity<sup>6</sup>. Based on current data, diclofenac should be avoided in patients at high risk of cardiovascular toxicity, with naproxen (250 mg bd prn) considered first-line<sup>7</sup>. NPC has reminded prescribers that:

- GI and cardiovascular adverse effects of NSAIDs may be minimised by selecting the lowest effective dose for the shortest duration necessary.
- Risks of GI toxicity are higher in the elderly.
- Diclofenac 150 mg daily has a thrombotic risk profile similar to that of selective COX-2 inhibitors.
- Epidemiological data suggest that naproxen 1000 mg daily or ibuprofen at lower doses ( $\leq$  1200 mg daily) are associated with a lower risk of thrombotic events.
- Ibuprofen, at doses of  $\leq$  1200 mg daily, is associated with the lowest GI risk of the traditional NSAIDs, but serious and fatal GI reactions have still been reported.

- Clinical trial data suggest that selective COX-2 inhibitors have GI safety advantages over standard NSAIDs, but serious and fatal GI reactions have nonetheless been associated with these drugs.
- Prescribing should be based on the safety profiles of individual NSAIDs or selective COX-2 inhibitors and on individual patient risk profiles (e.g. GI and cardiovascular).
- Prescribers should not switch between NSAIDs without careful consideration of the overall safety profile of the products, a patient's individual risk factors and patient preference.
- NSAIDs should only be prescribed for patients with heart failure when their use is considered essential.
- NSAID treatment is contraindicated in severe heart failure<sup>7</sup>.
- Co-prescription of a proton pump inhibitor to reduce GI adverse effects should be considered, in line with NICE guidance.
- Aspirin and another NSAID should only be used together when absolutely necessary; the combination substantially increases GI risk. Patients taking long-term aspirin should be reminded to avoid NSAIDs, including those bought without prescription<sup>8,9</sup>.

#### **Notes for prescribers and advisors**

- The AWMSG audit "Towards appropriate NSAID prescribing" can be found [here](#).
- The safety advantages of ibuprofen are only justified at dosages of  $\leq 1200$  mg daily.
- Hospital mapping of NSAID prescribing data to directorates can be effective.
- Review use of peri-operative analgesics and promote post-operative review.
- Encourage Yellow Card reporting.

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## 5.0 USE OF ANTIBIOTICS

**Purpose:** The development of antibiotic prescribing indicators supports the core aims of the Antimicrobial Resistance Programme in Wales to inform, support and promote the prudent use of antimicrobials<sup>1</sup>. The Welsh Antimicrobial Stewardship Forum supports the following national indicators.

**1. Unit of measure:** Antibacterial items per STAR-PU.

**Target for 2012–2013:** Maintain performance levels within the lower quartile, or show a reduction towards the quartile below.

**2. Unit of measure:** Usage of the top nine antibacterials (penicillin V, flucloxacillin, amoxicillin, oxytetracycline, doxycycline, erythromycin, clarithromycin, trimethoprim and nitrofurantoin) as a percentage of total antibacterial items.

**Target for 2012–2013:** Maintain performance levels within the upper quartile, or show an increase towards the quartile above.

**3. Unit of measure:** Quinolones as a percentage of total antibacterial items.

**Target for 2012–2013:** Maintain performance levels within the lower quartile, or show a reduction towards the quartile below.

**4. Unit of measure:** Cephalosporins as a percentage of total antibacterial items.

**Target for 2012–2013:** Maintain performance levels within the lower quartile, or show a reduction towards the quartile below.

**5. Unit of measure:** Co-amoxiclav as a percentage of total antibacterial items.

**Target for 2012–2013:** Maintain performance levels within the lower quartile, or show a reduction towards the quartile below.

The above indicators only cover antibacterials that appear in chapter 5 (Infections) of the British National Formulary (BNF)<sup>2</sup>.

### Background and evidence

The Public Health Wales report “Antimicrobial dispensing in primary care in Wales (2006–2008)” and the Health Protection Agency report “Antimicrobial resistance and prescribing in England, Wales and Northern Ireland, 2008” present the different prescribing and antimicrobial resistance patterns across Wales and the UK<sup>3,4</sup>. Data published by the Public Health Wales Antimicrobial Resistance Programme show that antimicrobial use across primary and secondary care is common and variable across Wales. The total number of antimicrobial prescription items dispensed in primary care across Wales over the last year has remained similar to that in 2008; it is currently 2,558,816 per annum, compared with 2,417,104 in 2008 (i.e. almost 1 antibiotic for every member of the population). Primary care prescribing rates vary from 505 to 606 items per 1,000 PUs across Welsh health boards<sup>5</sup>.

Concern has been expressed regarding the establishment of targets for antibiotic prescribing indicators, as there is no clear evidence-base for setting such targets. Data regarding indicators should be presented in a comparative form without targets. It is, however, recognised that for the purposes of establishing a set of national indicators, there needs to be an associated target despite this limitation. It is therefore proposed

that for indicators 1, 3, 4 and 5 this should be “maintain performance levels within the lower quartile, or reduction towards the quartile below” and for indicator 2, this should be “maintain performance levels within the upper quartile, or increase towards the quartile above”. Comparative trends for all antibiotic indicators should be interpreted with caution, with particular respect to seasonal variation.

### **1. Antibacterial items per STAR-PU**

The Department of Health Standing Medical Advisory Committee (which has since been superseded) Sub-Group on Antimicrobial Resistance report “The path of least resistance” stated that the evidence demonstrating that the use of antimicrobials causes resistance was overwhelming, although mostly circumstantial<sup>6</sup>. The evidence showed that resistance is greatest where use of antibacterial agents is heaviest. This applies at both national and clinical unit levels<sup>6,7</sup>. This has been corroborated in a European cross-national database study<sup>8</sup>. By contrast, a 12-year resistance surveillance study demonstrated that resistance was stable, despite an increase in cephalosporin dosage, and in another case, resistance increased with reduced trimethoprim-sulfamethoxazole treatment<sup>9</sup>.

