Grŵp Strategaeth Meddyginiaethau Cymru Gyfan
All Wales Medicines Strategy Group

National Prescribing Indicators 2025–2028

Supporting Safe and Optimised Prescribing

December 2024

(Please note: Due to the withdrawal of Audit+ by the end of 2024–25 it has not been possible to perform feasibility testing or collect relevant baseline data for some of the proposed indicators. This document will be updated as the situation develops.)

This document has been prepared by the All Wales Prescribing Advisory Group (AWPAG) with support from the All Wales Therapeutics and Toxicology Centre (AWTTC) and has subsequently been endorsed by the All Wales Medicines Strategy Group (AWMSG).

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Contents

Introduction

Prescribing indicators are used to highlight therapeutic priorities for NHS Wales and compare the ways in which different prescribers and organisations use particular medicines or groups of medicines. Prescribing indicators should be evidence-based, clear, easily understood and allow health boards, primary care clusters, GP practices and prescribers to compare current practice against an agreed standard of quality. Ideally, they should be validated by a group of experts, and should recommend the direction that prescribing should move, even if it is not possible to specify an exact value that represents 'good practice'. They should usually be standardised to allow comparison between health boards, primary care clusters, or practices serving different sized populations. Weighting can also consider the age and demographics of the population.

In October 2003, the All Wales Medicines Strategy Group (AWMSG) agreed that National Prescribing Indicators (NPIs) were useful tools to promote rational prescribing across NHS Wales, and since then, NPIs have evolved to include secondary care in addition to primary care. It was agreed that NPIs should address efficiency as well as quality and that targets should be challenging but achievable, and applicable at practice level. In order to undertake monitoring, the NPIs draw on a variety of data sources such as CASPACluster, Medusa, Audit+ and the Medicines and Healthcare products Regulatory Agency (MHRA).

For 2025–2028, the National Prescribing Indicators: Supporting Safe and Optimised Prescribing focuses on four priority areas, supported by safety and efficiency domains as shown in Figure 1. This continues with the philosophy of prudent healthcare, enabling higher quality and value through reducing variation, waste and harm. The four priority areas also support two themes in the Quadruple Aim of *A Healthier Wales*, Welsh Government's plan for health and social care[1], which itself supports the achievement of seven national wellbeing goals defined in the Well-being of Future Generations Act[2]. The two *A Healthier Wales* themes are:

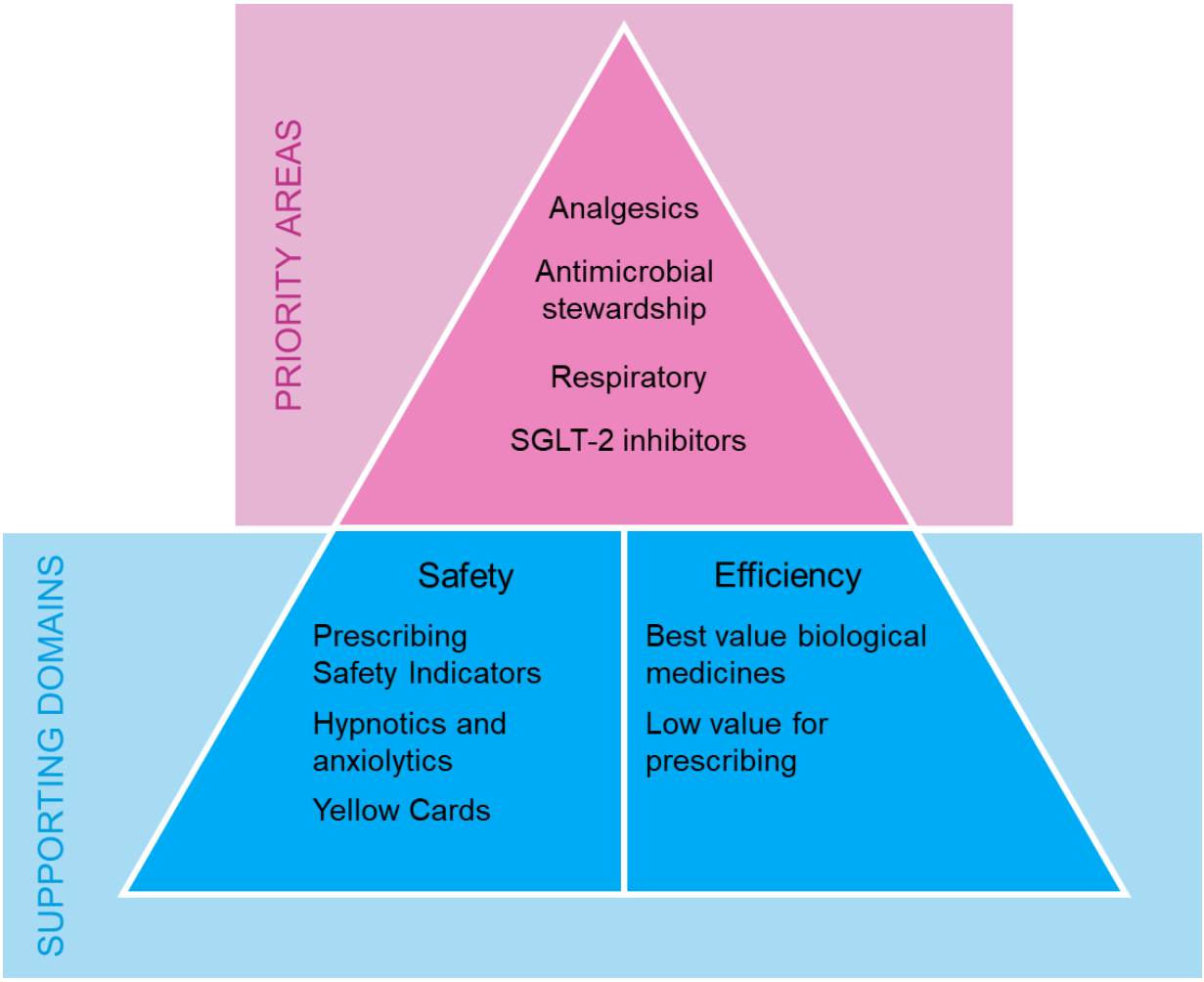
- Population health and wellbeing – better prevention and self-management
- Higher value health and social care – rapid improvement and innovation, enabled by data, focussed on outcomes.

The actions of *A Healthier Wales* were revised in September 2020 to support the stabilisation and recovery of services following the Covid-19 pandemic, as well as elements of *A Healthier Wales* brought to the forefront by the pandemic. An action within the *Determinants of Health* theme focuses on driving good practice to reduce health inequalities and outcomes[3]. The most recent *Wellbeing of Wales* annual report[4], which assesses progress against the seven national wellbeing goals of the Well-being of Future Generations Act, highlights:

- Limited progress made towards achieving the goal for a healthier Wales, with many of the healthier Wales indicators remaining stable.
- Healthy life expectancy continues to be worse for those living in more deprived areas but has remained relatively stable between 2011–2013 and 2018–2020. The national milestone is to increase healthy life expectancy of adults and narrow the gap between the least and most deprived by at least 15% by 2050[4].

Implementation of the NPIs supports the actions of *A Healthier Wales*.

Figure 1. National Prescribing Indicators: Supporting Safe and Optimised Prescribing – Priority areas and supporting domains



The measures for each of the priority and supporting areas, together with the background and evidence, reporting methods and data sources, are included within this document.

Method used to review and update NPIs

An NPI Task and Finish Group of the All Wales Prescribing Advisory Group (AWPAG) was established to review the 2022–2025 NPIs and discuss potential changes for 2025–2028.

Prior to the NPI Task and Finish Group meeting, a questionnaire was sent to health board medicines management teams, prescribing leads, GPs, cluster pharmacists, secondary care prescribers and pharmacists, and Medicines and Therapeutics Committees. This asked for comment on the continued relevance of the 2022–2025 NPIs that may be appropriate to monitor. This information then fed into the discussions of the NPI Task and Finish Group.

Key changes for 2025–2028

NPIs and PSIs for retirement:

- Anticoagulation in atrial fibrillation (AF), measured as the number of patients diagnosed with AF who:
  - Have a CHA2DS2-VASc score of 2 or more who are currently prescribed an anticoagulant, as a percentage of all patients diagnosed with AF.
  - Are currently prescribed an anticoagulant and have received an anticoagulant review (read codes 8BT3, 6A9, or 66QB) within the last 12 months, as a percentage of all patients diagnosed with AF who are prescribed an anticoagulant.
  - Are prescribed antiplatelet monotherapy, as a percentage of all patients diagnosed with AF.
- Number of female patients with a current prescription of oestrogen-only hormone replacement therapy (HRT) without any hysterectomy READ/SNOMED codes.

Retired indicators will continue to be monitored as Local Comparators on SPIRA for two years.

NPIs for inclusion:

- Course duration for respiratory tract infection (RTI) antibiotics.
- Short-Acting Beta-Agonist (SABA) inhalers.
- SGLT-2 inhibitors in patients with and without type 2 diabetes.
- Antimicrobials (nitrofurantoin and trimethoprim), to be included as additional PSIs.
- Topiramate in females aged 14-55 years, to be included as an additional PSI.

Amendments to current NPIs:

- Antimicrobial stewardship
  - Total antibacterial prescribing: Change in unit of measure to report on both items and DDDs per 1,000 STAR-PUs.
  - 4Cs (co-amoxiclav, cephalosporins, fluoroquinolones and clindamycin) antimicrobials: Change in unit of measure to report on items and DDDs per 1,000 patients.
- PSIs for amendment:
  - Number of patients with asthma who have been prescribed a beta-blocker to include only non-cardio-selective beta-blockers.
  - Sodium valproate safety indicator to include male patients.
- Low value for prescribing:
  - Tadalafil removed from the drug basket.
  - Chloral hydrate, rubefacients and alimemazine added to the drug basket.

2DRx data

Future developments during the 2025–2028 NPI timeframe include the potential availability of 2DRx barcoded data. All GP practices in Wales generate 2D barcoded prescriptions and barcoding technologies facilitate the transfer of all of the information on the prescription into the community pharmacy IT system. This includes patient and prescriber information, as well as information on the medication prescribed. This data could allow for more specific indicators to be introduced to supplement the existing NPIs, and Appendix 1 includes some examples. Any indicators developed utilising 2DRx data will require further development and feasibility testing once the data becomes available.

Measures

ADQ: The average daily quantity (ADQ) is a measure of prescribing volume based upon prescribing behaviour in England. It represents the assumed average maintenance dose per day for a medicine used for its main indication in adults. ADQ is not a recommended dose but an analytical unit to compare prescribing activity.

DDD: The defined daily dose (DDD) developed by the World Health Organization is a unit of measurement whereby each medicine is assigned a value within its recognised dosage range. The value is the assumed average maintenance dose per day for a medicine when used for its main indication in adults. A medicine can have different DDDs depending on the route of administration.

OME: Oral morphine equivalence (OME) is a measurement unit of 'mg of oral morphine equivalent dose' and aims to account for the variation in strength across all opioids. It is a widely reported and well understood unit used within healthcare and research, for both general therapeutic areas and in specialist pain management settings.

PU: Prescribing units (PUs) were adopted to take account of the greater need of elderly patients for medication in reporting prescribing performance in primary care. Patients aged 65 years and over are counted as three prescribing units; patients under 65 years and temporary residents are counted as one.

STAR-PU: Specific therapeutic group age–sex related prescribing units (STAR-PUs) are designed to measure prescribing weighted for age and sex of patients. There are differences in the age and sex of patients for whom medicines in specific therapeutic groups are usually prescribed. To make such comparisons, STAR-PUs have been developed based on costs of prescribing or items within therapeutic groups.

- Where possible, measures used should be accessible to all medicines management teams through CASPACluster, SPIRA, Audit+ or Medusa.
- The ADQ and STAR-PU measurements are used for certain indicators instead of the DDD measurement and PU weighting. ADQ measurements are available on CASPACluster and STAR-PU measurements are updated on a quarterly basis by the NHS Wales Shared Services Partnership (NWSSP): Primary Care Services.
- Digital Health and Care Wales (DHCW) will provide Audit+ data on the Prescribing Safety Indicators, which will be accessed by the Welsh Analytical Prescribing Support Unit (WAPSU) at a health board and cluster level.
- The MHRA will provide data on Yellow Card reporting which will be analysed by WAPSU.
- Secondary care medicines data will be supplied by DHCW through the Medusa data warehouse.
- Where data are provided by external sources, WAPSU cannot be held accountable for errors in data provided or delay in provision of data.
- An NPI specification document detailing drug baskets and targets/thresholds will be available on the awttc.nhs.wales website. This will be updated annually to include new targets/thresholds.

Targets

- Details of NPI targets are listed in Tables 1 and 2.
- NPI targets should be challenging but achievable and, unless otherwise stated, based on the principle of encouraging all health boards, local cluster groups and practices to achieve prescribing rates in the best quartile. In these instances, the target is therefore not an absolute value and can be achieved if there is movement towards the threshold set.
  - For primary care NPIs with a threshold, this will normally be set at the 75th percentile (i.e. the prescribing rate of the best performing 25% of practices), for the quarter ending 31st December of the preceding year.
  - Unless otherwise stated, the primary care thresholds are based on prescribing data for all general practices in Wales.

Tables 1 and 2 detail the 'priority area' and 'supporting domain' NPIs for 2025–2028 respectively, with units of measure and targets where applicable.

Evidence

The evidence, prescribing data (where available), and supporting prescribing messages are outlined in the body of the document.

Table 1. Priority area NPIs for 2025–2028

National Prescribing Indicator	Applicable to:	Unit(s) of measure	Target for 2025–2028	Data source
Priority Areas				
Analgesics	Primary care	Opioid burden user defined group (UDG) total OME per 1,000 patients. High strength opioids (UDG) with a likely daily dose of ≥ 120 mg OME per 1,000 patients.	Maintain performance levels within the lower quartile, or show a reduction towards the quartile below.	NWSSP
		Tramadol DDDs per 1,000 patients.	Maintain performance levels within the lower quartile, or show a reduction towards the quartile below.	NWSSP
		Gabapentin and pregabalin DDDs per 1,000 patients.	Maintain performance levels within the lower quartile, or show a reduction towards the quartile below.	NWSSP
Antimicrobial stewardship	Primary care	Total antibacterial DDDs per 1,000 STAR-PUs. Total antibacterial items per 1,000 STAR-PUs.	DDDs health board target: a quarterly reduction of 6%, 7% and 8% in subsequent years against a baseline of data from April 2019–March 2020. GP Practice target: Maintain performance levels within the lower quartile, or show a reduction towards the quartile below. GP Practice target: Maintain performance levels within the lower quartile, or show a reduction towards the quartile below.	NWSSP
		4C antimicrobials (co-amoxiclav, cephalosporins, fluoroquinolones and clindamycin) items combined, per 1,000 patients. 4C DDDs combined, per 1,000 patients.	Maintain performance levels within the lower quartile, or show a reduction towards the quartile below.	NWSSP

National Prescribing Indicator	Applicable to:	Unit(s) of measure	Target for 2025–2028	Data source
Priority Areas				
Antimicrobial stewardship	Primary care	• Proportion of amoxicillin 500 mg capsules prescribed for 5-day duration. • Proportion of doxycycline 100 mg capsules prescribed for 5-day duration. • Proportion of clarithromycin 500 mg tablets prescribed for 5-day duration.	• 75% of amoxicillin prescriptions issued as a 5-day duration versus a 7-day duration. • 75% of doxycycline prescriptions issued as a 5-day duration versus a 7-day duration. • 75% of clarithromycin prescriptions issued as a 5-day duration versus a 7-day duration.	NWSSP
Respiratory	Primary care	The number of dry powder inhalers (DPI) and soft mist inhalers (SMI) as a percentage of all inhalers prescribed.	80% of inhalers prescribed to be of low GWP, or show an increase towards the quartile above.	NWSSP
		Number of short acting beta agonist (SABA) inhalers as a percentage of all inhalers.	Maintain performance levels within the lower quartile, or show a reduction towards the quartile below.	NWSSP
SGLT-2 inhibitors	Primary care	Number of patients with type 2 diabetes and chronic heart failure who are prescribed an SGLT-2 inhibitor.	To increase the number of patients with type 2 diabetes and chronic heart failure prescribed an SGLT-2 inhibitor.	DHCW
	Primary care	Number of patients with type 2 diabetes and chronic kidney disease who are currently treated with an ARB or ACE inhibitor prescribed an SGLT-2 inhibitor.	To increase the number of patients with type 2 diabetes and chronic kidney disease prescribed an SGLT-2 inhibitor.	DHCW
	Primary care	Number of patients with non-diabetic chronic kidney disease who are currently treated with an ARB or an ACE inhibitor and have an ACR ≥ 22.6 mg/mmol prescribed an SGLT-2 inhibitor.	To increase the number of patients with non-diabetic chronic kidney disease prescribed an SGLT-2 inhibitor.	DHCW

Table 2. Supporting domain NPIs 2025–2028

National Prescribing Indicator	Applicable to:	Unit of measure	Target for 2025–2028	Data source
Supporting Domain: Safety				
Prescribing Safety Indicators	Primary care	Number of patients identified.	No target set.	DHCW
Hypnotics and anxiolytics	Primary care	Hypnotic and anxiolytic UDG ADQs per 1,000 STAR-PUs.	Maintain performance levels within the lower quartile, or show a reduction towards the quartile below.	NWSSP
Yellow Cards	Primary care	Number of Yellow Cards submitted.	One Yellow Card per 2,000 GP practice population.	MHRA
	Health board		One Yellow Card per 2,000 health board population. 10% or greater increase from baseline (previous financial year) for Yellow Cards submitted by secondary care. 25% or greater increase from baseline (previous financial year) for Yellow Cards submitted by members of the public.	
	Community pharmacy		No target set. Reported as the number of Yellow Cards submitted by health board.	
Supporting Domain: Efficiency				
Best value biological medicines	Primary + secondary care	Quantity of best value biological medicines prescribed as a percentage of total ‘biosimilar’ plus ‘reference’ product.	Increase the appropriate use of cost-efficient biological medicines, including biosimilar medicines.	NWSSP DHCW
Low value for prescribing	Primary care	Low value for prescribing UDG spend per 1,000 patients.	Maintain performance levels within the lower quartile or show a reduction towards the quartile below.	NWSSP

Please note: Implementation of the recommended NPIs 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. This is supported by the philosophy of prudent healthcare and *A Healthier Wales*, Welsh Government's plan for health and social care[1].

1.0 Priority areas

1.1 Analgesics

Analgesic medicines have been the mainstay of the treatment of pain for decades. Pain can be defined as acute or chronic, depending on the length of time the person has experienced pain. Chronic pain, also known as persistent pain, is usually defined as occurring when pain has been present for three months or more[5], and can be further categorised as chronic primary pain (CPP) or chronic secondary pain (CSP). CPP is pain with no clear underlying cause, or pain (or its impact) that is out of proportion to any observable injury or disease, with an estimated prevalence of 1%-6%[6]. CSP is pain caused by an underlining condition, for example rheumatoid arthritis or endometriosis. Chronic primary pain and chronic secondary pain can coexist[6]. In April 2021, NICE published a guideline for *Chronic Pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain,* which advocates a number of non-pharmacological options for the management of chronic primary pain, rather than analgesics[6]. The Welsh Pain Society recommends reserving opioids for patients who have defined conditions for which opioids have been shown to be effective but after all appropriate non-opioid and non-pharmacological options have been tried[7].

A number of analgesic medicines with different mechanisms of action and licensed indications are available; however, the current analgesic NPIs focus on total opioid use; high strength opioids; tramadol; and gabapentin and pregabalin. They have been included as concerns have been raised regarding their appropriate use and review, in addition to their potential for dependence, diversion and misuse.

There is increasing evidence that many analgesics, including opioids, gabapentin and pregabalin, have the potential for harm and abuse. Cases of dependency have been described and there are reports of an increasing street value and risk of drug misuse[8]. Patients should be given information on the potential benefits of their medicine, and its risks and reported side effects, including the potential for such medicines to lead to abuse or dependence[8]. In September 2019, due to the growing problem of dependence and addiction to prescription medicines, Public Health England published a review of the evidence for dependence on and withdrawal from prescribed medicines, which included opioids and gabapentinoids. The review made a number of recommendations, including: increasing the availability and use of data on the prescribing of medicines that can cause dependence or withdrawal to support greater transparency and accountability and help ensure practice is consistent and in line with guidance; and improving information for patients on prescribed medicines and other treatments, and increasing informed choice and shared decision-making between clinicians and patients[9].

1.1.1 Opioid burden

Purpose:
To encourage the appropriate use and review of opioids in primary care, minimising the potential for dependence, diversion, misuse and ADRs.
Units of measure:
1. Opioid burden UDG total oral morphine equivalence (OME) per 1,000 patients. 2. High strength opioids UDG with a likely daily dose of ≥ 120 mg OME per 1,000 patients.
Target for 2025–2028:
Maintain performance levels within lower quartile, or show a reduction towards the quartile below.

Note
Monitoring of trends in total analgesic prescribing and other analgesics should be undertaken alongside these NPIs in order to assess the overall picture of analgesia prescribing in Wales.

Figure 2. Trend in opioid burden OME per 1,000 patients to quarter ending June 2024

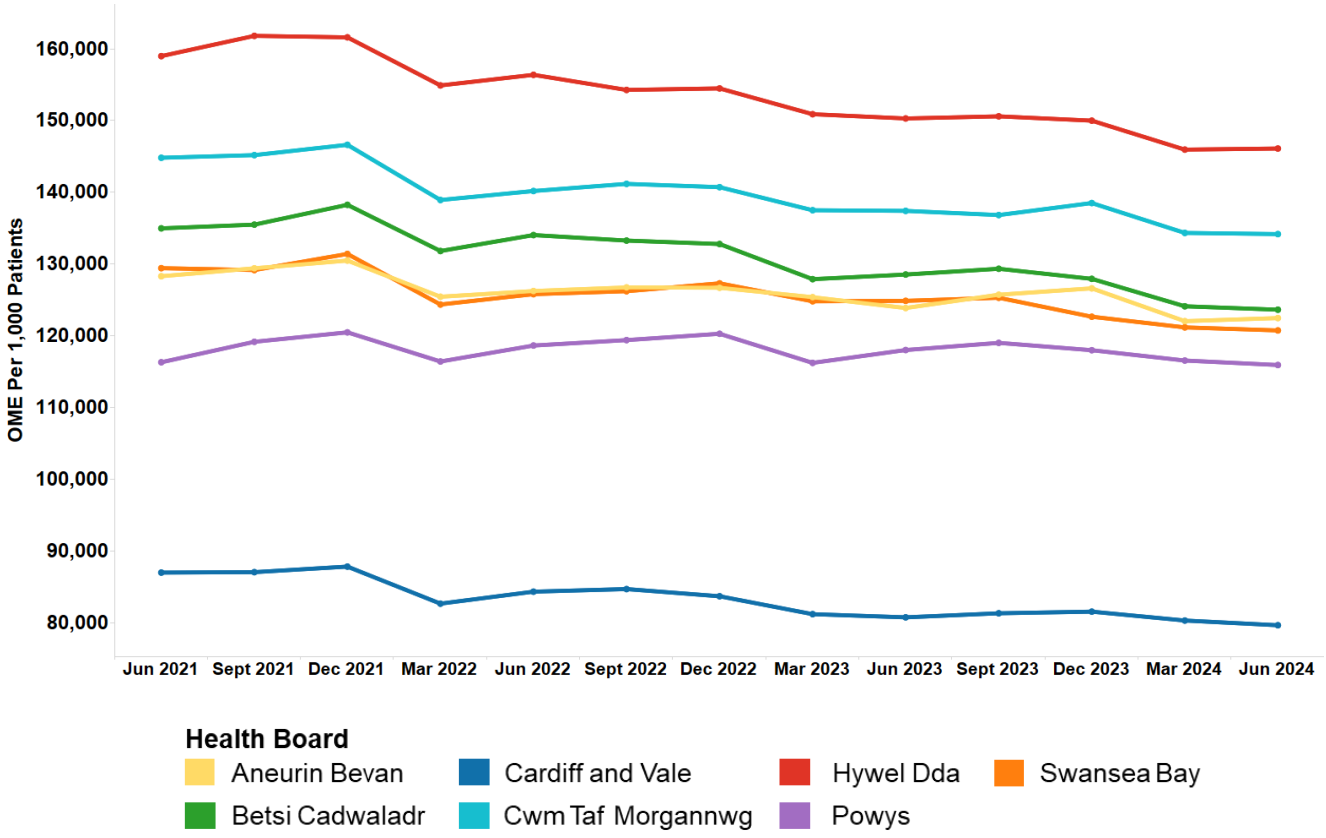


Figure 3. Opioid burden OME per 1,000 patients in Welsh health boards and English CCGs – Quarter ending June 2024

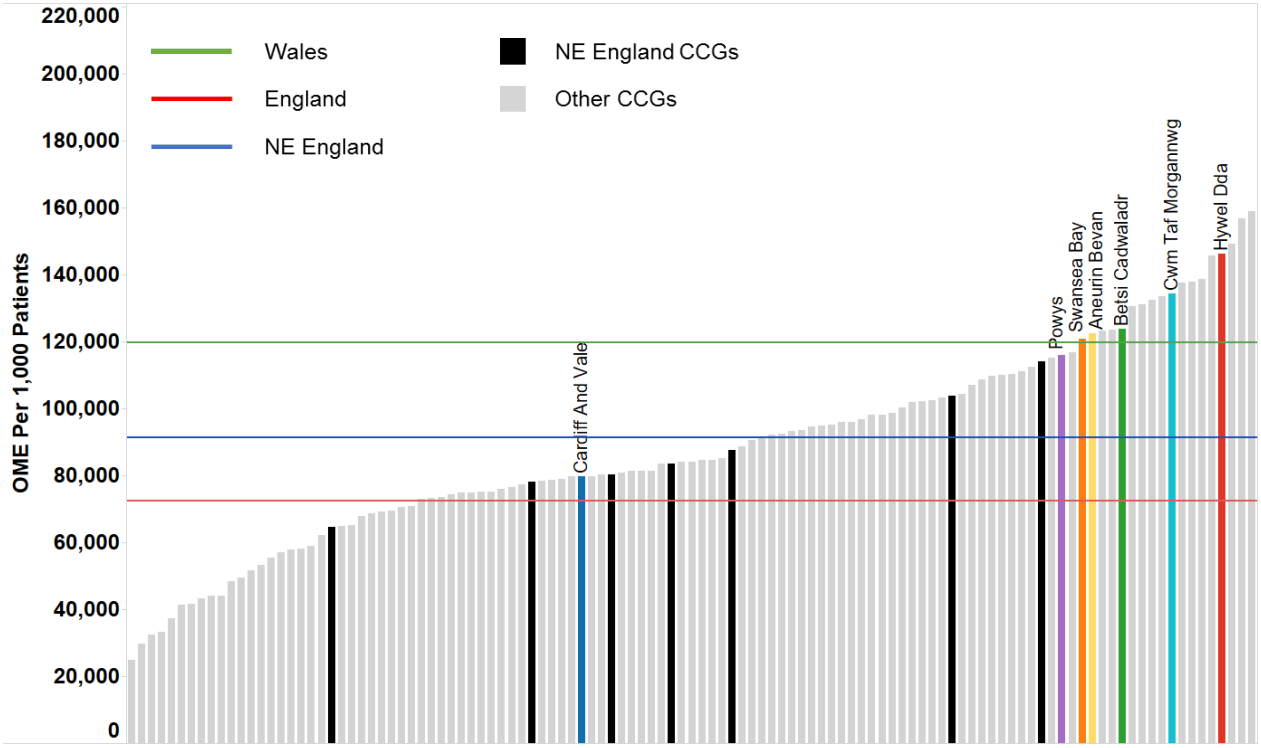


Figure 4. Trend in high strength opioids OME per 1,000 patients to quarter ending June 2024

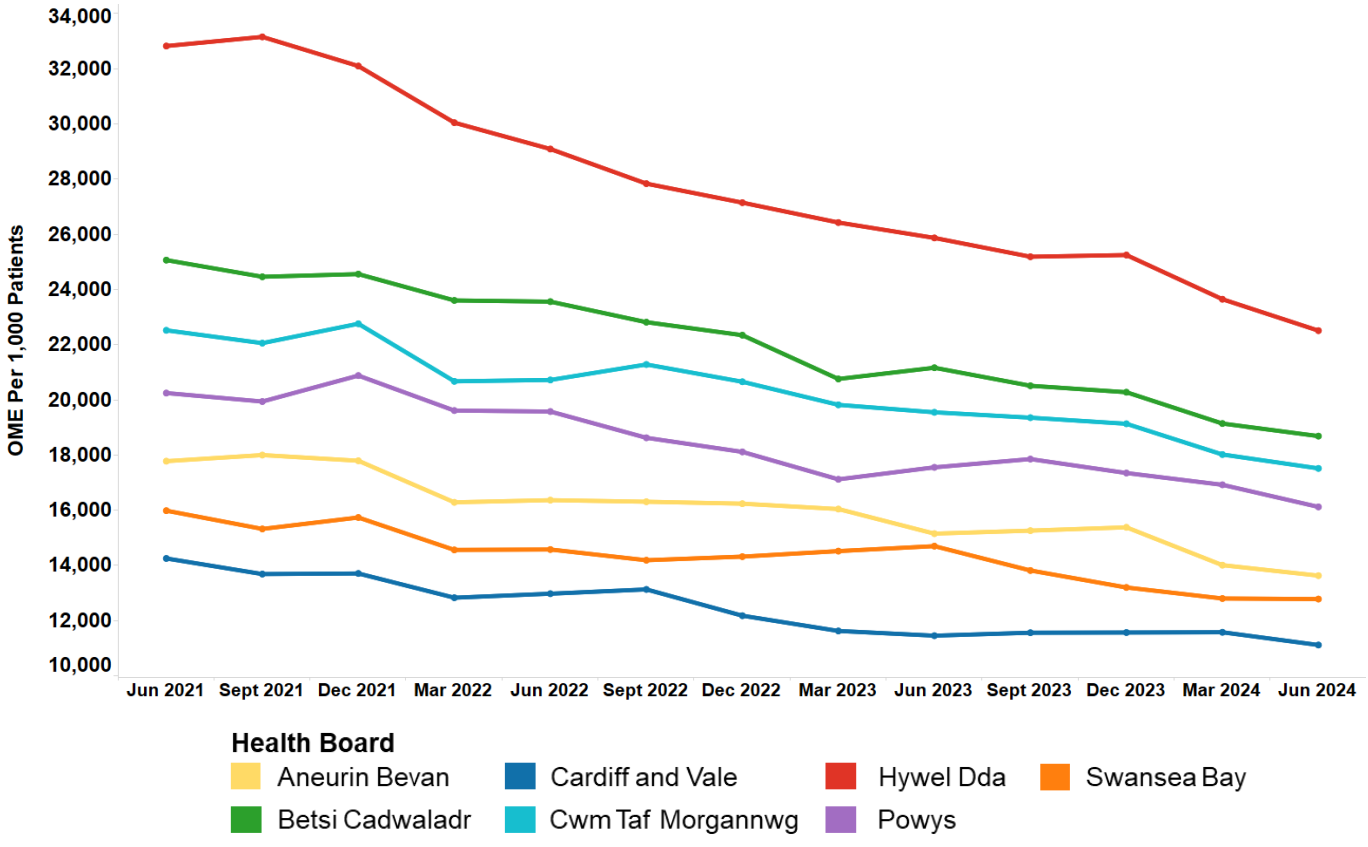
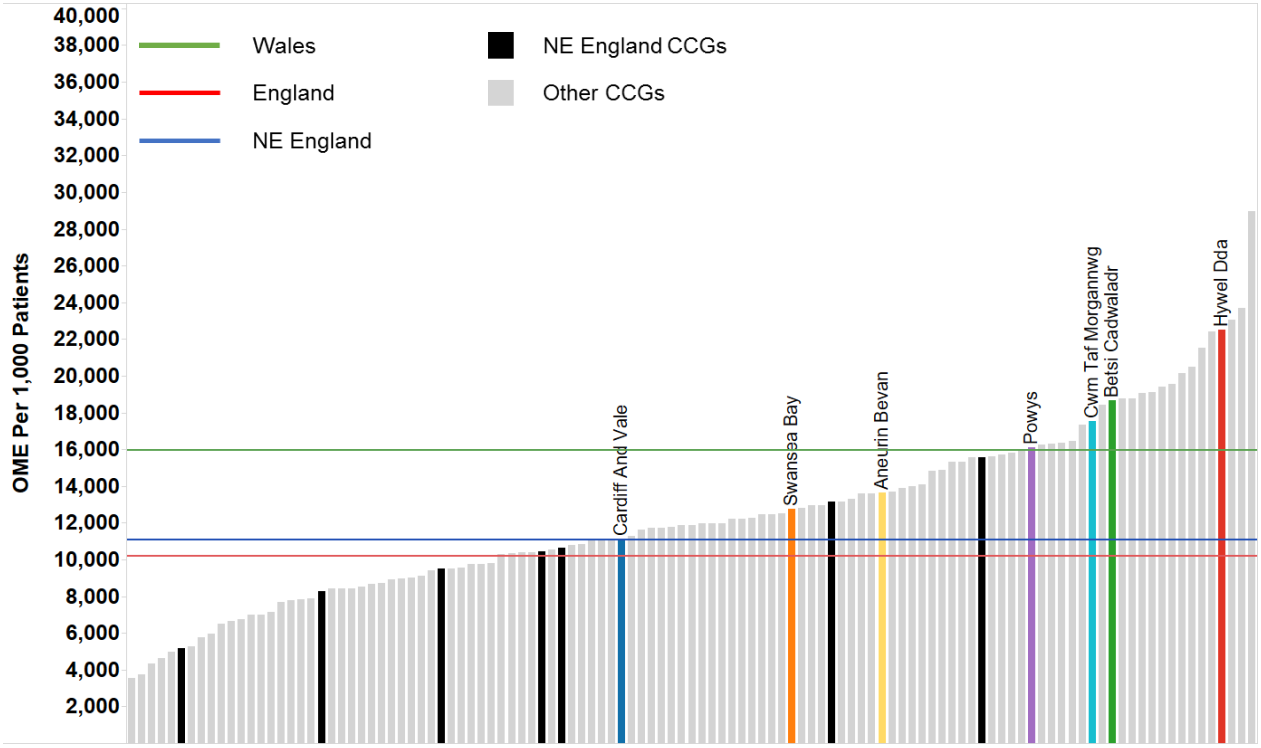


Figure 5. High strength opioids OME per 1,000 patients in Welsh health boards and English CCGs – Quarter ending June 2024



Background and evidence

Opioid analgesics have long been used as the gold standard to treat severe pain, most notably for acute pain and in palliative care[10]. The WHO analgesic ladder advocates a stepwise approach from non-opioid analgesics to opioids for mild to moderate pain, followed by opioids for moderate to severe pain. It was developed with the aim of helping patients with cancer achieve freedom from pain[11], but has often been used as a guide to the treatment of chronic pain. This has resulted in patients with chronic pain receiving increasing doses of strong opioids, however, it has never been validated in this setting[12], and this simple approach is not appropriate for chronic pain, which is highly complex[13].

Due to a lack of evidence of effectiveness, opioids are not recommended as a treatment option for the management of chronic primary pain. NICE states that opioids should not be initiated to manage chronic primary pain for this reason[6]. In addition, evidence from non-randomised studies on the use of long-term opioids for chronic pain suggests an increased risk of dependence, although it is acknowledged that there were limitations on the studies[6].

Opioid analgesics have well established side effects including constipation, nausea and vomiting, and respiratory depression, and repeated administration may cause tolerance and dependence[14]. Whilst concerns regarding tolerance and dependence should be no deterrent in the control of pain in terminal illness[14], they should be considered when prescribing for other causes of pain. A systematic review in 2015 suggested that rates of misuse of opioids in patients treated for chronic pain ranged from 21% to 29% and that addiction resulted in between 8% and 12% of patients taking opioids[15,16].