### **2. Usage of the top nine antibacterials (penicillin V, flucloxacillin, amoxicillin, oxytetracycline, doxycycline, erythromycin, clarithromycin, trimethoprim and nitrofurantoin) as a percentage of total antibacterial items**

The Health Protection Agency guidance for primary care identifies the most appropriate treatment protocol and antibiotics for common infections experienced in primary care<sup>10</sup>. The top nine antibacterials provide sufficient cover to treat: upper and lower respiratory tract infections, urinary tract infections (UTIs) except acute pyelonephritis, and common skin infections. The use of simple generic antibiotics, and the avoidance of broad-spectrum antibiotics (e.g. co-amoxiclav, quinolones and cephalosporins) preserves these antibiotics from resistance and reduces the risk of *Clostridium difficile* (*C. difficile*), methicillin-resistant *Staphylococcus aureus* (MRSA) and resistant UTIs.

### **3. Quinolones as a percentage of total antibacterial items**

There is an association between quinolone use and the incidence of *C. difficile* associated diarrhoea (CDAD)<sup>11,12</sup>; therefore, use should be restricted to specific indications in order to reduce the risk of potential antimicrobial resistance. The average cost of a *C. difficile* infection has been estimated to be £4,007<sup>13</sup>.

### **4. Cephalosporins as a percentage of total antibacterial items**

The cephalosporins are broad-spectrum antibiotics which are used for the treatment of septicaemia, pneumonia, meningitis, biliary-tract infections, peritonitis, and UTIs<sup>2</sup>. There is an association between cephalosporin use and the incidence of CDAD<sup>10</sup>; therefore, use should be restricted to specific indications in order to reduce the risk of potential antimicrobial resistance. Cephalosporins are not listed as first- or second-line treatments in the Health Protection Agency report “Management of infection guidance for primary care”<sup>10</sup>. The five most commonly prescribed cephalosporins in the community are cefalexin, cefaclor, cefradine, cefuroxime and cefixime; with cefalexin accounting for 86% of all cephalosporin items and 8% of all antibacterial items prescribed<sup>5</sup>.

### **5. Co-amoxiclav as a percentage of total antibacterial items**

Co-amoxiclav is broad-spectrum penicillin with activity against beta-lactamase-producing organisms such as *Staphylococcus aureus* and *Escherichia coli*. In 1997, CSM (now the MHRA) issued guidance which limited the indications for co-amoxiclav due to an increased risk of cholestatic jaundice compared with other antibacterial agents<sup>14</sup>. The use of co-amoxiclav is also associated with a moderate risk of *C. difficile* infection<sup>15</sup>, which is increased with the duration of treatment and use in at-

risk patient groups, such as those aged over 65. Primary care prescribing data from April 2009 to June 2011 shows that co-amoxiclav prescribing as a percentage of total antibacterial items remained constant at approximately 6%<sup>5</sup>.

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## 6.0 MORPHINE AS A PERCENTAGE OF STRONG OPIOID PRESCRIBING

**Purpose:** Encourage the use of morphine as the first-line strong opioid.

**Unit of measure:** Morphine as a percentage of strong opioid prescribing (excluding buprenorphine and methadone preparations prescribed for the management of opioid dependence; see BNF chapter 4.10.3<sup>1</sup>).

**Target for 2012–2013:** Maintain performance levels within upper quartile, or show an increase towards the quartile above.

### **Background and evidence**

The following are classed as strong opioids<sup>1,2</sup>:

- Buprenorphine
- Diamorphine
- Dipipanone
- Fentanyl
- Hydromorphone
- Meptazinol
- Methadone
- Morphine
- Oxycodone
- Papaveretum
- Pethidine
- Tapentadol \*

\* Please note that tapentadol prolonged-release tablets (Palexia SR) is the only formulation of tapentadol which has been recommended by AWMSG and ratified by the Health Minister for use within NHS Wales to date.

Opioids are increasingly being used to treat persistent pain. Opioids have a well-established role in the management of acute pain following trauma (including surgery), and in the management of pain associated with terminal illness. There is evidence from clinical trials that opioids can be effective, in the short- and medium-term, in providing symptomatic improvement in a variety of non-cancer pain conditions. There is a propensity for these drugs to cause problems of tolerance, dependence and addiction. The benefits of opioid treatment for the patient must be balanced against burdens of long-term use, as therapy for persistent pain may need to be continued for months or years<sup>3</sup>. There are many palliative care guidelines, such as those developed in Fife<sup>4</sup>, as well as guidance on the use of opioids in chronic non-malignant pain, such as those produced in Gwent<sup>5</sup>. These are based on the World Health Organisation (WHO) guidelines, which state “*If pain occurs, there should be prompt oral administration of drugs in the following order: non-opioids (aspirin and paracetamol); then, as necessary, mild opioids (codeine); then strong opioids such as morphine, until the patient is free of pain*”<sup>6</sup>.

Morphine remains the most valuable opioid analgesic for severe pain. It is the standard against which other opioid analgesics are compared<sup>1</sup>. Where possible, modified release opioids administered at regular intervals should be used to manage patients with persistent pain. Clinical experience suggests that immediate release preparations are more strongly associated with tolerance and problem drug use. Use of flexible dosing regimens using immediate release preparations (alone or in combination with modified release preparations) can, in some circumstances, provide effective

symptomatic relief and allow an overall reduction in opioid dose<sup>3</sup>. Use of such regimens may be justified when:

- the pain is intermittent and short-lived;
- pain intensity has significant diurnal variation;
- background pain is well controlled with modified release preparations, but the patient has infrequent, short-lived episodes of increased pain.

The clinical response to morphine is highly variable, with approximately 10–30% of patients unable to tolerate it, mainly due to adverse side effects; treatment with other opioids is required to optimise the balance between adequate pain relief and side effect profile. The need to use immediate release opioids for persistent pain should prompt specialist review<sup>3</sup>. The current Welsh average for morphine prescribing as a percentage of strong opioids is 38.7%<sup>3</sup>.