A briefing paper by the British Medical Association (BMA), *Chronic Pain: supporting safer prescribing of analgesics,* notes that too many people with chronic pain are

prescribed opioids at high doses. Doses above an oral morphine equivalence (OME) of 120 mg/day increases the risk of harm without any increased benefit for the patient [17,18]. A table providing approximate OME values for opioids can be found in Appendix 2.

Despite the lack of evidence for use in chronic non-cancer pain, research in the UK has found an escalation of strong opioid prescribing in primary care, predominantly for non-cancer patients[10]. A retrospective cohort study looking at opioid prescribing in primary care in Wales between 2005 and 2015, found that the annual number of prescriptions for opioids increased by 44%, while the total daily OME per 1,000 patients increased by 95%[19]. During the same period, the annual number of opioid related deaths increased from 82 in 2005 to 141 in 2015. Since then, the annual number of opioid related deaths in Wales has fluctuated, with the most recent data reporting a total of 124 deaths in 2022[20]. A November 2018 briefing statement to health professionals on the management of opioid medications, issued by the Faculty of Pain Medicine of the Royal College of Anaesthetists, highlights that there is professional and governmental concern regarding misuse of prescription medicines and the number of prescriptions of opioid analgesics. Key messages from the briefing statement include the urgent need to screen and assess people on opioids, and to make clinical decisions about opioid reduction and optimal pain management[21].

NICE guidance recommends that if a person with chronic primary pain is already taking an opioid analgesic, this should be reviewed[6]. As part of the shared decision-making process, it should be explained that there is a lack of evidence for efficacy of these medicines for chronic primary pain. A plan for continuing taking an opioid analgesic safely should be agreed if the patient reports a benefit at a safe dose with few harms. The risks of continuing opioid analgesic use should be explained if they report little benefit and/or significant harm. Where this is the case, the patient should be encouraged and supported to reduce and stop the opioid if possible[6].

The decision to taper and stop an established opioid regimen needs to be discussed carefully with the patient, it should include an explanation of the rationale for stopping opioids and the potential benefits of opioid reduction (avoidance of long-term harms and the ability to engage in self-management strategies); agree outcomes of opioid tapering; outline arrangements for monitoring and support during opioid tapering; and document an agreed tapering schedule. The dose of drug can be tapered by 10% weekly or fortnightly[17].

Chronic pain is a complex condition which has a substantial impact on the lives of those affected. The relief of pain should be seen as a clinical priority, yet the prescribing of opioids is often not the most appropriate or effective treatment option for many patients with chronic pain, and can risk exposing patients to unnecessary harm[12]. Complete pain relief is rarely achieved, therefore management should focus not only on reduction in pain intensity but also on improved function. An estimated 49% of patients in the UK suffering from chronic pain also suffer from depression[12], and there is variable interplay between biological, psychological and social factors[22]. Although off label use, NICE recommends consideration of an antidepressant in the pharmacological management of chronic primary pain, to help with quality of life, sleep and psychological distress, even in the absence of a diagnosis of depression[6].

This NPI promotes a prudent approach to prescribing opioid analgesics, taking into account the indication, assessing risks and benefits, and encouraging timely review of patients prescribed opioids for chronic pain.

Useful resources

- AWMSG (2023) Resources for pharmacological management of pain
- Health Education and Improvement Wales (undated) Analgesic Stewardship and Pain Management
- Live Well with Pain (2024) Living Well with Pain resources and training for social prescribers, clinicians and other practitioners in supporting pain self-management
- NICE guideline (2021) Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain
- PrescQIPP (2023) Bulletin 336: Reducing opioid prescribing in chronic pain
- PrescQIPP (2022) Bulletin 284: Chronic pain
- RCoA Faculty of Pain Medicine (2022) Opioids Aware
- RCoA Faculty of Pain Medicine (2019) Opioids Aware: Tapering and stopping opioids
- RCoA Faculty of Pain Medicine (2019) Checklist for Prescribers

1.1.2 Tramadol

Purpose:
To encourage the appropriate use and review of tramadol in primary care, minimising the potential for dependence, diversion, misuse and ADRs.
Unit of measure:
Tramadol DDDs per 1,000 patients.
Target for 2025–2028:
Maintain performance levels within lower quartile, or show a reduction towards the quartile below.

Note
Monitoring of trends in total analgesic prescribing and other analgesics should be undertaken alongside these NPIs in order to assess the overall picture of analgesia prescribing in Wales.

Figure 6. Trend in tramadol DDDs per 1,000 patients to quarter ending June 2024

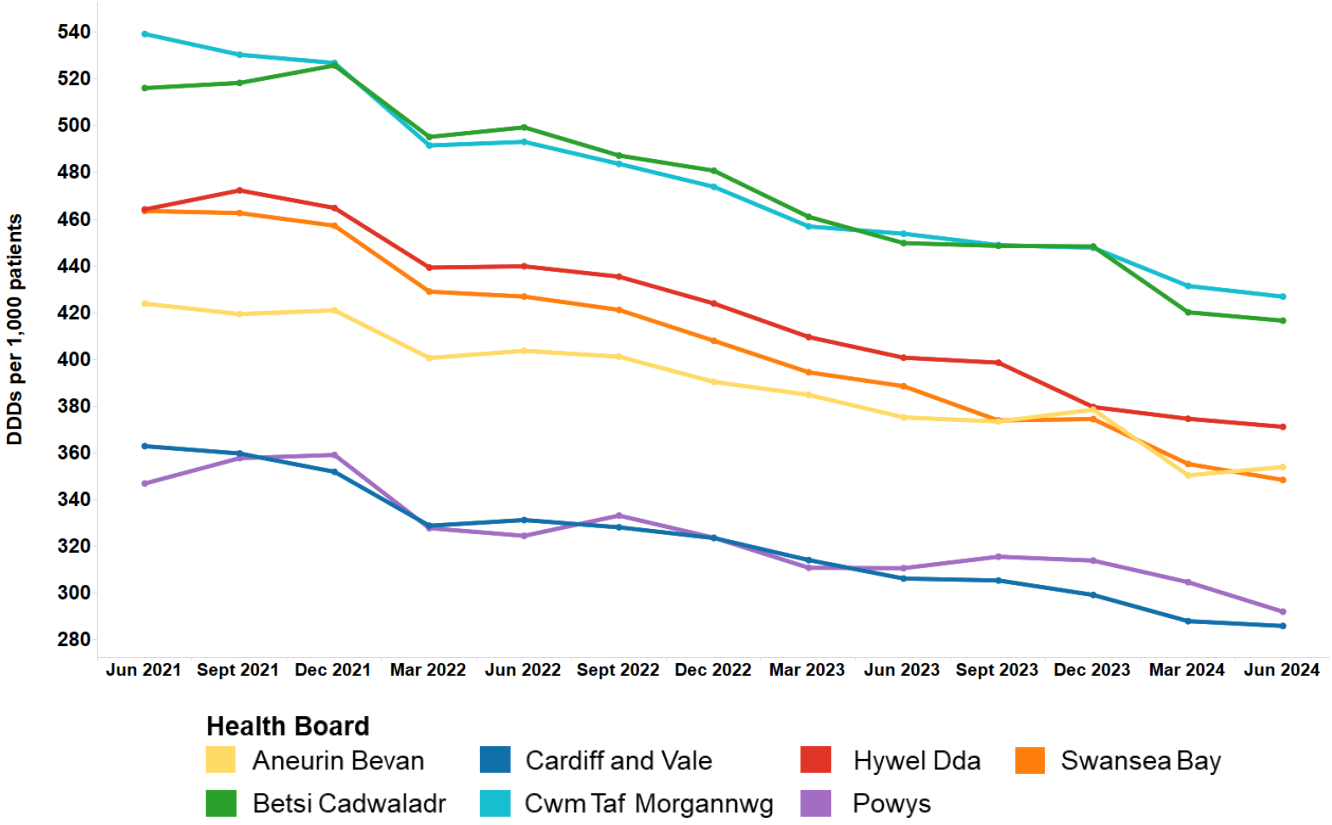
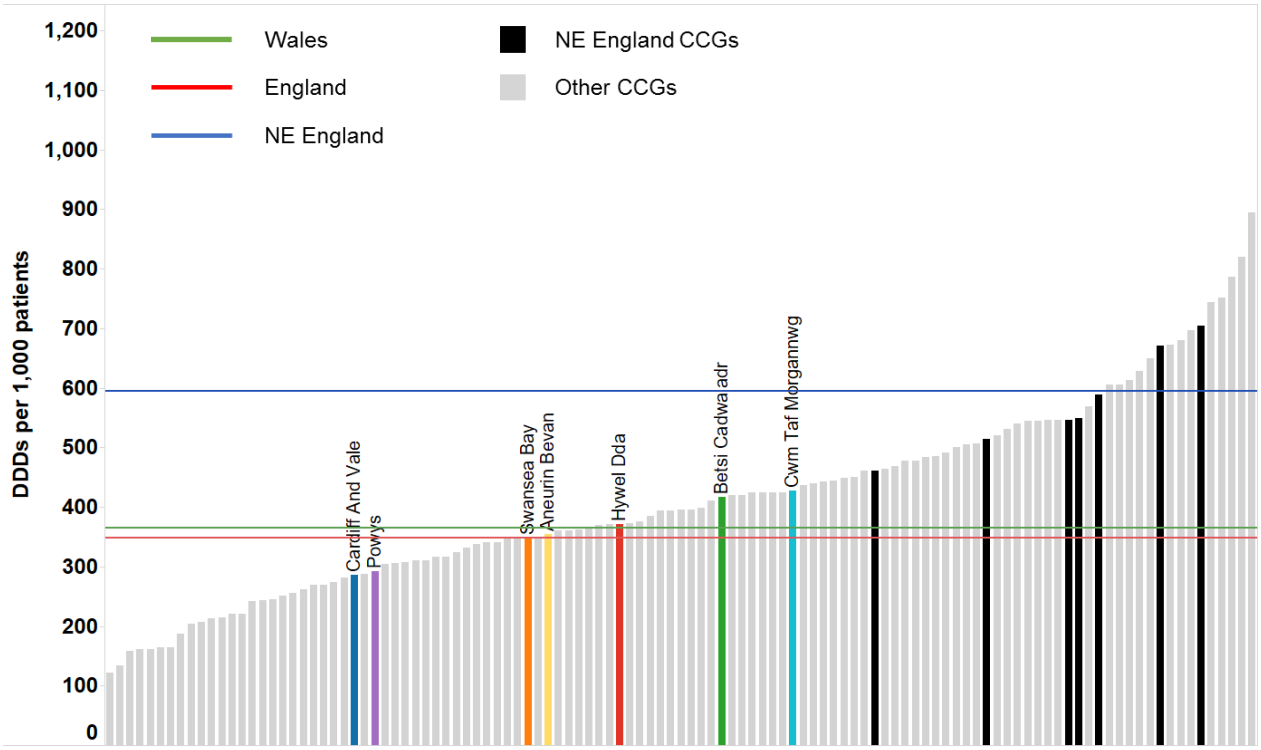


Figure 7. Tramadol DDDs per 1,000 patients in Welsh health boards and English CCGs – Quarter ending June 2024



Background and evidence

Tramadol is an opioid analgesic licensed for the treatment of moderate to severe pain. Tramadol produces analgesia by two mechanisms: an opioid effect and an enhancement of the serotonergic and adrenergic pathways[14]. It has fewer of the typical opioid side effects (notably, less respiratory depression, less constipation and less addiction potential); psychiatric reactions have been reported[14]. The unique dual-action pharmacological profile of tramadol increases the risk of adverse effects seen in overdose[23].

In 2013, the Advisory Council on the Misuse of Drugs recommended that the UK Government should reclassify tramadol as a class C substance, and place it within Schedule III of the Misuse of Drugs Regulations 2001, due to concerns regarding abuse, dependence and an increasing number of deaths involving tramadol[23]. The changes came into force in June 2014, since then, the number of deaths involving tramadol in Wales has fluctuated annually with the most recent data reporting seven deaths in 2022[20]. Concerns remain regarding the potential for abuse and dependence.

Dizziness and nausea are the most commonly reported adverse effects, with headache, drowsiness, vomiting, constipation, dry mouth, fatigue and sweating also frequently reported[24]. Rare adverse effects include hallucinations, confusion, sleep disturbance, anxiety and nightmares, as well as cases of dependence and withdrawal[24]. To minimise the risk of convulsions, patients with a history of epilepsy or those susceptible to seizures should only be treated with tramadol if there are compelling reasons to do so[24]. In addition, tramadol should be used with caution in patients also taking medicines that can lower the seizure threshold, such as tricyclic antidepressants or selective serotonin reuptake inhibitors (SSRIs)[24]. The use of tramadol is contraindicated in uncontrolled

epilepsy and in patients receiving, or who have recently discontinued (within the previous two weeks) monoamine oxidase inhibitors[24].

If it is appropriate for a patient's tramadol to be stepped down or stopped, it is important to note that the dose must be reduced slowly to ensure the patient's safety and to minimise the risk of withdrawal symptoms and/or adverse reactions. Where physical dependence to tramadol develops, the withdrawal syndrome can be severe, with symptoms typical of opiate withdrawal sometimes accompanied by atypical symptoms including seizures, hallucinations and anxiety[23,25]. To encourage patient engagement and concordance, a suggested approach would be to reduce the dose at each reduction step, e.g. by one 50 mg dose, and to titrate according to how the patient manages, rather than by setting time limits for the next reduction. Every patient and their circumstances will be different, and a prudent and individually tailored approach is required[26].

This NPI does not measure the prescribing of tramadol and paracetamol combination products as there are no DDDs available; however, these products are included in the *Medicines Identified as Low Priority for Funding in NHS Wales – Paper 2*, due to a lack of advantage over the individual preparations, with prescribing data made available on SPIRA.

While there is a recognised place in pain management for tramadol, concerns regarding the risks associated with misuse and diversion prompted a review of tramadol prescribing, in addition to a larger package of resources for pharmacological management of pain, in NHS Wales[26,27]. AWMSG's *Tramadol Educational Resources* outlines prescribing key points and provides audit materials to support healthcare professionals undertaking reviews of tramadol prescribing in order to ensure it is appropriately prescribed. It advises prescribing tramadol only where it is clearly indicated and if it improves pain and function. A suite of patient information leaflets (including Easy Read versions) were also developed to support prescriber-patient conversations[26]. It must be noted that pain management is often complex and prescribers need to make evidence-based, informed decisions based on the individual needs of the patient.

This NPI promotes a prudent approach to prescribing tramadol, taking into account the risks and benefits of tramadol while encouraging timely review.

Useful resources

- AWMSG (2023) Resources for pharmacological management of pain
- AWMSG (2021) Tramadol educational resources

1.1.3 Gabapentin and pregabalin

Purpose:
To encourage the appropriate use and review of gabapentin and pregabalin in primary care, minimising the potential for dependence, diversion, misuse and ADRs.
Unit of measure:
Gabapentin and pregabalin DDDs per 1,000 patients.
Target for 2025–2028:
Maintain performance levels within lower quartile, or show a reduction towards the quartile below.

Note
Monitoring of trends in total analgesic prescribing and other analgesics should be undertaken alongside these NPIs in order to assess the overall picture of analgesia prescribing in Wales.

Figure 8. Trend in gabapentin and pregabalin DDDs per 1,000 patients to quarter ending June 2024