#### **Notes for prescribers and advisors**

- Prescribers are **recommended** to prescribe oral modified release and transdermal strong opioid preparations by brand to avoid confusion and allow for continuity of supply. Such practice should reduce the potential for dosing, dispensing and administration errors and reduce confusion for patients<sup>2</sup>.
- Concomitant use of a weak opioid, such as co-codamol or tramadol, should be avoided.

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## 7.0. LONG- AND INTERMEDIATE-ACTING INSULIN ANALOGUES

**Purpose:** Ensure prescribing of long-acting insulin analogues in type 2 diabetes mellitus is in line with NICE guidance<sup>1</sup>. It is intended that this indicator should be a collaborative indicator for hospital and primary care prescribing.

**Unit of measure:** Long-acting insulin analogues as a percentage of total long- and intermediate-acting insulin (excluding biphasics).

**Target for 2012–2013:** Maintain performance levels within the lower quartile, or show a decrease towards the quartile below.

### Background and evidence

NICE guidance on the management of type 2 diabetes recommends that when insulin therapy is necessary, human isophane (NPH) insulin is the preferred option<sup>1</sup>. Long-acting insulin analogues have a role in some patients, and can be considered for those who fall into specific categories, e.g. those who require assistance from a carer or healthcare professional to administer their insulin injections, or those with problematic hypoglycaemia. The All Wales Diabetes Forum and Welsh Endocrine and Diabetes Society support the current NICE guidelines. However, for most people with type 2 diabetes, long-acting insulin analogues offer no significant advantage over human NPH insulin, and are much more expensive.

A health economic analysis by NICE found that the cost effectiveness of long-acting insulin analogues was not favourable. The incremental cost per quality-adjusted life-year (compared with conventional insulin) was greater than £100,000 in all scenarios, and in some scenarios in excess of £400,000. Importantly, this analysis incorporated the anticipated health-related quality of life gain associated with the reduced fear of severe hypoglycaemic episodes. These issues are discussed in a MeReC Rapid Review 826<sup>2</sup>.

A Canadian health technology assessment concluded that most estimates of differences in HbA1c between patients treated with conventional insulins and insulin analogues were not statistically significant. These results are consistent with the health economic analysis conducted by NICE for long-acting insulin analogues in type 2 diabetes. See MeReC Rapid Review 318<sup>3</sup>.

Nevertheless, the prescribing of these agents has increased substantially over the past few years. England has also developed a prescribing comparator to support this QIPP topic; entitled “Long/intermediate acting insulin analogues”<sup>4</sup>. English comparative data shows that in the majority of primary care trusts, more than 80% of all intermediate- or long-acting insulin items (excluding biphasic insulins) are now the long-acting insulin analogues insulin glargine or insulin detemir<sup>5</sup>. The average prescribing rate for Wales is currently 93%, at an annual cost of £8 million<sup>6</sup>.

People with glycaemic control problems should be properly assessed for underlying causes before these newer, more expensive insulins are considered. This includes education, and checking the patient’s understanding of how to manage their disease and treatment. Any decision to start a long-acting insulin analogue needs to be balanced carefully against the lack of long-term safety data available for these agents, and their high prescribing costs. Prescribers and patients should also consider the concern about a possible association between higher doses of insulin glargine and cancer. This has been suggested in some studies, but current evidence is conflicting. See MeReC Rapid Review 1652<sup>7</sup>.

More information regarding the use of long-acting insulin analogues in type 2 diabetes can be found within the type 2 diabetes NPC e-Learning materials<sup>8</sup> and in the June 2011 MeReC bulletin<sup>9</sup>.

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**APPENDIX 1. Performance of NHS Wales against 2011–2012 indicators (1<sup>st</sup> quarter – June 2011)**

Please note that the following graphs show progress against the current target, which has increased over the time period measured.

**Understanding the histograms**

The **green** line shows the total number of practices that have achieved the target.

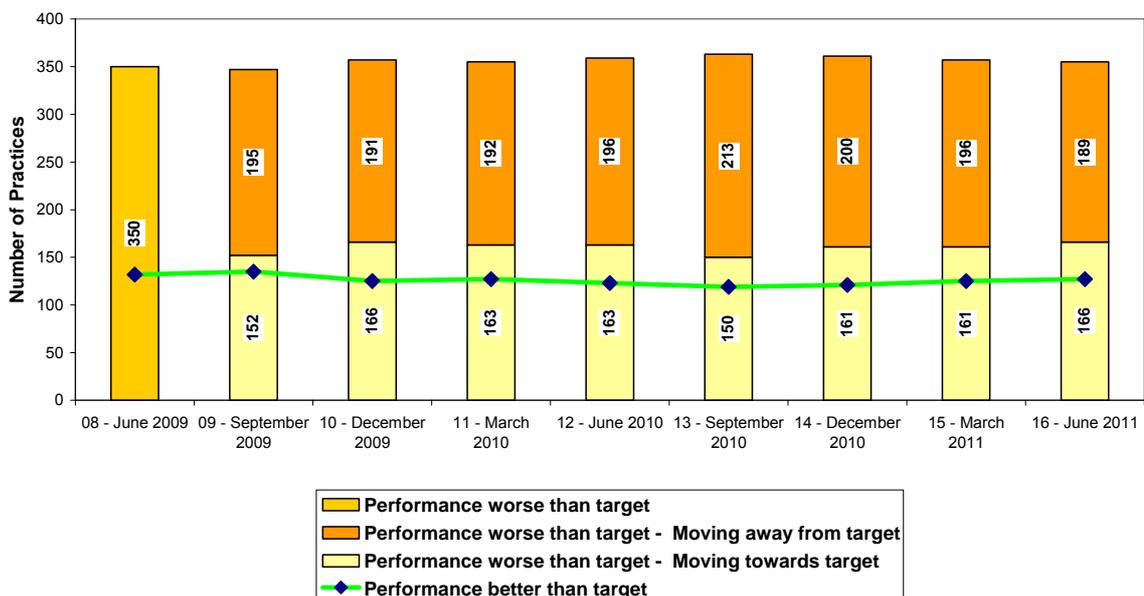
The **amber** bar to the left shows the total number of practices not achieving the target in the quarter ending June 2009. The value each practice has at this point is used as a reference value.