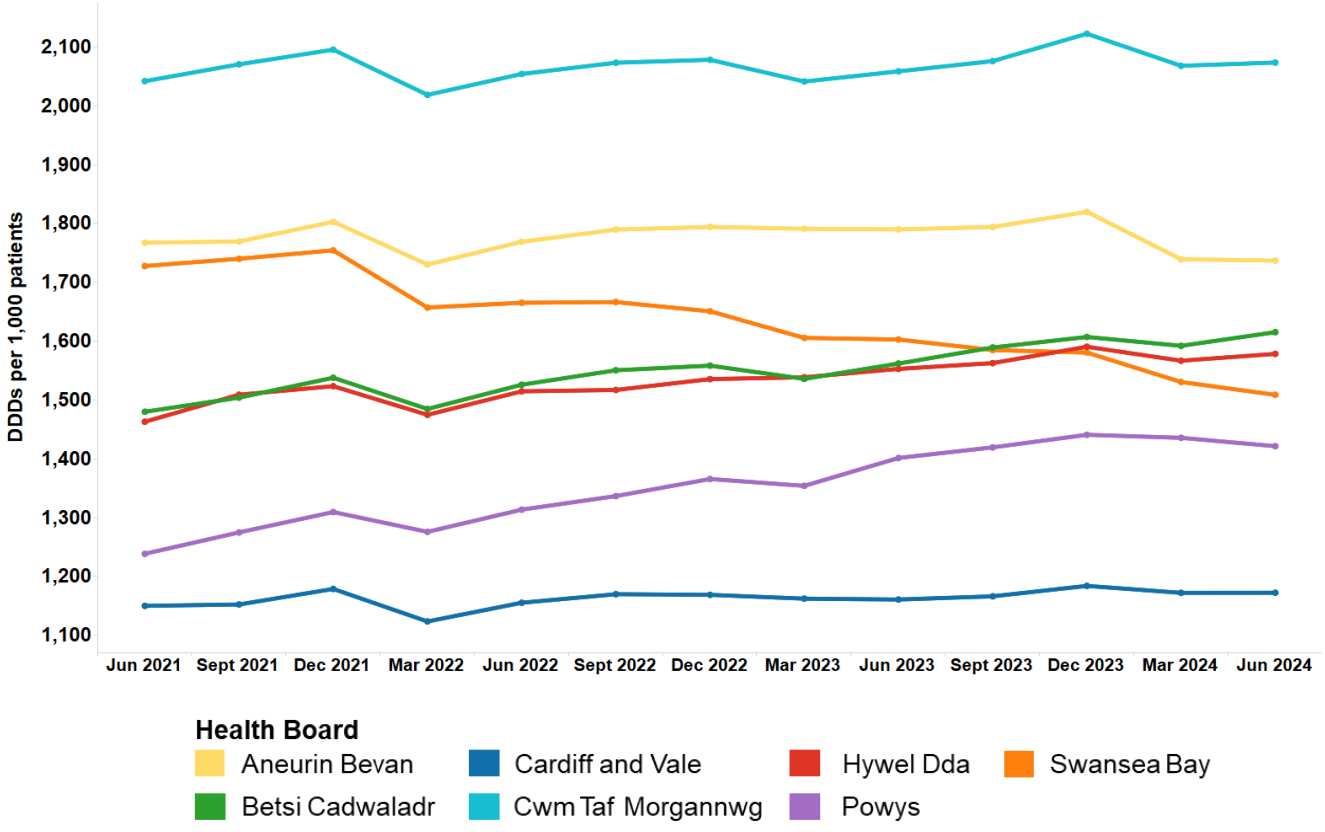
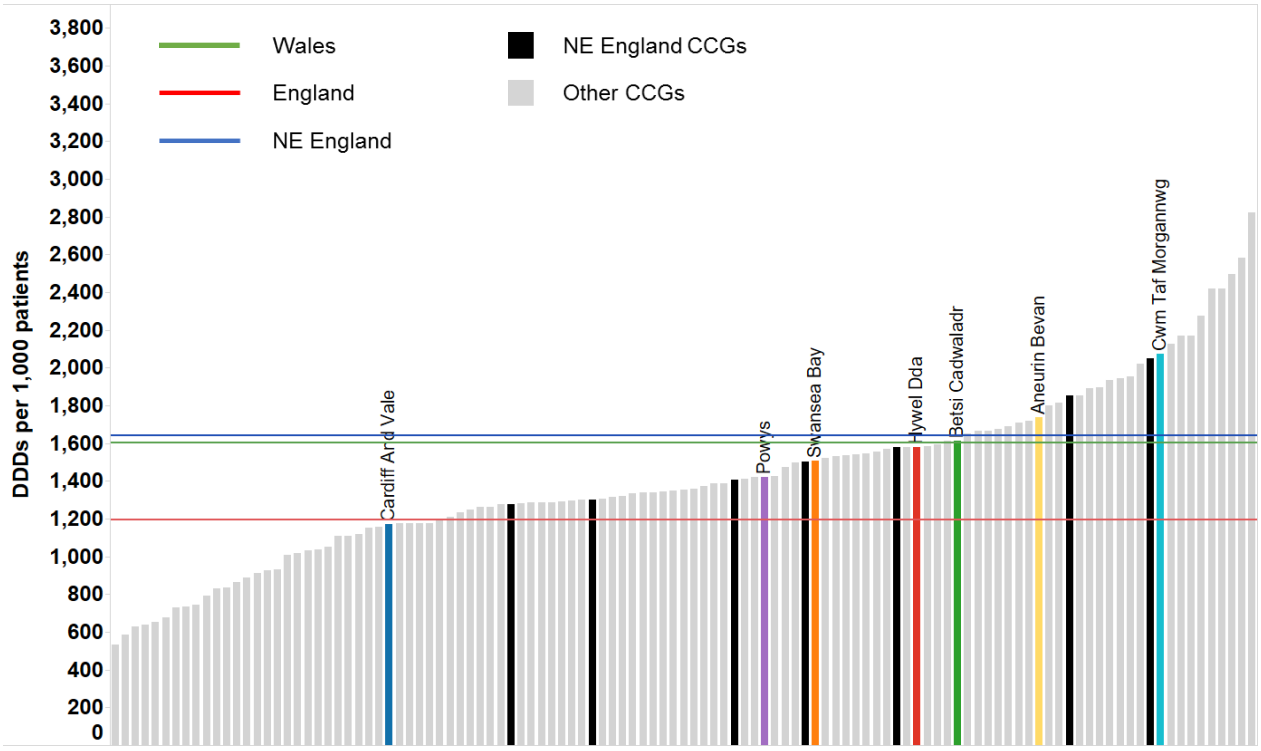


Figure 9. Gabapentin and pregabalin DDDs per 1,000 patients in Welsh health boards and English CCGs – Quarter ending June 2024



Background and evidence

NICE recommends gabapentin or pregabalin as first-line options in the treatment of neuropathic pain, along with amitriptyline and duloxetine[28]. Gabapentin is licensed for peripheral neuropathic pain and epilepsy[29-31], whilst pregabalin is licensed for peripheral and central neuropathic pain, in addition to epilepsy and as a third line option for the treatment of generalised anxiety disorder (GAD)[32-35]. In April 2019, gabapentin and pregabalin were reclassified as Schedule 3 controlled drugs in response to recommendations made by the Advisory Council on the Misuse of Drugs, due to concerns regarding the potential risk of dependence, misuse and diversion[36].

NICE guidance, *Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain*, recommends that prescribers do not initiate gabapentinoids to manage chronic primary pain, unless as part of a trial for complex regional pain syndrome, as the evidence suggest a lack of benefit[6]. As gabapentinoids are currently recommended for neuropathic pain, expert opinion within the committee suggested that complex regional pain syndrome (CRPS) is sometimes understood as a neuropathic pain disorder. Based on the expert opinion of some committee members they therefore decided to make a recommendation for research on the use of gabapentinoids for CRPS to inform future guidance. There is currently variation in the use of drugs to treat chronic primary pain. The recommendations are likely to have a resource impact in the short term because there may be increased resource use from helping people to stop treatments, particularly opioids and gabapentinoids.

There has been increasing use of gabapentin and pregabalin in primary care with prescribing data from the quarter ending December 2023, compared with the quarter ending December 2013, demonstrating an increase of over 85% in prescription items across Wales[37]. Current prescribing of gabapentin and pregabalin in Wales is high in

comparison with England, with 1,640 DDDs per 1,000 patients in Wales[37], compared with 1,204 DDDs per 1,000 patients in England[38] for the quarter ending December 2023. The number of deaths where pregabalin was mentioned on the death certificate has also increased, from a total of 10 deaths in Wales in 2019, to 30 deaths in 2022[20]. The number of deaths where gabapentin was mentioned on the death certificate has remained relatively consistent across the same timeframe. Increasing numbers of deaths in Northern Ireland involving pregabalin has led to its removal from the country's formulary for use in neuropathic pain. The Northern Ireland Health and Social Care Board made the decision in August 2021 due to a significant increase in deaths involving pregabalin, and the risks of dependence, misuse and diversion[39].

Dependence, diversion and misuse

The Summaries of Product Characteristics (SPCs) for both gabapentin and pregabalin highlight that cases of misuse, abuse and dependence have been reported. Caution should be exercised in prescribing either drug for patients with a history of substance abuse, and patients should be monitored for symptoms of misuse or dependence[29-34]. A Welsh Health Circular in 2016 noted that patients should be made aware of the risk of harms, including dependence[40]. Their mechanism for producing dependence is not yet well understood, though there may be direct or indirect effects on the dopaminergic 'reward' system[41,42]. An NHS Scotland resource, *Gabapentinoid Prescribing for Chronic Pain in Primary Care*, highlights that there appears to be more evidence of misuse than for dependence[43,44].

Misuse of gabapentin and pregabalin has been noted for some years in clients attending substance misuse services and within prisons; currently, pregabalin appears to be more sought after for misuse than gabapentin[40]. Pregabalin may have a higher abuse potential than gabapentin due to its rapid absorption, faster onset of action and higher potency[45]. Pregabalin causes a 'high' or elevated mood in users[45], and individuals misusing gabapentin and pregabalin describe improved sociability, euphoria, relaxation and a sense of calm[46]. Pregabalin misusers achieve these effects by taking large quantities, ranging from 200 mg to 5 g as a single dose[46].

Individuals at risk of misusing or diverting gabapentinoids may include those who: have a history of substance misuse; make specific requests for initiation of either gabapentin or pregabalin, particularly after release from prison; repeatedly make requests for an early prescription or repeatedly report lost medication, and those who contact out of hours services for supplies of medication[43]. Prescribers must give careful consideration to the individual patient when prescribing gabapentinoids to minimise the risk of misuse, dependence and diversion, an assessment of both the risks and benefits is essential[43].

In September 2019, Public Health England published an evidence review, *Dependence and withdrawal associated with some prescribed medicines*, which noted that gabapentinoids have come to be used for a wider range of indications than is supported by the evidence or their licensing. They have sometimes been prescribed in place of opioids or benzodiazepines in the belief that they are less liable to misuse or dependence, and with a lack of awareness of the withdrawal problems that can arise when prescribing is stopped[9]. This is concerning given the increased number of deaths associated with gabapentin and pregabalin, and highlights the importance of appropriate initiation, review, and tapering and stopping of medication where the patient is not benefitting or there are concerns regarding misuse or diversion.

With prevalence of neuropathic pain estimated to be 9.2%[47], estimated prevalence of GAD estimated to be 5.9%[48] and prevalence of epilepsy at 1.0%[49], it is likely that the majority of gabapentin and pregabalin prescribed is for neuropathic pain. However the same considerations regarding the potential for dependence, misuse and diversion apply when prescribing for patients with GAD or epilepsy, and The Advisory Council on the Misuse of Drugs issued advice to prescribers in 2016 noting the importance of appropriate prescribing to minimise these risks[45].

Neuropathic pain

Neuropathic pain can be defined as pain that arises as a direct consequence of a lesion or diseases affecting the somatosensory nervous system[50], and can be very challenging to manage with only a minority of people experiencing a clinically relevant benefit from any one intervention[51].

Before initiating any treatment for neuropathic pain, it is good practice to assess the type, severity and impact of pain to guide management and gauge its success; there are brief and well-validated tools available for use in non-specialist settings[52]. Tools to aid assessment of neuropathic pain include the Leeds assessment of neuropathic symptoms and signs (LANSS Pain Scale)[53] and the painDETECT questionnaire[54].

No single drug works for all neuropathic pain and, given the diversity of pain mechanisms, patient's responses and diseases, treatment must be individualised[55]. When agreeing a treatment plan with the patient, pain severity, the underlying cause of pain, comorbidities, concurrent medications and vulnerability to adverse effects should be taken into account[28]. Patients should be informed that response to drug treatment in neuropathic pain is often inadequate, with no more than 40–60% of people obtaining partial pain relief[56]. A 2015 systematic review and meta-analysis found that the number needed to treat (NNT) for 50% pain relief was 7.2 for gabapentin and 7.7 for pregabalin[57]. A 2019 Cochrane systematic review of pregabalin for neuropathic pain in adults concluded that pregabalin at daily oral doses of 300 mg to 600 mg can provide good levels of pain relief for some people with post-herpetic neuralgia and painful diabetic neuropathy, however evidence for use in other types of neuropathic pain is very limited. In addition, the review noted that more than half of patients treated with pregabalin will not attain worthwhile pain relief, while a similar proportion (around 6 or 7 out of 10) will experience at least one adverse event[58].

NICE guidance, *Neuropathic pain in adults*, recommends early assessment once treatment has commenced. This should be followed by regular clinical reviews to assess and monitor effectiveness, including pain control, impact on lifestyle, physical and psychological wellbeing, adverse effects and continued need[28]. If the patient has not shown sufficient benefit within eight weeks of reaching the maximum tolerated dose, drug treatment should be reduced and stopped[55]. The SPCs for both gabapentin and pregabalin indicate that they can be discontinued gradually over a minimum of one week, independent of indication[30,33]; however, a more gradual dose taper allows observation of emergent symptoms that may have been controlled by the drug[46]. Public Health England suggests reducing the daily dose by a maximum of 300 mg every four days in the case of gabapentin and by a maximum of 50–100 mg per week in the case of pregabalin[46].

If pain does not appear to be neuropathic in nature and is not currently well controlled, consider a change of treatment as gabapentin and pregabalin are only licensed for neuropathic pain[55]. Both gabapentin and pregabalin are commonly prescribed for

non-neuropathic pain syndromes; however, there is little evidence to support this practice[46]. A 2017 Canadian systematic review and meta-analysis highlighted that gabapentin and pregabalin are increasingly being used for non-specific chronic lower back pain, despite the significant risk of adverse effects without any demonstrated benefit[59]. This highlights the need for treatment to be reviewed when either pregabalin or gabapentin are prescribed outside of their licensed indications.

Neuropathic pain management is often complex and prescribers need to make evidence-based, informed decisions based on the individual needs of the patient. Overall, treatment gains in neuropathic pain with even the most effective available treatments are modest[58]. Prescribers should be aware not only of the potential benefits of gabapentin and pregabalin, but also that they may be misused or diverted. Individuals who are misusing analgesics need to be distinguished from those who are using higher or more frequent doses because their symptoms are not being adequately treated. It is vitally important that any individual whose condition warrants an increase in pain relief is reassessed and subsequently receives the appropriate evidence-based prescribing[60]. The reclassification of gabapentin and pregabalin as class C controlled substances has resulted in stronger controls with regards to the prescribing and supply of these items; it is now illegal to be in possession of these drugs without a prescription.

This NPI promotes a prudent approach to prescribing gabapentin and pregabalin, taking into account the risks and benefits, and encouraging timely review.

Useful resources

- AWMSG (2023) Resources for pharmacological management of pain
- The Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) Pain Scale (2021)
- PrescQIPP (2022) Bulletin 216: Neuropathic pain (log in required for access)
- Public Health England (2014) Advice for prescribers on the risk of the misuse of pregabalin and gabapentin
- SIGN (2019) SIGN 136. Management of chronic pain

1.2 Antimicrobial stewardship

Antimicrobial resistance (AMR) is a growing threat to global health, and sporadic outbreaks of untreatable 'super-bugs' is now a reality in hospitals across the UK. In 2019, it was estimated that approximately 1.27 million deaths globally were caused by infections resistant to antibiotics, and without intervention, that figure could rise to 10 million by 2050, eclipsing the number of deaths caused by cancer and malaria. The financial impact on the global economy would be extreme, at an estimated cost of $100 trillion[61].

In 2015, member states of the World Health Organisation endorsed a Global Action Plan (GAP) on Antimicrobial Resistance, encompassing five key strategic objectives[62]. This provides a framework from which National Action Plans (NAP) can be developed and delivered by individual member states. The UK was one of the first countries to establish a NAP, with strategies and action plans in place since 2000, pre-dating the United Nations GAP. In 2018, the four devolved administrations of the UK worked together to produce a new 20-year vision, designed to deliver the key strategies of the United Nations GAP. The vision was published in January 2019[63] and aims to contain, control and mitigate AMR by 2040 through lowering the burden of infection, optimising the use of antimicrobials and developing new diagnostics, therapies and vaccines. These documents are 'One-health', reflecting a need for coordinated action across human health, animal health, agriculture and the environment.

The first UK 2019–2024 NAP contained four overarching targets aimed at human health and, in Wales, was supported by annual Welsh Health Circulars (WHCs) published by Welsh Government. The UK's second 5-year NAP, *Confronting antimicrobial resistance 2024 to 2029*[64] contains outcomes and commitments that will make progress towards the 20-year vision for AMR to be contained, controlled and mitigated. The action plan has nine strategic outcomes organised under four themes:

- Reducing the need for, and unintentional exposure to, antimicrobials;
- Optimising the use of antimicrobials;
- Investing in innovation, supply and access and;
- Being a good global partner.

Five of the nine targets are aimed at human health, developed by working groups with representation from across the UK:

- To prevent any increase in a specified set of drug-resistant infections from the 2019 to 2020 baseline by 2029.
- To prevent any increase in Gram-negative bloodstream infections in humans from the 2019 to 2020 baseline by 2029.
- To increase UK public and healthcare professionals' knowledge on AMR by 10%, using 2018 and 2019 baselines, respectively by 2029.
- To reduce total antibiotic use in human populations by 5% from the 2019 baseline by 2029.
- To achieve 70% of total use of antibiotics from the Access category (new UK category) across the human healthcare system[64].

Ensuring the continued effectiveness of antibiotics is essential to the success of *A Healthier Wales*, which supports the achievement of the Well-being of Future Generations Act's wellbeing goals[65]. In support of the new UK 5-year NAP, Welsh Government have published an AMR & Healthcare Associated Infections (HCAI)

WHC, designed to provide sequential targets to the NHS in Wales, enabling them to meet the overall UK targets. The WHC issued in September 2024 includes a number of improvement goals for primary and secondary care[66]. Antimicrobial stewardship indicators may be used to underpin further improvements in antimicrobial prescribing.

1.2.1 Total antibacterial prescribing

Purpose:

To encourage the appropriate prescribing of all antibiotics in primary care.

Unit of measure:

- Total antibacterial DDDs per 1,000 STAR-PUs.
- Total antibacterial items per 1,000 STAR-PUs.

Target for 2025–2028:

- Health board target:
  - DDDs/1,000 STAR-PUs: a quarterly reduction of 6%, 7% and 8% in subsequent years against a baseline of data from April 2019–March 2020.
- GP practice targets:
  - DDDs/1,000 STAR-PUs: maintain performance levels within the lower quartile, or show a reduction towards the quartile below.
  - Items/1,000 STAR-PUs: maintain performance levels within the lower quartile, or show a reduction towards the quartile below.

Note
Comparative trends for antimicrobial NPIs should be interpreted with caution, with particular respect to seasonal variation.