For all subsequent quarters, practices which fail to meet the target are split into two groups shown in cream or orange:

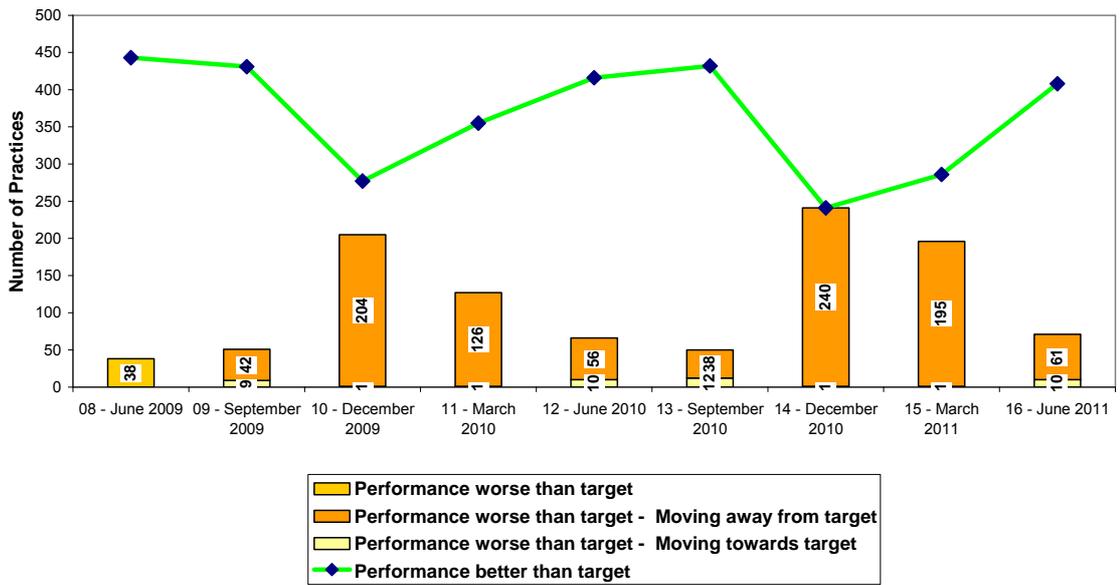
- Practices included in the **cream** (lower) part of the bar have not met the target, but their value in this quarter is closer to the target than their value in the first period. An assumption is made that they are moving towards the target.
- Practices included in the **orange** (upper) part of the bar have not met the target, and their value in this quarter is further away from the target than their value in the first period. An assumption is made that they are moving away from the target.

(See Figure legends)

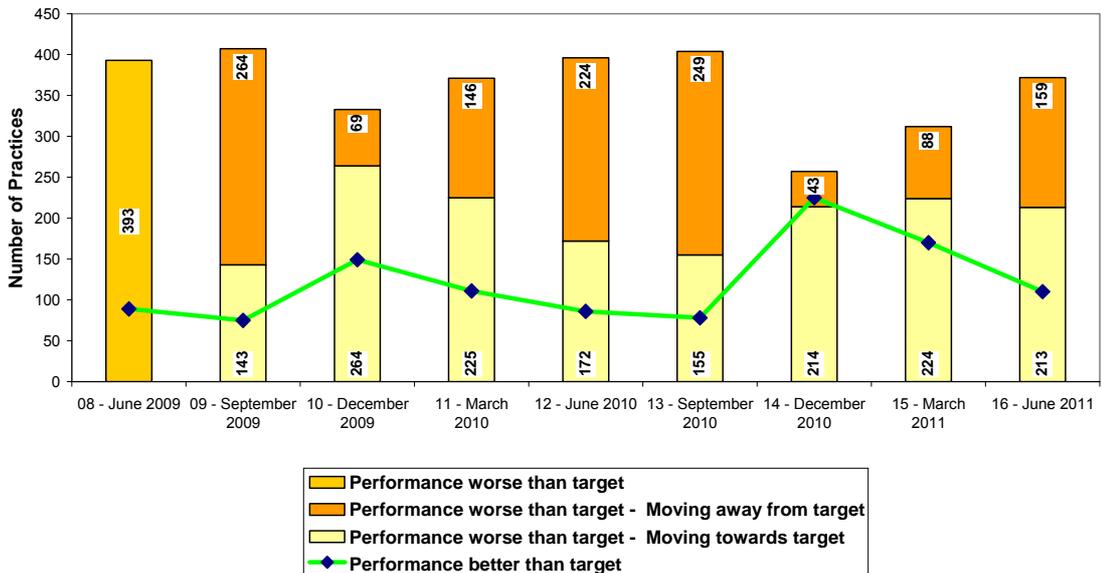
**Welsh GP Practices - Practice Level data - ACEI % of Angio II and Acel - (Threshold of Upper Quartile - 79.88 %)**



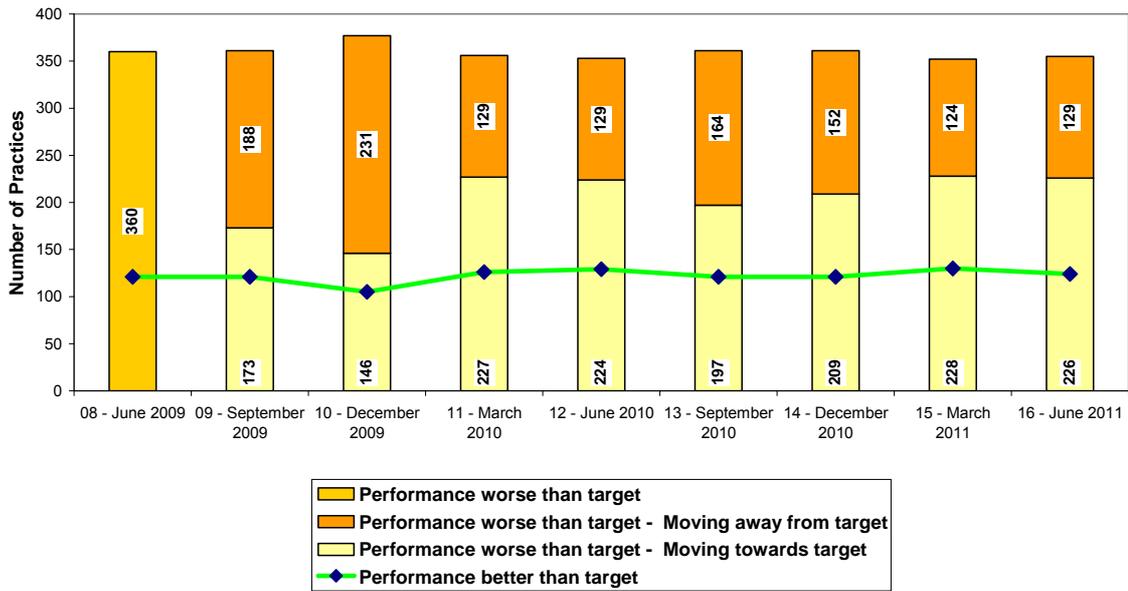
Welsh GP Practices - Practice Level data - Antibacterial Items Per 1000 PU - (Threshold of Lower Quartile - 161.57)



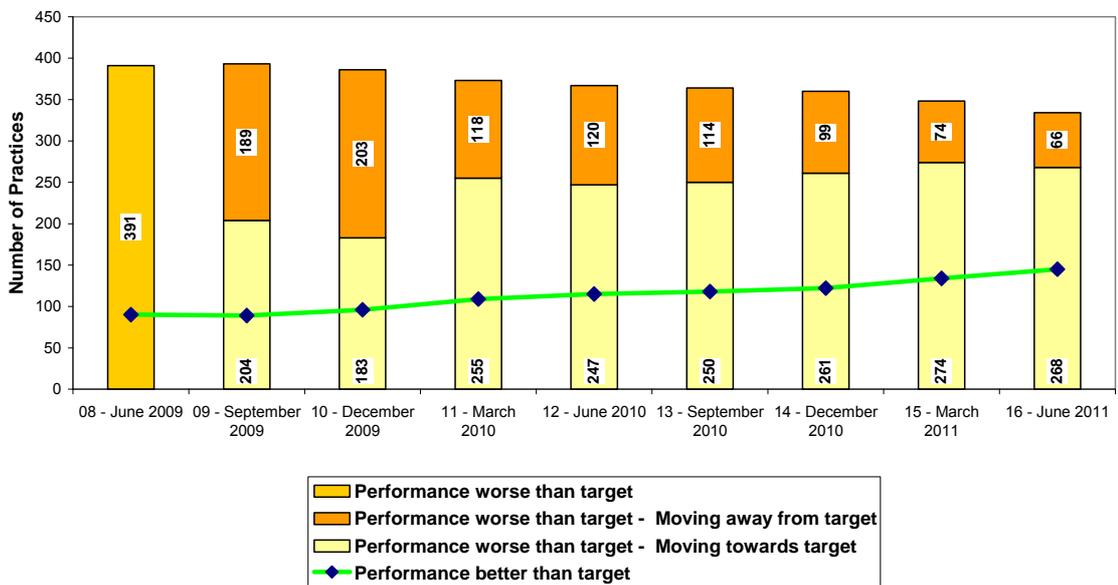
Welsh GP Practices - Practice Level data - Top 9 Antibacterials as a % of Antibacterials Items - (Threshold of Upper Quartile - 80.26%)



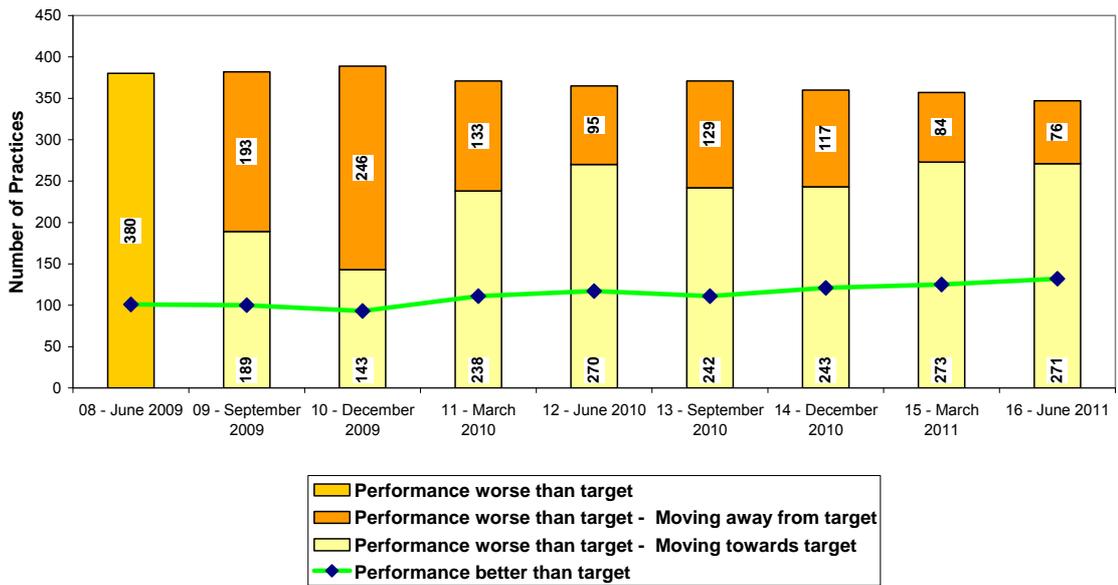
Welsh GP Practices - Practice Level data - Anxiolytics DDD per 1000 Patients - (Threshold of Lower Quartile - 410)