Table 3. Health board baseline data: DDDs per 1,000 STAR-PUs 2019–2020[67]

Health board	June 2019	September 2019	December 2019	March 2020
Aneurin Bevan	2,540	2,452	2,727	2,739
Betsi Cadwaladr	2,421	2,386	2,703	2,530
Cardiff and Vale	2,423	2,388	2,674	2,577
Cwm Taf Morgannwg	2,886	2,782	3,088	2,986
Hywel Dda	2,563	2,452	2,723	2,668
Powys	2,196	2,206	2,422	2,373
Swansea Bay	2,651	2,543	2,826	2,719

Figure 10. Trend in total primary care antibacterial DDDs per 1,000 STAR-PUs to quarter ending June 2024

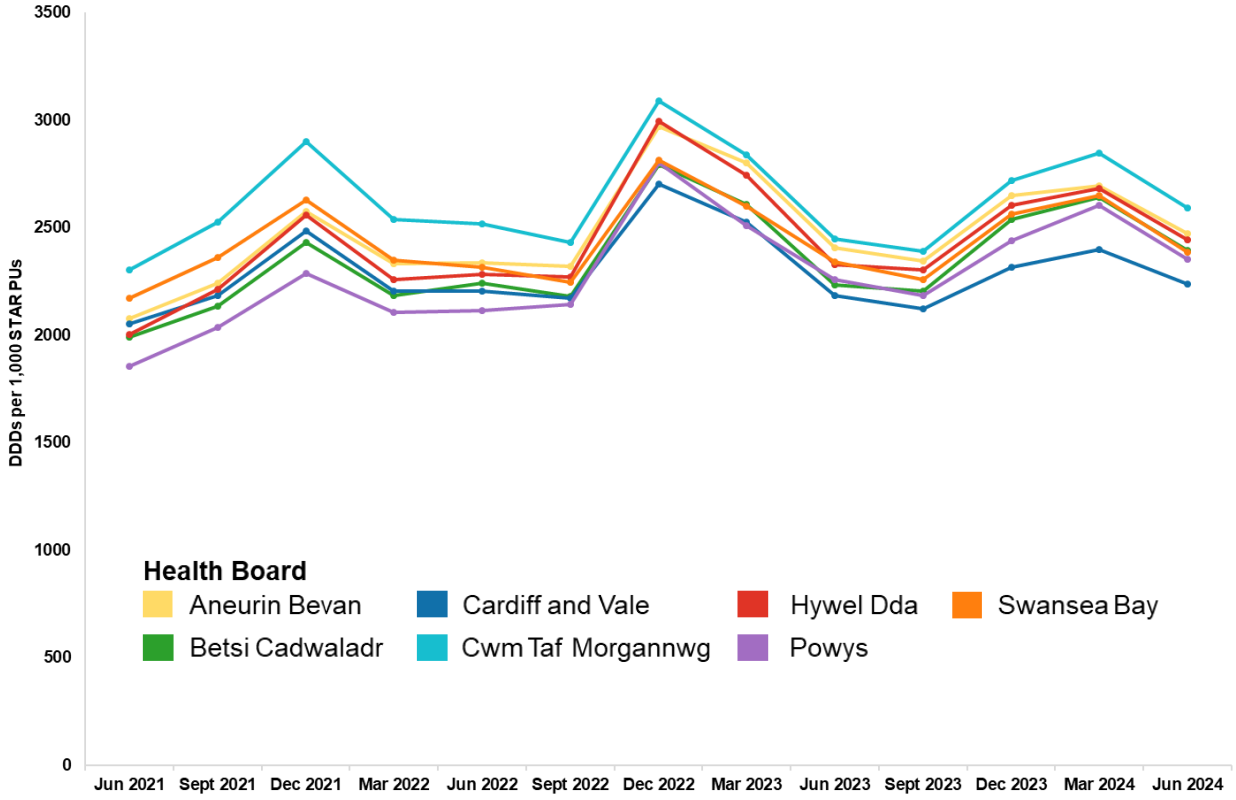


Figure 11. Trend in total primary care antibacterial items per 1,000 STAR-PUs to quarter ending June 2024

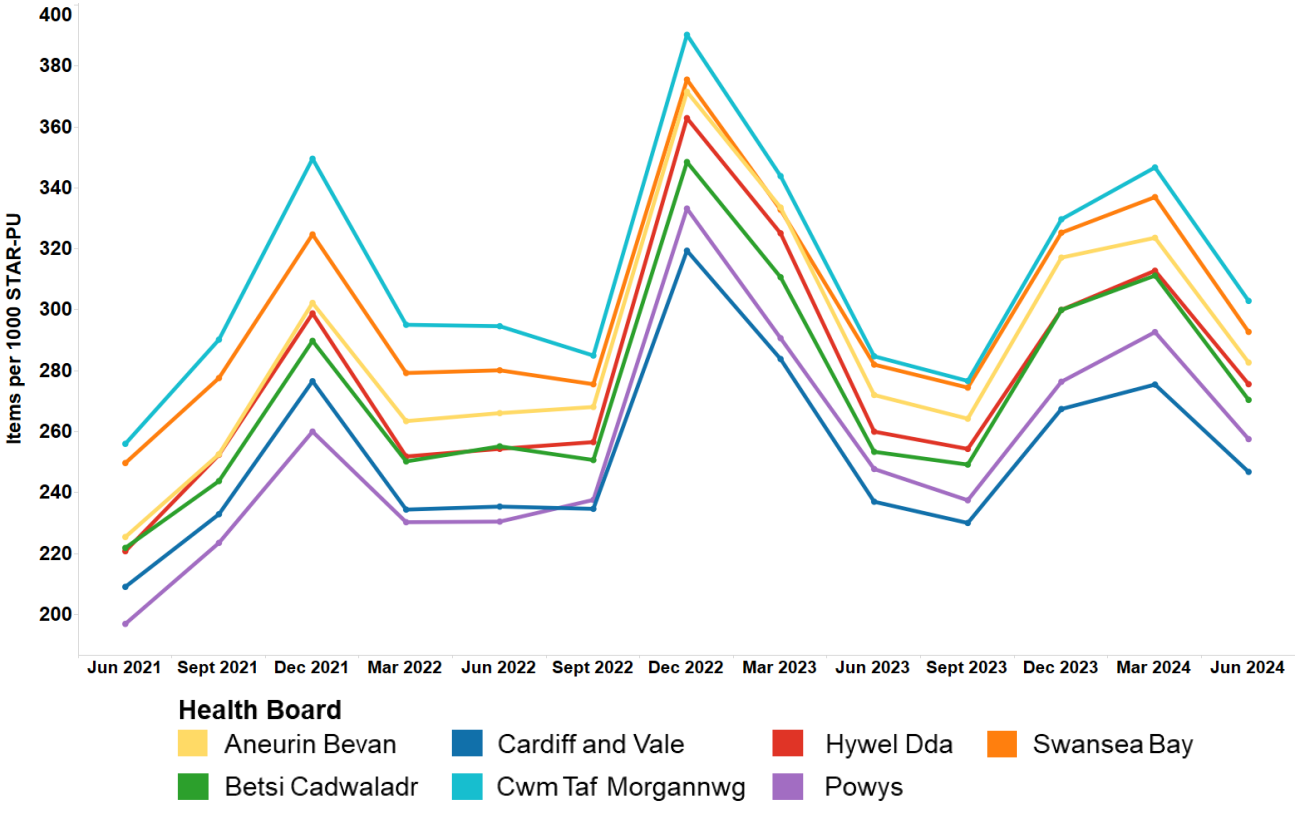
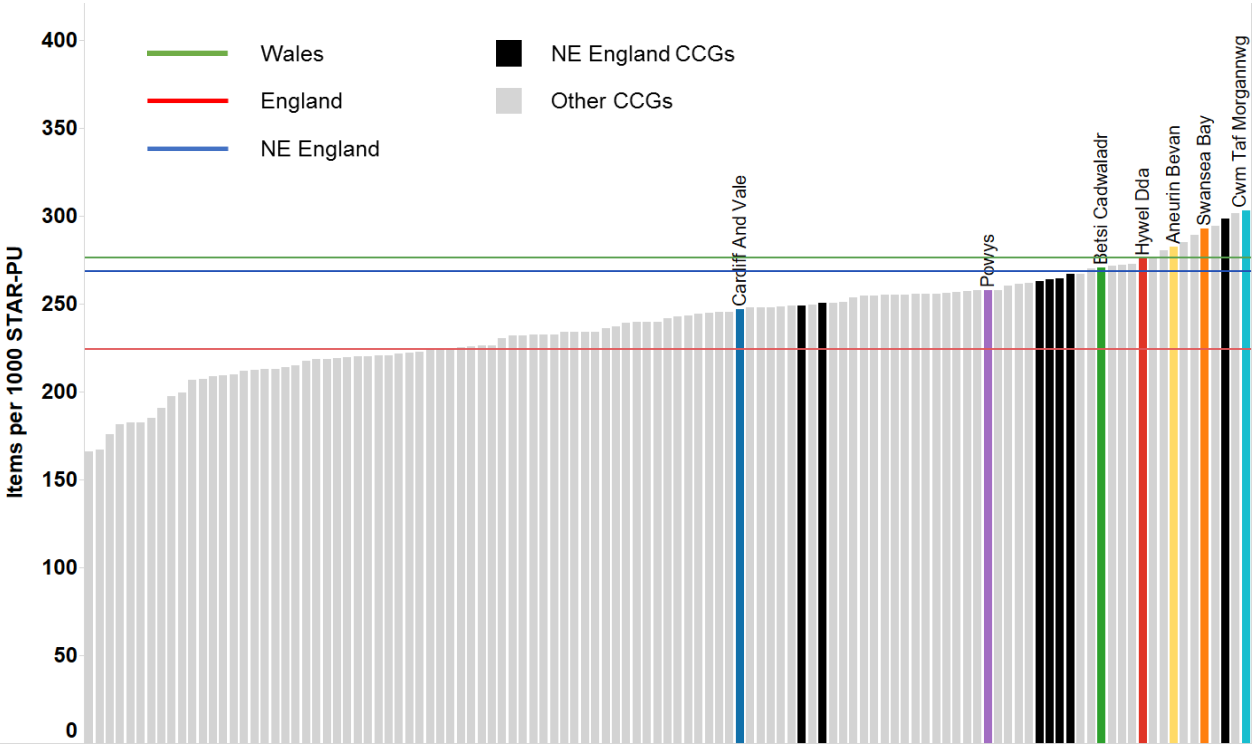


Figure 12. Total primary care antibacterial items per 1,000 STAR-PUs in Welsh health boards and English CCGs – Quarter ending June 2024



Comparison data with England will be available for DDDs per 1,000 STAR-PUs.

Background and evidence

The widespread and often excessive use of antimicrobials is one of the main factors contributing to the increasing emergence of AMR. Within Wales, antimicrobial usage in primary care has decreased over recent years, however, variation still exists. For the quarter ending December 2023, primary care prescribing rates varied from 267 to 330 items per 1,000 STAR-PUs across Welsh health boards[67].

The Public Health Wales reports *Antimicrobial Resistance in urine cultures in Wales 2016–2023* and *Antimicrobial resistance in blood cultures in Wales 2016–2023* presents different AMR patterns across Wales[68,69]. They show resistance trends in Wales for drug-bug combinations. In some cases there is considerable variability in resistance rates between different areas and hospitals[70].

NICE Guideline 15, *Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use*, makes recommendations for organisations on antimicrobial stewardship programmes, antimicrobial stewardship interventions and communication strategies[71]. In addition, it makes recommendations for individual prescribers in both primary and secondary care. Key recommendations include:

- Follow local or national guidelines, prescribing antibiotics for the shortest effective course at the most appropriate dose;
- Consider the risk of antimicrobial resistance for individual patients and the population as a whole;
- Document the clinical diagnosis in the patient's record and the reason for prescribing, or not prescribing, an antimicrobial[71].

Ultimately, indiscriminate or inappropriate use of antibiotics is a key driver in the spread of antibiotic resistance[72]. Therefore, the ultimate aim has to be the reduction in inappropriate prescribing, measured as volume of antimicrobials.

1.2.2 4C antimicrobials

Purpose:
To reduce the prevalence of healthcare associated infection (HCAI), including *Clostridioides difficile* infection and *Staphylococcus aureus* bacteraemia caused by Methicillin-resistant *Staphylococcus aureus* (MRSA), by encouraging a reduction in variation and reduce overall prescribing of the 4C antimicrobials (co-amoxiclav, cephalosporins, fluoroquinolones and clindamycin) in primary care.
Units of measure:
• Co-amoxiclav, cephalosporin, fluoroquinolone and clindamycin DDDs combined, per 1,000 patients. • Co-amoxiclav, cephalosporin, fluoroquinolone and clindamycin items combined, per 1,000 patients.
Target for 2025–2028:
Maintain performance levels within lower quartile, or show a reduction towards the quartile below.

Note
Comparative trends for antimicrobial NPIs should be interpreted with caution, with particular respect to seasonal variation.

Figure 13. Trend in 4C antimicrobial DDDs per 1,000 patients to quarter ending June 2024

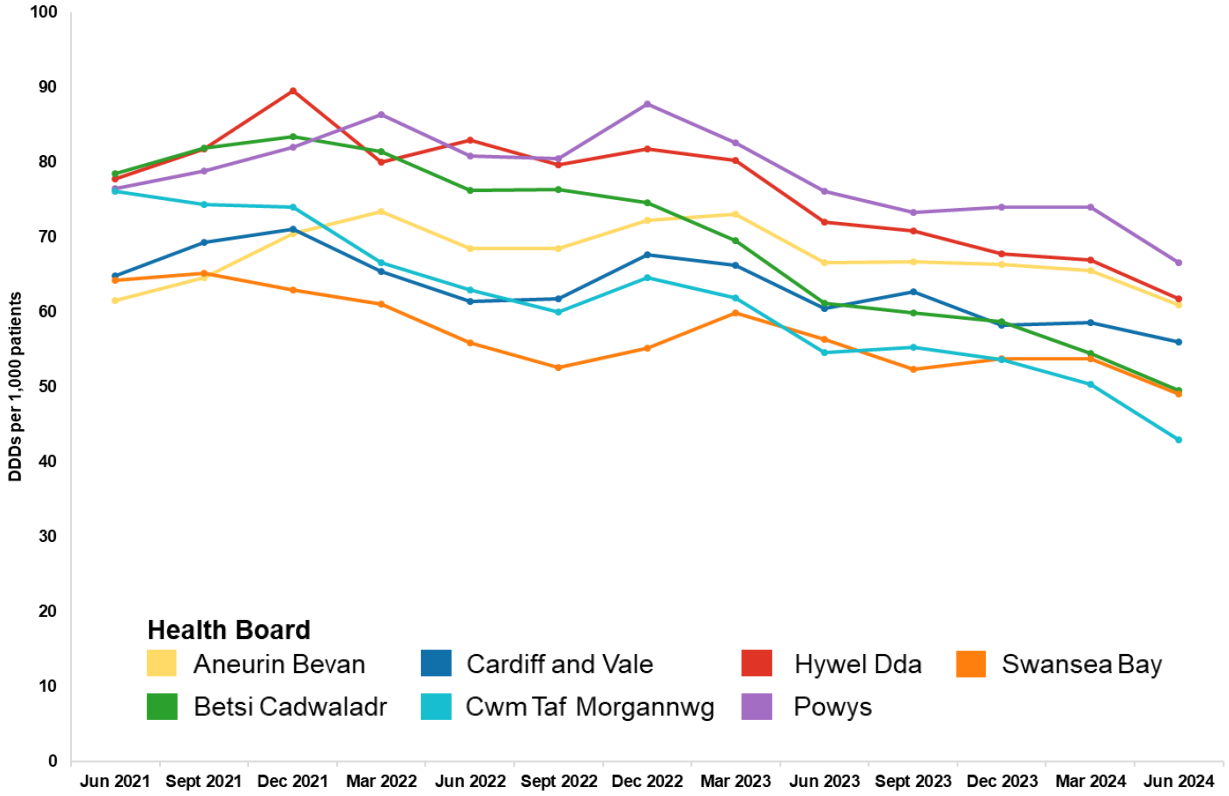


Figure 14. Trend in 4C antimicrobial items per 1,000 patients to quarter ending June 2024

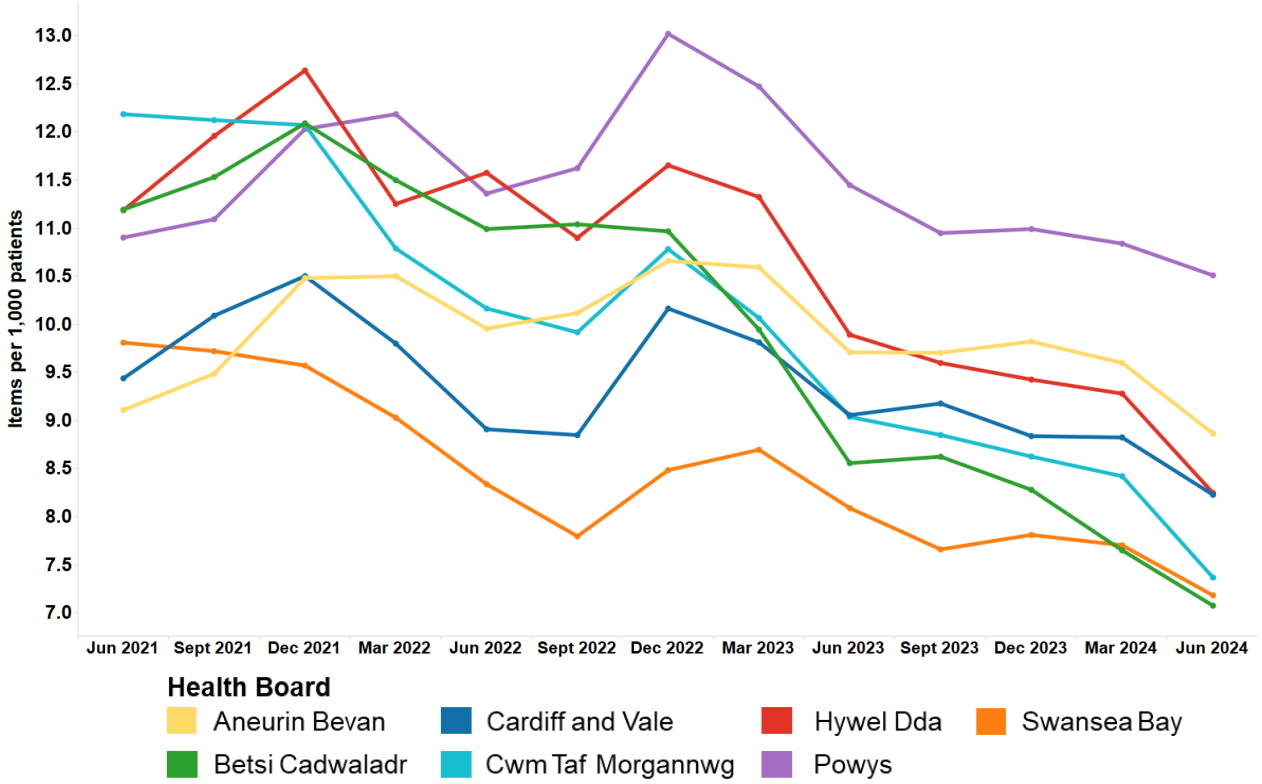
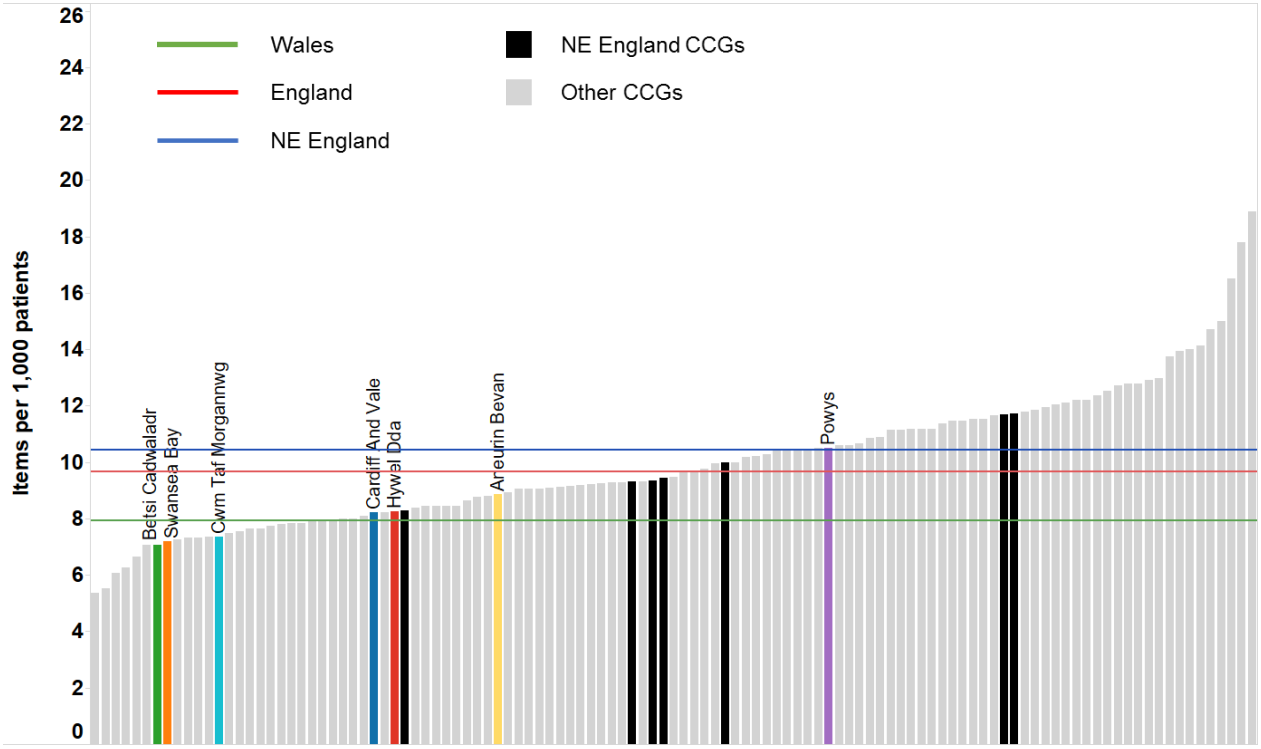


Figure 15. 4C antimicrobial items per 1,000 patients in Welsh health boards and English CCGs – Quarter ending June 2024



Comparison data with England will be available for DDDs per 1,000 patients.

Background and evidence

AWMSG's *Primary care antimicrobial guidelines* state "Use simple generic antibiotics if possible. Avoid broad spectrum antibiotics (e.g. co-amoxiclav, quinolones and cephalosporins) when narrow spectrum antibiotics remain effective, as they increase the risk of *C. difficile*, methicillin-resistant *Staphylococcus aureus* (MRSA) and resistant urinary tract infections"[73].

The term '4C antimicrobials' refers collectively to four broad-spectrum antibiotics, or groups of antibiotics: co-amoxiclav, cephalosporins, fluoroquinolones and clindamycin. The use of simple generic antibiotics and the avoidance of these broad-spectrum antibiotics preserve them from resistance and reduce the risk of *C. difficile*, MRSA and resistant UTIs. Compared with narrow-spectrum antibiotics, broad-spectrum antibiotics are more likely to significantly change the gut flora, potentially allowing other bacteria, such as *C. difficile*, to become established. *C. difficile* may be found in the gut of people with no symptoms. When the normal bacteria in the gut are disrupted (for example, by antibiotics) the numbers of *C. difficile* bacteria may increase to unusually high levels, particularly in people whose immune system is compromised. Symptoms of *C. difficile* infections vary from mild, self-limiting diarrhoea to severe complications, including pseudomembranous colitis, toxic megacolon, perforation of the colon, sepsis and death[74]. The most commonly implicated antibiotics in *C. difficile* infection include clindamycin, cephalosporins (in particular second and third generation cephalosporins), fluoroquinolones and co-amoxiclav[74]. However, these antimicrobials have a very useful role in specific clinical situations, so should be reserved for use as per local guidelines.

There have been a number of Drug Safety Updates from the MHRA in recent years regarding risk of adverse events related to the use of fluoroquinolones. A 2018 Drug Safety Update highlighted the small increased risk of aortic aneurysm and dissection, particularly in older patients[75]. A further update in March 2019 informed prescribers of new restrictions and precautions for use of fluoroquinolones due to very rare reports of disabling and potentially long-lasting or irreversible side effects mainly affecting musculoskeletal and nervous systems. Following an EU-wide review of safety, new restricted indications were introduced for ciprofloxacin; levofloxacin; moxifloxacin and olfloxacin[76], in addition the marketing authorisation for the quinolone nalidixic acid, licensed for UTIs, was suspended[77]. A December 2020 Drug Safety Update highlighted that systemic and inhaled fluoroquinolones have been associated with a small increased risk of heart valve regurgitation[78]. An August 2023 Drug Safety update reminded fluoroquinolones should not be prescribed for non-severe or self-limiting infections, or for mild to moderate infections unless other antibiotics that are commonly recommended for these infections are considered inappropriate[79]. A January 2024 Drug Safety update further restricted the use of fluoroquinolones and highlighted systemic fluoroquinolones must now only be prescribed when other commonly recommended antibiotics are inappropriate due to the risk of potentially long-term or irreversible side effects with fluoroquinolones[80]. Where prescribing is unavoidable, all patients should be counselled and consented using the MHRA Patient Information leaflet and this shared care discussion documented in the patient record.

Useful resources

- AWMSG (2024) Primary care antimicrobial guidelines
- AWMSG (2024) Back-up antibiotic prescribing: Good practice guide
- AWMSG (2023) CEPP National Audit: Focus on Antibiotic Prescribing
- RCGP TARGET Antibiotics toolkit

1.2.3 Course duration for respiratory tract infection (RTI) antibiotics

Purpose:

To increase the proportion of antibiotics prescribed for an appropriate duration when prescribing for RTIs to reduce the risk of antimicrobial resistance and adverse effects.

Unit of measure:

- Proportion of amoxicillin 500 mg capsules prescribed for 5-day duration.
- Proportion of doxycycline 100 mg capsules prescribed for 5-day duration.
- Proportion of clarithromycin 500 mg tablets prescribed for 5-day duration.

Target for 2025–2028:

- Health board and GP practice target: 75% of amoxicillin prescriptions issued as a 5-day duration versus a 7-day duration.
- Health board and GP practice target: 75% of doxycycline prescriptions issued as a 5-day duration versus a 7-day duration.
- Health board and GP practice target: 75% of clarithromycin prescriptions issued as a 5-day duration versus a 7-day duration.

Figure 16. Trend in the percentage of amoxicillin 500 mg capsules issued as a 5-day duration versus a 7-day duration to June 2024

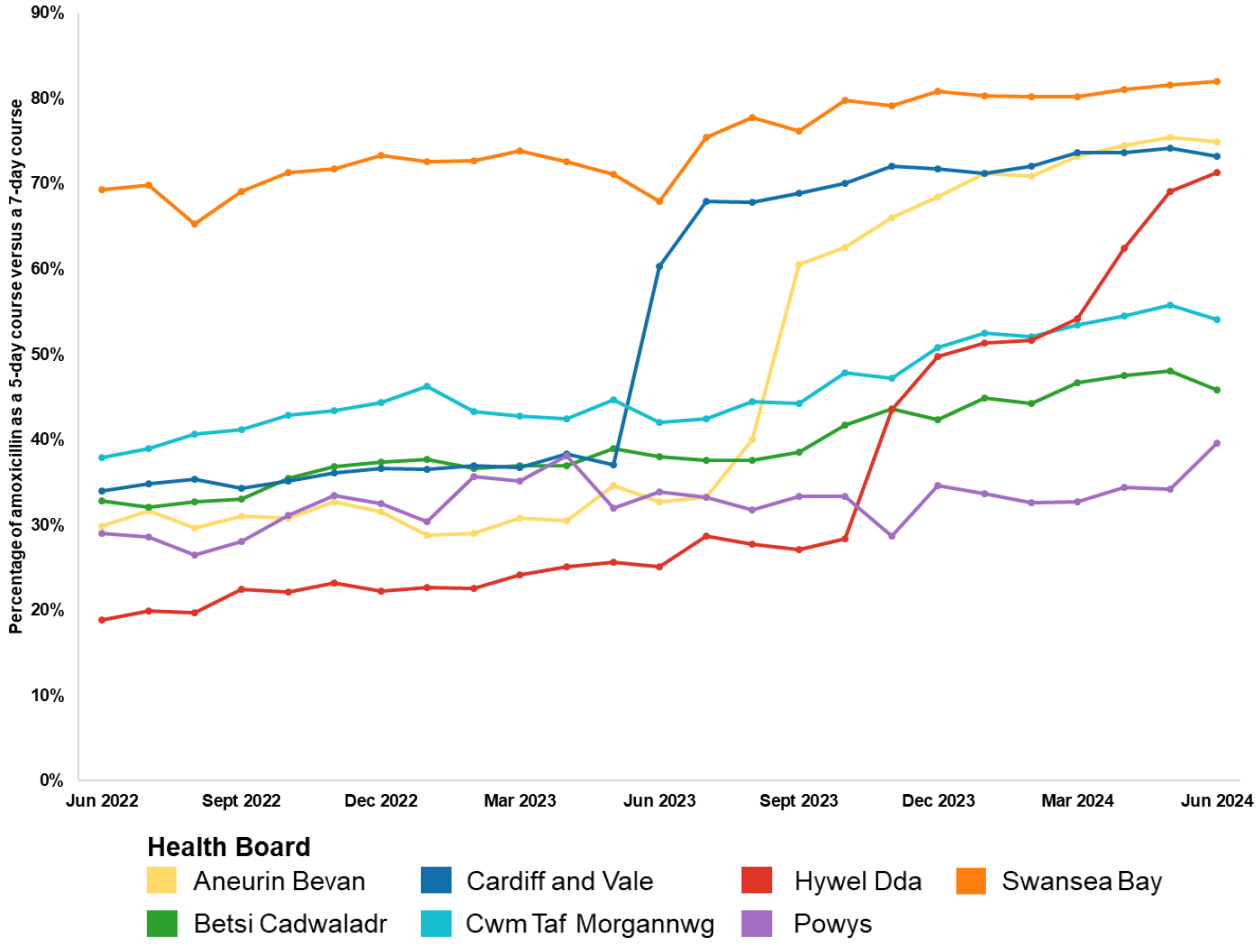


Figure 17. Trend in the percentage of doxycycline 100 mg capsules prescribed as a 5-day duration versus a 7-day duration to June 2024

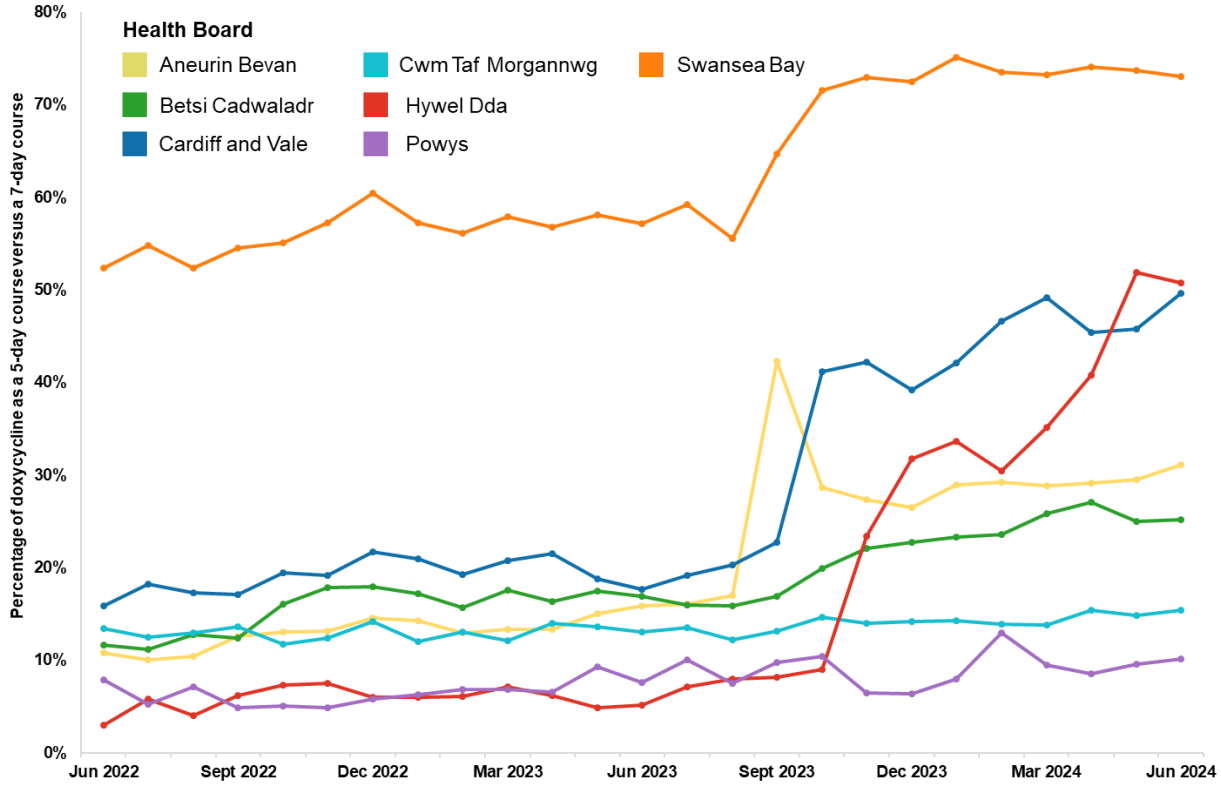
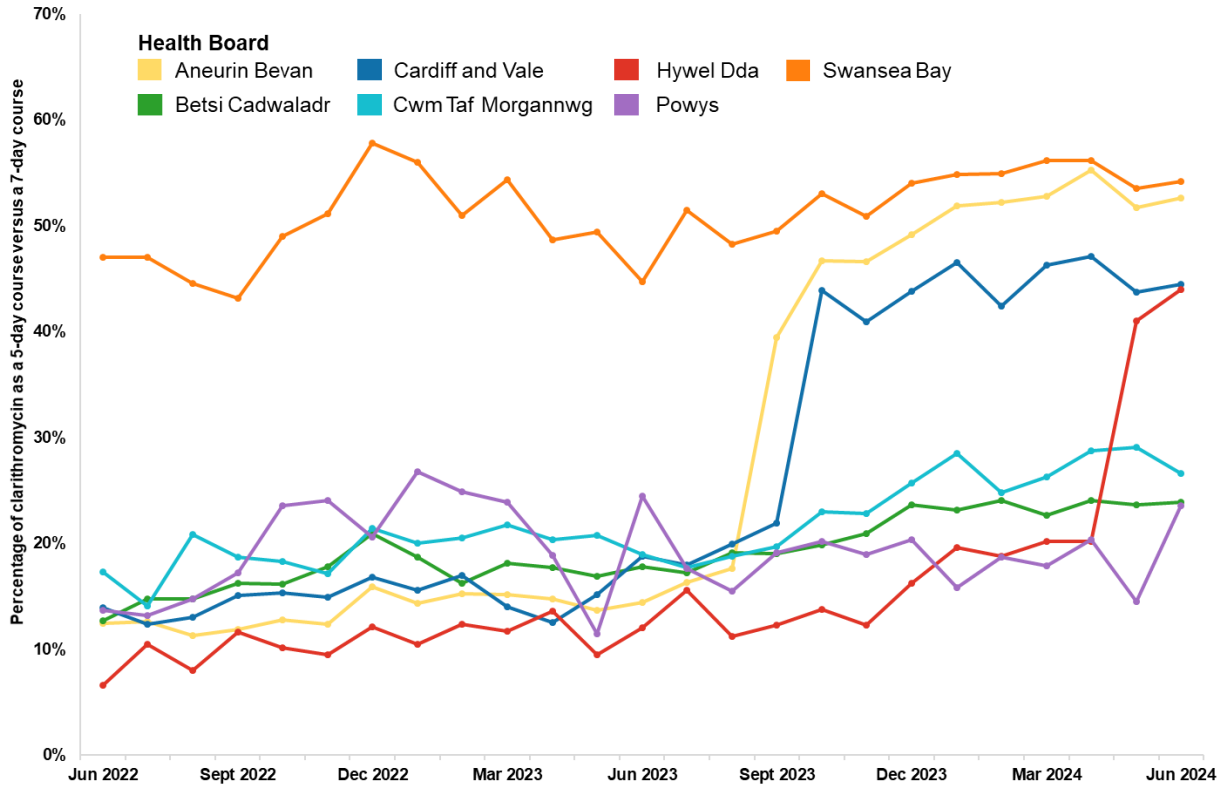


Figure 18. Trend in the percentage of clarithromycin 500 mg tablets prescribed as a 5-day duration versus a 7-day duration to June 2024



Background and evidence

Antimicrobial overuse is a driver of antimicrobial resistance. A core component of antimicrobial stewardship is optimal duration of use[64]. Recent studies are increasingly demonstrating that shorter treatment durations are as effective as longer courses when treating uncomplicated infection[81-83]. The aim of this indicator is to reduce patient exposure to antibiotics and address antimicrobial resistance by supporting the prescribing of the shortest effective antibiotic course for acute respiratory tract infections (RTIs). This indicator supports the implementation of the recent quality statement produced by NICE relating to antibiotic duration for acute RTIs, that adults prescribed an antibiotic for an acute RTI are given a 5-day course[84].