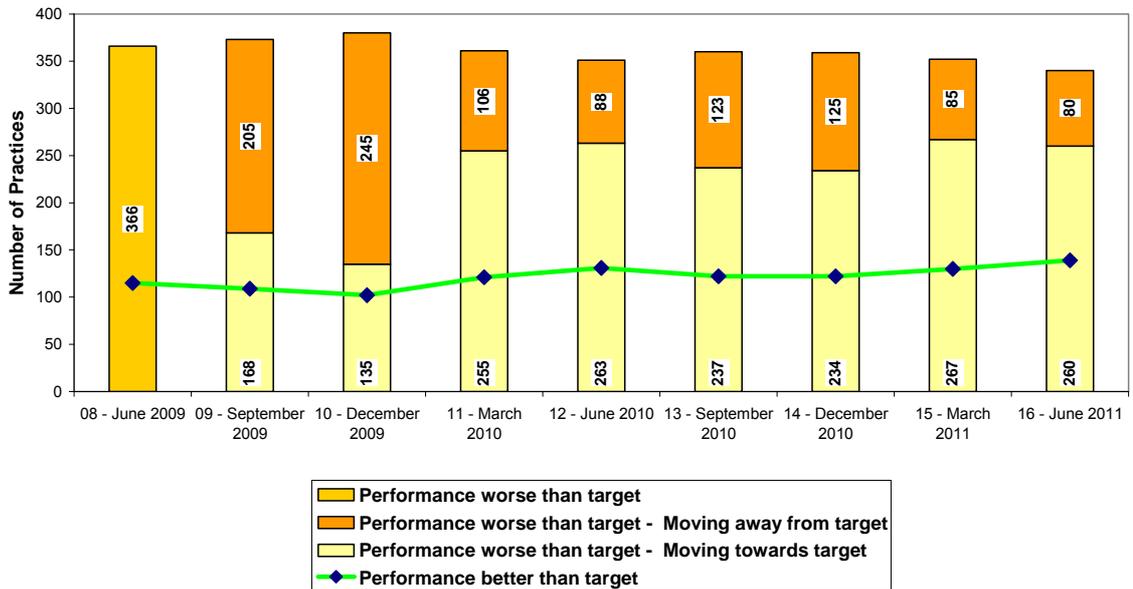
Welsh GP Practices - Practice Level data - Dosulepin DDDs per 1000 PU - (Threshold of Lower Quartile - 73)



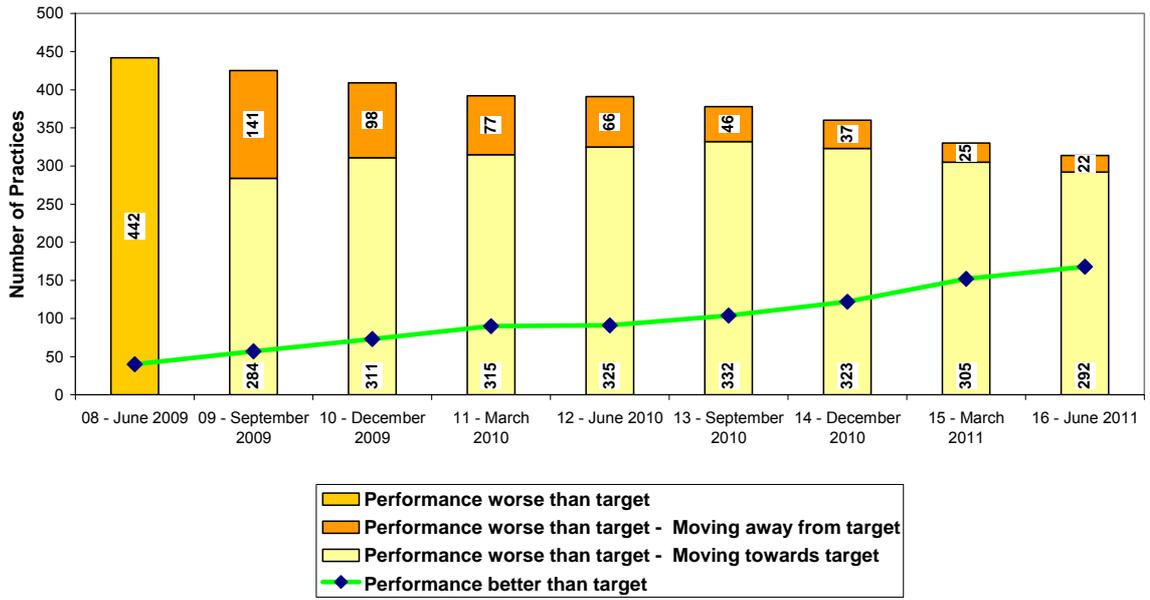
Welsh GP Practices - Practice Level data - Hypnotics DDD per 1000 Patients -  
(Threshold of Lower Quartile - 892)