The vast majority of indications for acute RTIs in the AWMSG Primary Care Antimicrobial Guidelines recommend the shortest effective course of treatment[73]. NICE quality statement states, when a decision is made to prescribe antibiotics for acute RTI, the shortest course that is likely to be effective should be prescribed to reduce the risk of antimicrobial resistance and adverse effects. AWMSG Primary Care Antimicrobial Guidelines and NICE guidance for antimicrobial stewardship recommend five-day antibiotics courses for sinusitis, sore throat, COPD infective exacerbation, cough (acute) and pneumonia (community-acquired)[73,85].

The shortest effective courses of amoxicillin (Figure 16), doxycycline (Figure 17) and clarithromycin (Figure 18) are not consistently prescribed within Welsh primary care, with considerable variation across health boards apparent[37]. Within this there may be factors associated with health inequalities in patient exposure leading to unnecessary treatment while driving antimicrobial resistance[64].

Potential benefits of the introduction of course duration for RTI antibiotics NPI include:

- Reducing the risk of adverse drug reactions and toxicity.
- Contributing to the reduction in antimicrobial resistance.
- Reducing the risk of patients inappropriately self-treating future infections with unused antibiotics or of patients giving them to others.
- Contributing to the UK AMR NAP goal to reduce human exposure to antibiotics in primary care.

Useful resources

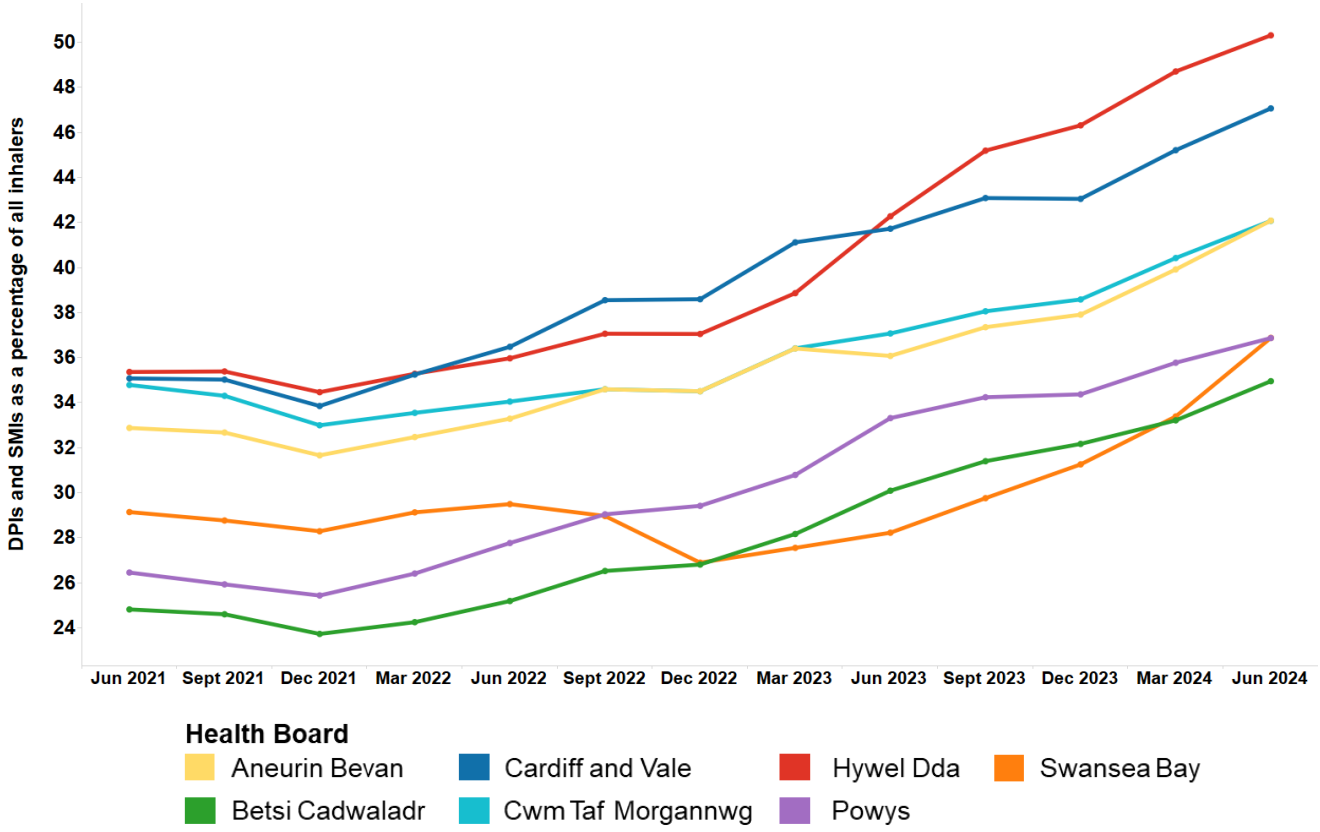
- AWMSG (2024) Primary care antimicrobial guidelines
- AWMSG (2024) Back-up antibiotic prescribing: Good practice guide
- NICE (2023) Acute respiratory infection in over 16s: initial assessment and management including virtual wards (hospital at home)
- NHS Futures Antimicrobial Resistance Programme, (log-in required)
- PrescQIPP Bulletin 313: Antimicrobial stewardship

1.3 Respiratory

1.3.1 Decarbonisation of inhalers

Purpose:
To encourage an increase in the use of low Global Warming Potential (GWP) inhalers (dry powder inhalers (DPI) and soft mist inhalers (SMI)), to reduce the carbon footprint of inhaler prescribing in Wales.
Unit of measure:
The number of DPIs and SMIs as a percentage of all inhalers prescribed.
Target for 2025–2028:
80% of inhalers prescribed to be DPIs or SMIs, or show an increase towards the quartile above.

Figure 19. Trend in the percentage of DPI and SMI as a percentage of all inhalers prescribed to quarter ending June 2024



Background and evidence

The *NHS Wales Decarbonisation Strategic Delivery Plan*, launched in March 2021, sets out NHS Wales' plan for addressing the climate emergency declared by Welsh Government in 2019. The plan contains a number of initiatives and targets for the decarbonisation of NHS Wales that will be assessed and reviewed in 2025 and 2030, and includes several key actions related to inhalers[86]. A separate national strategy for Wales, *Decarbonisation: inhaler prescribing, use and disposal 2023–2030*, to reduce its carbon footprint of inhaler use in Wales[87]. It outlines 12 key actions for the NHS and its partners to:

- Reduce over-reliance on reliever inhalers (e.g. SABAs)
- Reduce the use of inhalers that have a high global warming potential (GWP) by prescribing lower GWP inhalers as an alternative where appropriate; and
- Responsible disposal of inhalers[87].

Metered dose inhalers (MDIs) contain hydrofluorocarbons (HFC) which are powerful greenhouse gases, with a global warming effect several thousand times that of carbon dioxide. These gases are used as the propellant in MDIs[86] and the impact that they have on global warming is known as the carbon footprint. In 2018, these propellants were estimated to be responsible for 4% of the NHS's entire carbon footprint[88]. Dry powder inhalers (DPIs) have a carbon footprint 18 times lower than MDIs, and clinical studies have shown them to be equally effective and cost effective as MDIs[88]. Soft mist inhalers do not contain a propellant, therefore have a lower carbon footprint that MDIs[89]. As of February 2024, MDI use in Wales accounts for 61% of all inhalers prescribed, a decrease from 67% in February 2023[90], however MDIs accounted for only 13% of inhalers prescribed in Sweden in 2017[91]. There is clearly scope to increase the proportion of lower global warming potential inhalers prescribed in Wales.

The British Thoracic Society (BTS) last updated its position statement regarding the environment and lung health in 2020, and made a number of recommendations by which the environmental impact of inhaler prescribing can be reduced[88]. The recommendations include prescribing a DPI when a new class of inhaler is commenced; during respiratory reviews, recommending low carbon alternatives to patients currently using MDIs; and where patients are using several classes of inhalers and poor technique is identified with one device, that a DPI is prioritised. It is noted that these changes should only take place where the patient is able to use the device safely[88].

One of the key actions within the *NHS Wales Decarbonisation Strategic Delivery Plan* is to transition patients to low GWP inhalers, but only where patient care will not be impacted. The target is a shift to 80% of inhalers being low GWP alternatives by 2025[86]; as of February 2024 Wales has reached 39%[90,92]. It is crucial that while efforts are made to reduce the emissions associated with inhalers, patient choice is maintained and that changes are only made where clinically appropriate[87,88,93]. The NICE Asthma Patient Decision Aid can support shared decision-making between patients and prescribers and enable the patient to consider a range of factors when considering the best type of inhaler for them, including how important it is for their inhaler to have a low carbon footprint[89]. The 2024 AWMSG *All Wales Asthma Diagnosis and Management Guidelines* and 2023 AWMSG *All Wales COPD Management and Prescribing Guidelines*, developed by the Respiratory Health Implementation Group (RHIG), can aid prescribers to easily identify inhalers with a low GWP[93,94].

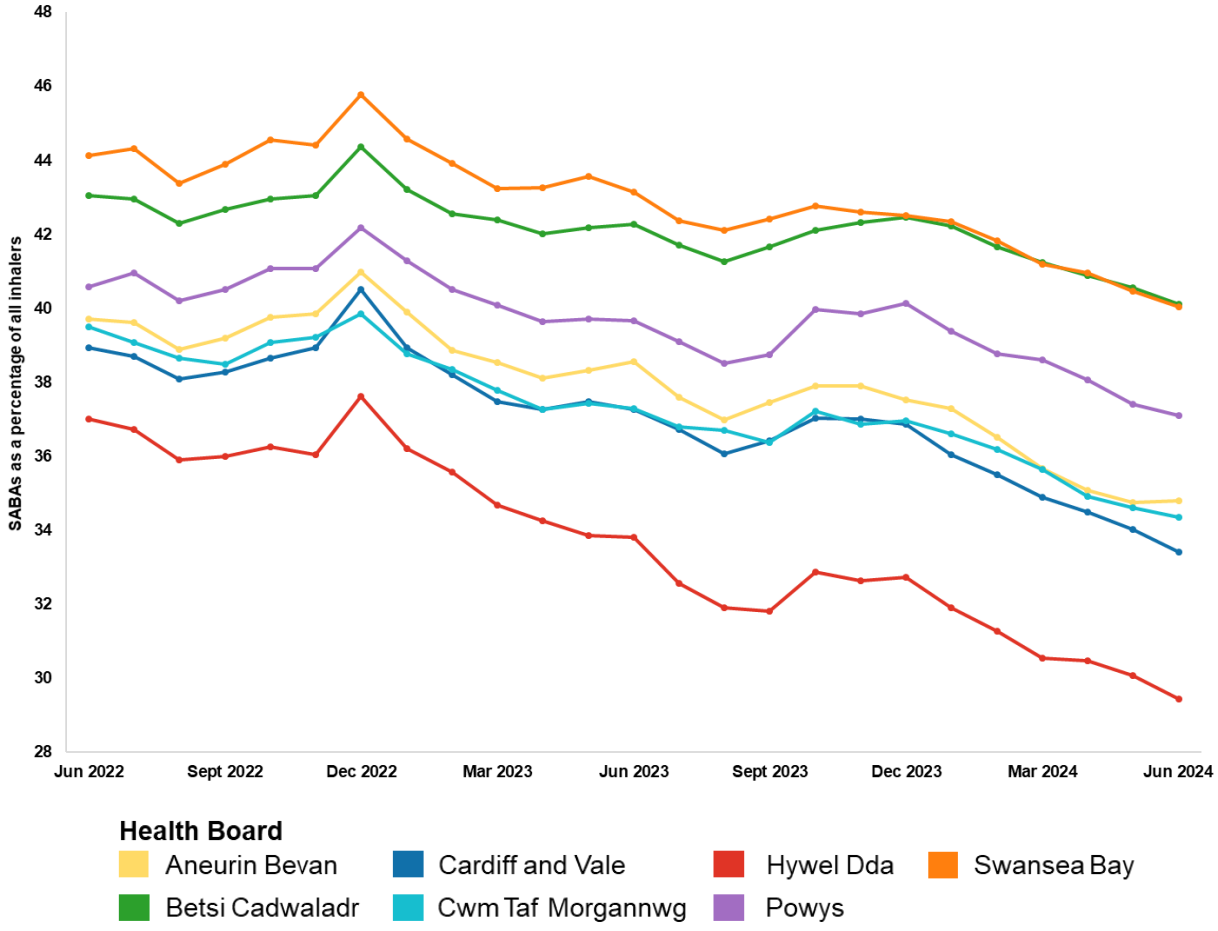
Useful resources

- AWMSG (2024) All Wales Asthma Diagnosis and Management Guidelines
- AWMSG (2023) All Wales COPD Management and Prescribing Guidelines
- AWMSG (2023) Decarbonisation: inhaler prescribing, use and disposal 2023–2030
- AWTTC (2024) SPIRA - Decarbonisation Dashboard (NHS Wales network connection required)
- NICE (2022) Patient decision aid: Inhalers for asthma
- PrescQIPP (2021) Bulletin 295: Inhaler carbon footprint

1.3.2 Short Acting Beta Agonist (SABA) inhalers

Purpose:
To reduce over reliance on SABA inhalers to improve asthma control in patients and asthma related health outcomes.
Unit of measure:
Number of SABA inhalers as a percentage of all inhalers.
Target for 2025–2028:
Maintain performance levels within lower quartile, or show a reduction towards the quartile below.

Figure 20. Trend in the number of SABA inhalers as a percentage of all inhalers prescribed to June 2024



Background and evidence

Short-Acting Beta-Agonist (SABA) reliever inhalers are intended for use in acute situations only; they should not be required more than twice per week in asthma[93]. Overuse of SABA inhalers, defined as three or more 200 dose SABA inhalers per year has been recognised as a problem for many years and reflects very poorly controlled asthma[93,95]. Evidence from the National Review of Asthma Deaths (2014) and the global SABINA trial (2020) link SABA prescribing to a higher risk of severe exacerbation and asthma deaths due to poor disease control[96-98]. The Global Initiative on Asthma (GINA) 2023 report also acknowledges risks associated with SABA overuse as patients who tend to underuse inhaled corticosteroids (ICS) tend to overuse SABA relievers[95].

SABA overprescribing is more common in the UK than other European countries[97]. Asthma-related healthcare use (e.g. hospital visits) and related costs could potentially be decreased by reducing SABA overuse, through improved asthma control[99,100]. Asthma-related healthcare costs are 61% higher for people who overuse SABAs compared with those who do not[99] and, in instances where SABA overuse is reduced, up to 70% fewer hospital admissions are anticipated[101].

In addition, SABA MDIs are a significant contributor to the carbon footprint of respiratory treatment being responsible for 60.7% of per capita greenhouse gas emissions in the UK[102,103]. Reducing over reliance on SABAs, will help reduce the carbon emissions from SABA inhalers while also improving the control of respiratory disease[87]. The *NHS Wales Decarbonisation Strategic Delivery Plan* emphasises providing support and education to improve patient understanding and non-pharmacological interventions such as smoking cessation, exercise and the correct use of preventative therapies[104].

Useful resources

- AWMSG (2024) All Wales adult asthma management and prescribing guideline
- AWMSG (2023) All Wales paediatric asthma management and prescribing guidelines
- NICE (2022) Asthma. Patient decision aid on asthma inhalers
- RCP (2024) Green physician toolkit

1.4 SGLT-2 inhibitors

Please note: Due to the withdrawal of Audit+ by the end of 2024–25 it has not been possible to perform any feasibility testing of the exact proposed indicators. Where available we have included graphs based on data available on the primary care information portal to give an indication of baseline data.

Background and evidence

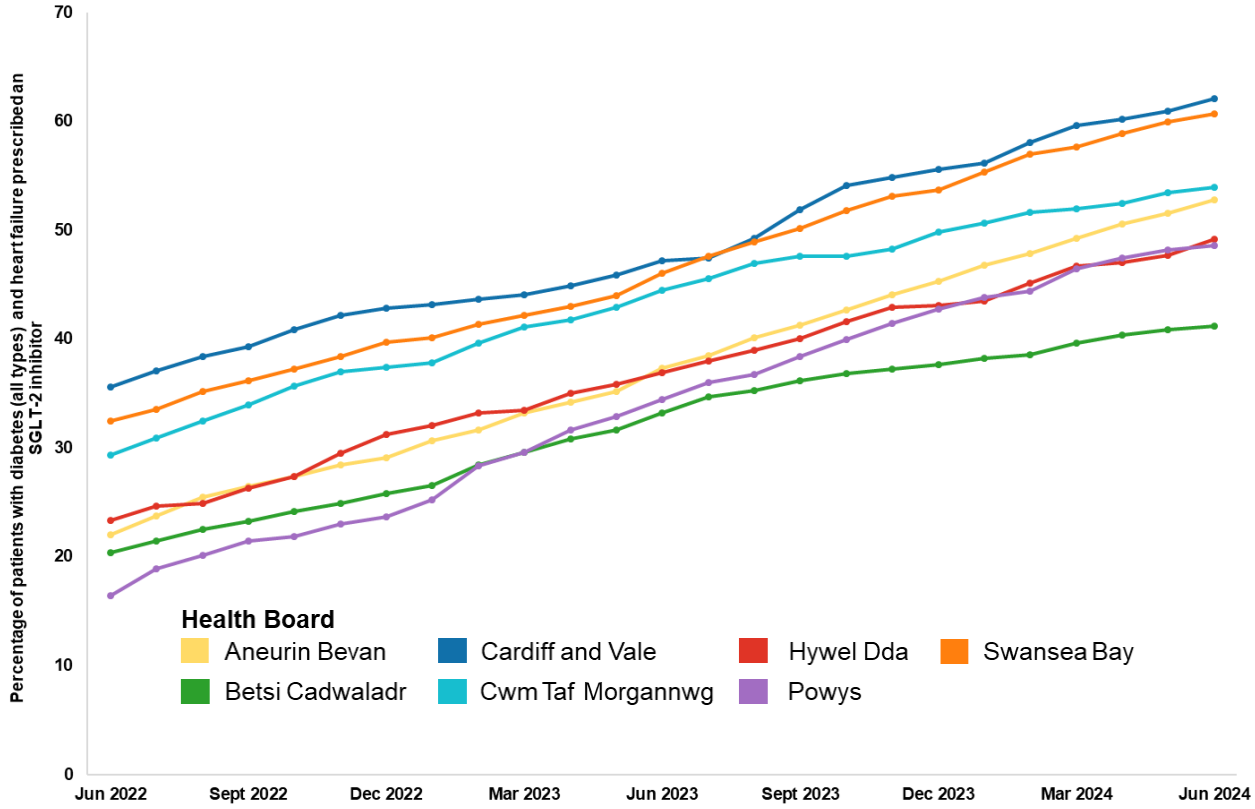
This area contains measures looking at the use of sodium-glucose co-transporter-2 (SGLT-2) inhibitors in patients with a diagnosis of type 2 diabetes mellitus (T2DM) and chronic heart failure, in patients with T2DM and chronic kidney disease (CKD) and in patients with non-diabetic CKD; with the aim of ensuring that patients are appropriately treated.