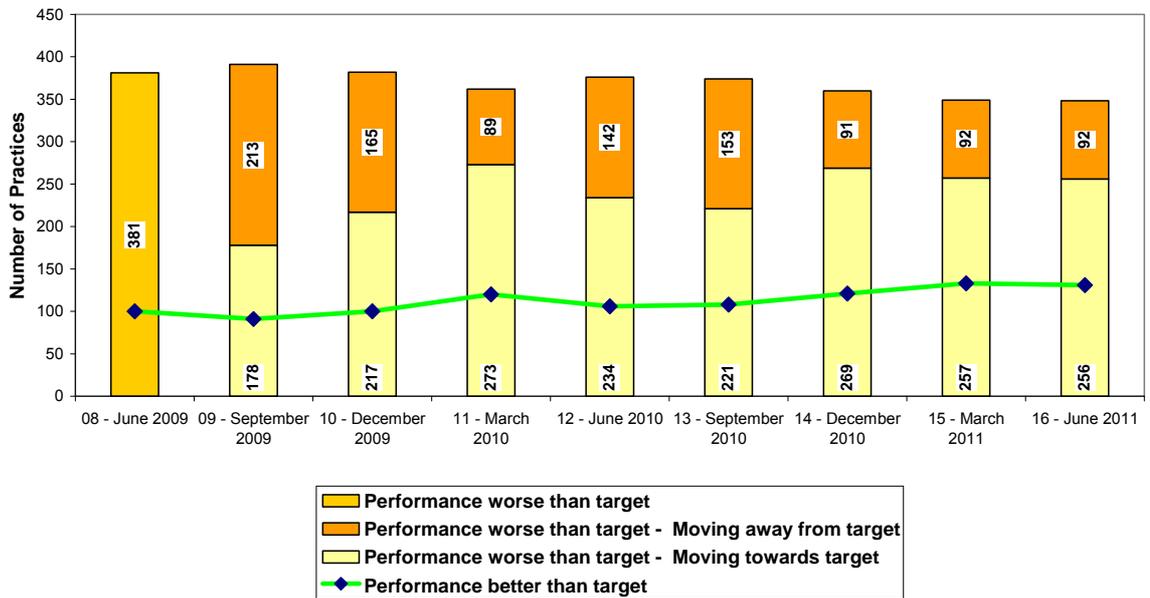
Welsh GP Practices - Practice Level data - Hypnotics and Anxiolytics DDD Quantity  
per 1000 Patients - (Threshold of Lower Quartile - 1,454)



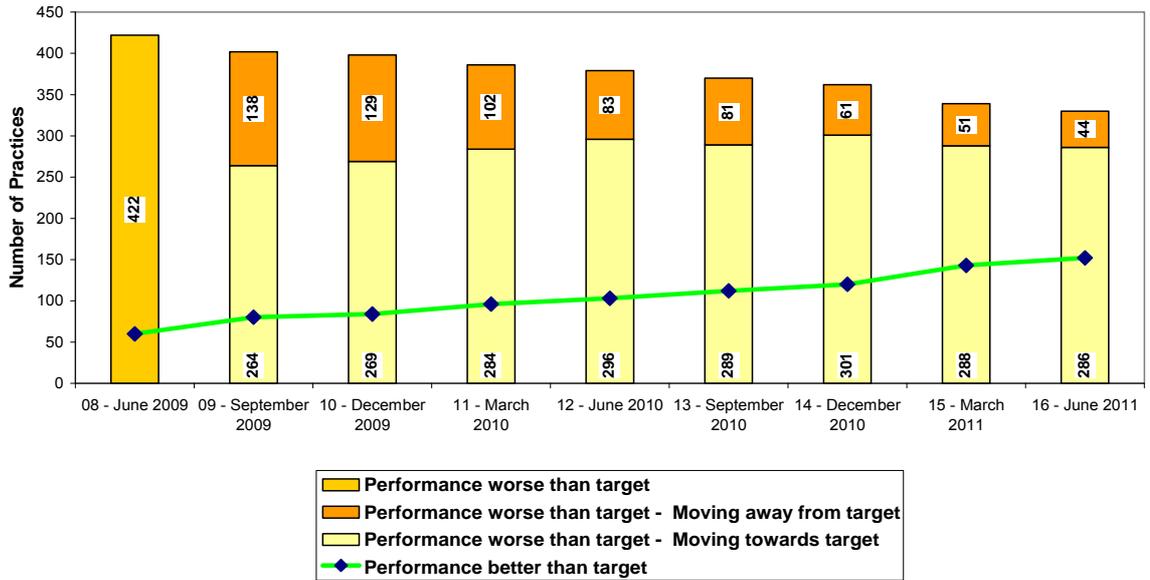
Welsh GP Practices - Practice Level data - Ibuprofen And Naproxen as % of NSAIDs - (Threshold of Upper Quartile - 62.12%)



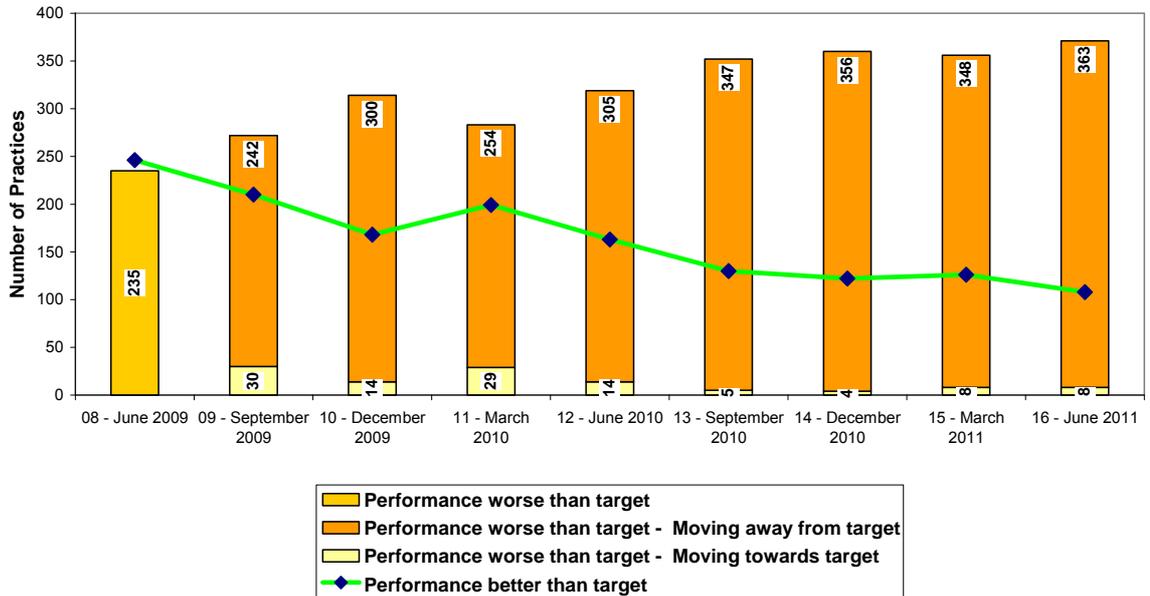
Welsh GP Practices - Practice Level data - NSAIDs ADQ Per 1000 PU - (Threshold of Lower Quartile - 1,690)



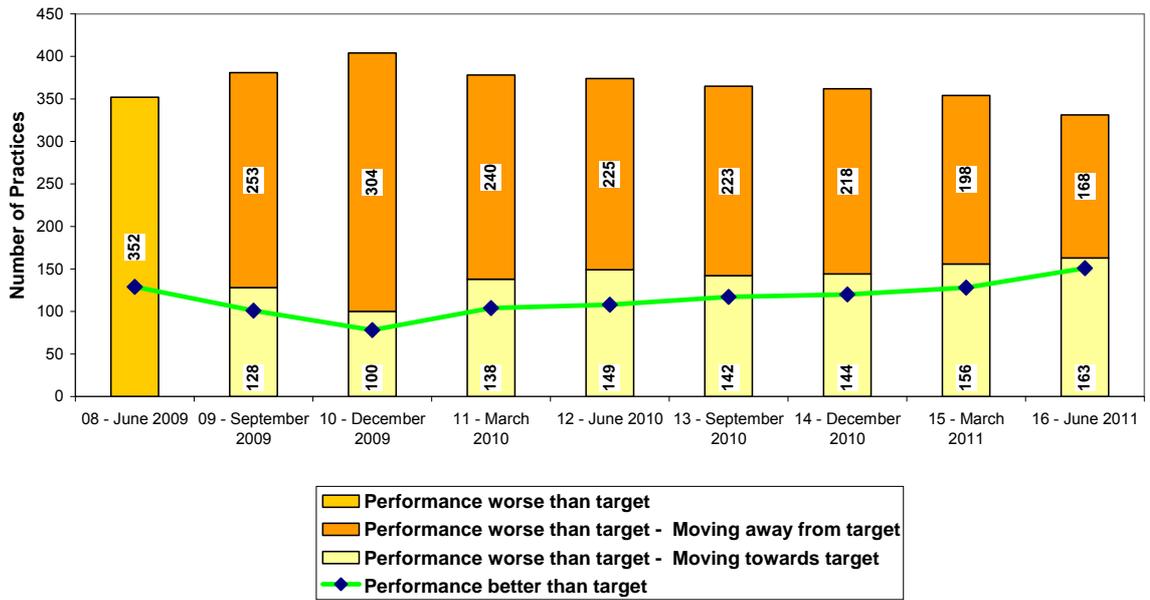
Welsh GP Practices - Practice Level data - LAC PPI as % of all PPIs - (Threshold of Upper Quartile - 94.29%)



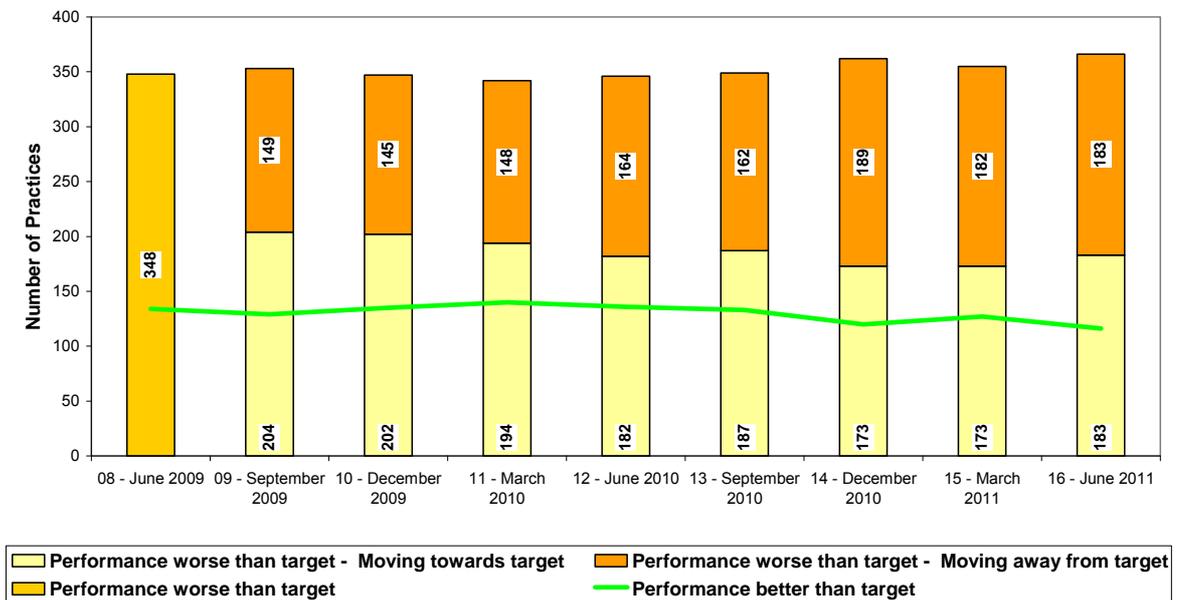
Welsh GP Practices - Practice Level data - PPIs DDDs per 1000 PU - (Threshold of Lower Quartile - 4,748)



Welsh GP Practices - Practice Level data - Quinolones Items Per 1000 PU -  
(Threshold of Lower Quartile - 2.45)



Welsh GP Practices - Practice Level data - Simvastatin and Pravastatin as % of all  
Statins - (Threshold of Upper Quartile - 78.35%)



Welsh GP Practices - Practice Level data - Trimethoprim 200mg 3 day treatment courses - (Threshold of Upper Quartile - 57.86%)