SGLT-2 inhibitors were developed as a treatment for T2DM[105,106]. Since their introduction, benefits for a wide range of other indications have been demonstrated as they have been found to promote protective mechanisms that may contribute to the slowing of related cardiovascular, renal and metabolic complications. Evidence from well conducted randomised controlled trials show that SGLT-2 inhibitors reduce the risk of CKD progression and the number of cardiovascular and end stage renal events in adults with T2DM[106,107].

1.4.1 Patients with type 2 diabetes and chronic heart failure

Purpose:
To improve cardiovascular outcomes in patients with T2DM and chronic heart failure.
Unit of measure:
Number of patients with T2DM and chronic heart failure who are prescribed an SGLT-2 inhibitor.
Target:
To increase the number of patients with T2DM and chronic heart failure prescribed an SGLT-2 inhibitor.

Figure 21. Percentage of patients with type 2 diabetes and heart failure prescribed an SGLT-2 inhibitor to June 2024*



Background and evidence

Heart failure is a long-term clinical syndrome where the heart does not effectively pump blood around the body. It often requires lifelong management that involves medications, including SGLT-2 inhibitors[108]. Patients with heart failure and T2DM are at a higher risk of adverse outcomes and of cardiovascular mortality[109]. This indicator supports the implementation of *Quality Statement 5: Treatment with an SGLT-2 inhibitor*, produced by NICE in relation to T2DM[110].

SGLT-2 inhibitor trials in people with symptomatic heart failure have demonstrated that SGLT-2 inhibition reduces the risk of cardiovascular death or hospitalisation for heart failure among this population[111]. These findings have also been demonstrated in people with reduced and preserved ejection fraction, and in people with recent hospitalisation for worsening heart failure[111].

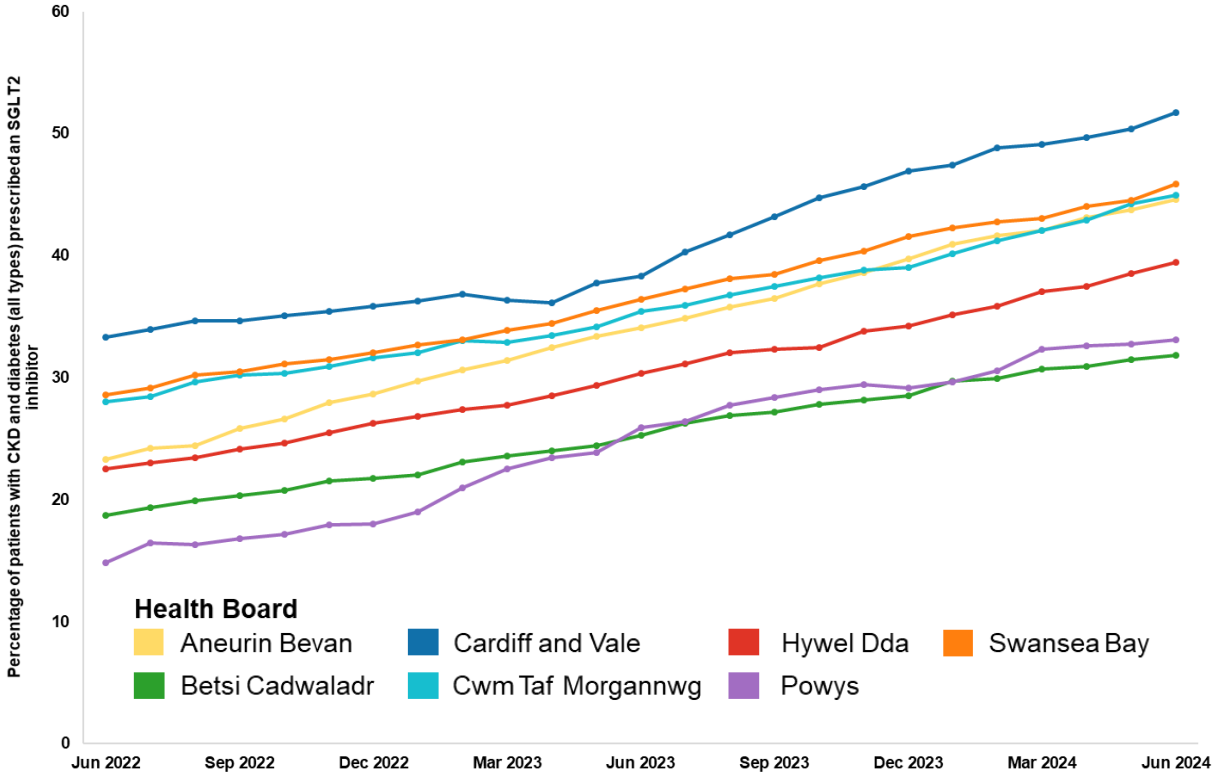
The NICE guideline, Type 2 diabetes in adults: management, recommends that patients with T2DM are assessed for cardiovascular status and risk to determine whether they also have chronic heart failure or established atherosclerotic cardiovascular disease[107]. NICE recommend SGLT-2 inhibitors in addition to metformin as a first-line treatment for T2DM in patients who have or develop chronic heart failure or established atherosclerotic cardiovascular disease. If metformin is contraindicated or not tolerated, SGLT-2 inhibitors should be offered as first-line treatment in this patient group[107]. Dapagliflozin (Forxiga®) and empagliflozin (Jardiance ®) are currently licensed in adults for the treatment of both symptomatic chronic heart failure and T2DM[112,113].

* based on data available on the primary care information portal

1.4.2 Patients with type 2 diabetes and chronic kidney disease

Purpose:
To reduce the risk of CKD progression and mortality and risk of cardiovascular events in patients with CKD and type 2 diabetes.
Unit of measure:
Number of patients with type 2 diabetes and CKD who are currently treated with an ARB or an ACE inhibitor prescribed an SGLT-2 inhibitor.
Target:
To increase the number of patients with type 2 diabetes and CKD prescribed an SGLT-2 inhibitor.

Figure 22. Percentage of patients with CKD and diabetes (all types) prescribed an SGLT-2 inhibitor to June 2024*



Background and evidence

CKD is a long-term condition characterised by abnormal kidney function or structure (or both) that is present for more than three months with implications for health[114]. It is staged by categories of glomerular filtration rate (GFR) and albuminuria (albumin:creatinine [ACR] ratio) whereby increased risk of adverse outcomes is associated with decreased GFR and/or increased ACR (with the risk multiplied when both markers are at play)[114,115]. CKD is a serious public health problem associated with significant morbidity, premature mortality and high healthcare costs[116]. The economic burden of kidney disease accounts for 3.2% of NHS budgets (£6.4 billion) as more than 10% of the UK population live with CKD (at any stage). The economic burden is

* based on data available on the primary care information portal

projected to rise to £13.9 billion by 2033[116]. The most common cause of CKD is diabetes, 40% of those with T2DM go on to develop diabetic kidney disease[117].

Management of CKD aims to prevent and delay disease progression and the development of complications with guidelines (both UK and international) regularly updated to reflect the growing body of evidence for SGLT-2 inhibitors place in treatment pathways[111,114,115]. The current NICE quality standard (March 2023) for T2DM in adults state SGLT-2 inhibitors should be offered to people with T2DM and CKD who are taking an angiotensin-converting enzyme (ACE) inhibitor or angiotensin-receptor blocker (ARB) and who have an ACR over 30 mg/mmol and meet the criteria in the marketing authorisation for the SGLT-2 inhibitor (including relevant eGFR thresholds)[110]. While, the UK Kidney Association (UKKA) guideline published in October 2023 recommend SGLT-2 inhibitors in CKD and T2DM patients with a broader range of eGFR and lower ACR thresholds[103]. The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines published in April 2024, recommend SGLT-2 inhibitors in CKD and T2DM patients who have an eGFR ≥ 20 ml/min/1.73m^2 (no ACR threshold)[114]. The current guidelines make differing recommendations for the role of SGLT-2 inhibitors in CKD and T2DM due to the fast-evolving clinical trial evidence.

Canagliflozin (Invokana®), dapagliflozin (Forxiga®) and empagliflozin (Jardiance®) are the SGLT-2 inhibitors approved for the treatment of CKD in patients with T2DM[112,113,118]. Increasing the proportion of people with T2DM and CKD on SGLT-2 inhibitors will slow CKD progression and reduce the number of cardiovascular and end-stage renal events[110,111], however there is much work to be done to ensure that those people who are likely to benefit from treatment are identified and provided with appropriate medication[121].

1.4.3 Patients with non-diabetic chronic kidney disease

Purpose:
To reduce the risk of CKD progression and mortality and risk of cardiovascular events in patients with non-diabetic CKD.
Unit of measure:
Number of patients with non-diabetic CKD who are currently treated with an ARB or an ACE inhibitor and have an ACR ≥ 22.6 mg/mmol prescribed an SGLT-2 inhibitor.
Target:
To increase the number of patients with non-diabetic CKD prescribed an SGLT-2 inhibitor.

Please note: Due to the withdrawal of Audit+ by the end of 2024–25 it has not been possible to perform any feasibility testing of this proposed indicator or collect any baseline data.

Background and evidence

SGLT-2 inhibition has been shown to be effective in people with CKD and albuminuria, including people without T2DM[111]. A recent systematic review and meta-analysis of SGLT-2 inhibitor trials (which included four CKD trials) demonstrated that the renal benefits of SGLT-2 inhibition were similar for people with or without diabetes[122]. There is evidence for benefits in terms of CKD progression, cardiovascular events and mortality

when SGLT-2 inhibitors are used as an add on to standard care with ACE inhibitors and ARBs for people with CKD[122].

Dapagliflozin (Forxiga®) and empagliflozin (Jardiance®) are the SGLT-2 inhibitors approved for the treatment of CKD in patients without T2DM[112,113]. Associated NICE technology appraisal guidance recommendations for dapagliflozin (Forxiga®) and empagliflozin (Jardiance®) specify an ACR threshold (≥ 22.6 mg/mmol) for non-diabetic patients with CKD but not for those with T2DM and CKD[119,120]. The existing evidence base indicates that increasing the proportion of people on SGLT-2 inhibitors will lead to a meaningful improvement in patient outcomes[111].

Useful resources

- AWMSG (2021) All Wales advice on sodium-glucose cotransporter-2 (SGLT-2) inhibitors in type 2 diabetes and cardiovascular disease
- European Society of Cardiology (2023) Guidelines for the management of cardiovascular disease in patients with diabetes
- Kidney Care UK (2023) Let's talk kidneys. Opportunities for early intervention in chronic kidney disease
- NICE (2023) Type 2 diabetes in adults (QS209)
- NICE (2022) Type 2 diabetes in adults: management (NG208)
- UKKA (2023) UK Kidney Association Clinical Practice Guideline: Sodium-Glucose Co-transporter-2 (SGLT-2) Inhibition in Adults with Kidney Disease 2023 UPDATE

2.0 Supporting domains

2.1 Safety

2.1.1 Prescribing Safety Indicators

Please note: Due to the withdrawal of Audit+ by the end of 2024–25 it has not been possible to perform any feasibility testing or collect any baseline data for some of the proposed new indicators.

Purpose:

To identify patients at high risk of adverse drug reactions and medicines-related harm in primary care.

Units of measure:

Prescribing Safety Indicators related to acute kidney injury (AKI)

- Number of patients on the CKD register (CKD stage 3–5) who have received a repeat prescription for an NSAID within the last 3 months.
- Number of patients who are not on the CKD register but have an eGFR of < 59 ml/min and have received a repeat prescription for an NSAID within the last 3 months.
- Number of patients with concurrent prescriptions of an NSAID, renin-angiotensin system (RAS) drug and a diuretic.
- Number of patients aged 75 and over with a current prescription for an ACE Inhibitor or loop diuretic without a check of renal function and electrolytes in the previous 15 months.

Prescribing Safety Indicators related to antimicrobial stewardship

- Number of patients with recurrent prescriptions for nitrofurantoin, with an eGFR of < 45 ml/min.
- Number of trimethoprim items prescribed to patients aged ≥ 65 years, per 1,000 patient list size aged ≥ 65 years.

Prescribing Safety Indicators related to bleeds

- Number of patients with a peptic ulcer who have been prescribed NSAIDs without a PPI.
- Number of patients with concurrent prescriptions of warfarin and an oral NSAID.
- Number of patients with concurrent prescriptions for a DOAC and an oral NSAID.
- Number of patients aged 65 years or over prescribed an NSAID plus aspirin and/or clopidogrel but without gastroprotection (PPI or H_2-receptor antagonist).
- Number of patients with concurrent prescriptions of an oral anticoagulant (warfarin or DOAC) and an SSRI.

Prescribing Safety Indicators related to cognition

- Number of patients aged 65 years or over prescribed an antipsychotic.
- Number of patients aged 75 and over with an Anticholinergic Effect on Cognition (AEC) score of 3 or more for items on active repeat.

Prescribing Safety Indicators specific to females

- Number of female patients with a past medical history of venous or arterial thrombosis who have been prescribed combined hormonal contraceptives.
- Number of female patients aged 14–55 with a prescription for oral retinoids.
- Number of female patients aged 14–55 with a prescription for topiramate

Prescribing Safety Indicators related to 'other'

- Number of patients under 16 with a current prescription of aspirin.
- Number of patients with asthma who have been prescribed a non-cardioselective beta-blocker.
- Number of patients with concurrent prescriptions of verapamil and a beta-blocker.
- Number of female patients aged ≤ 55 years with a prescription for sodium valproate.
- Number of male patients who have been prescribed sodium valproate.

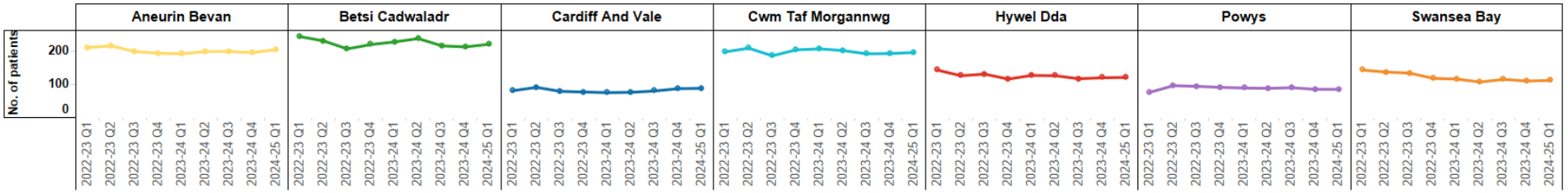
Target for 2025–2028:

No target set

Figure 23. Prescribing Safety Indicators

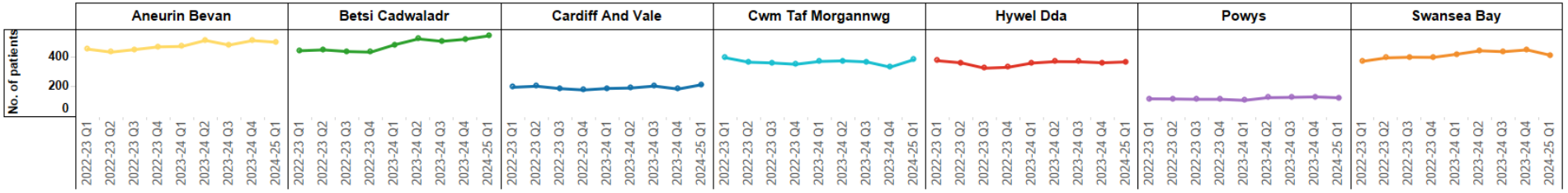
Prescribing Safety Indicators related to acute kidney injury (AKI)

01. Number of patients on the CKD register (CKD stage 3–5) who have received a repeat prescription for an NSAID within the last 3 months.



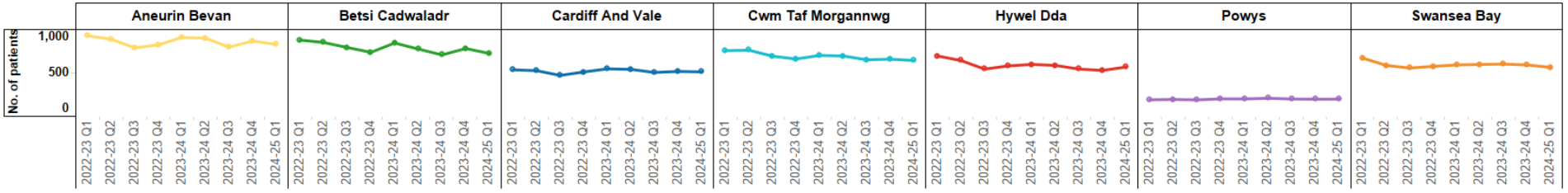
No Measure Value	2022-23 Q1	2022-23 Q2	2022-23 Q3	2022-23 Q4	2023-24 Q1	2023-24 Q2	2023-24 Q3	2023-24 Q4	2024-25 Q1
Aneurin Bevan	211	216	199	194	192	199	199	196	205
Betsi Cadwaladr	244	231	207	220	228	238	216	213	221
Cardiff And Vale	81	91	79	77	75	76	80	87	88
Cwm Taf Morgannwg	198	209	186	204	207	202	192	193	196
Hywel Dda	143	126	131	116	127	126	117	120	121
Powys	76	96	94	91	89	88	90	85	85
Swansea Bay	143	137	134	118	116	107	115	110	112

02. Number of patients who are not on the CKD register but have an eGFR of < 59 ml/min and have received a repeat prescription for an NSAID within the last 3 months.



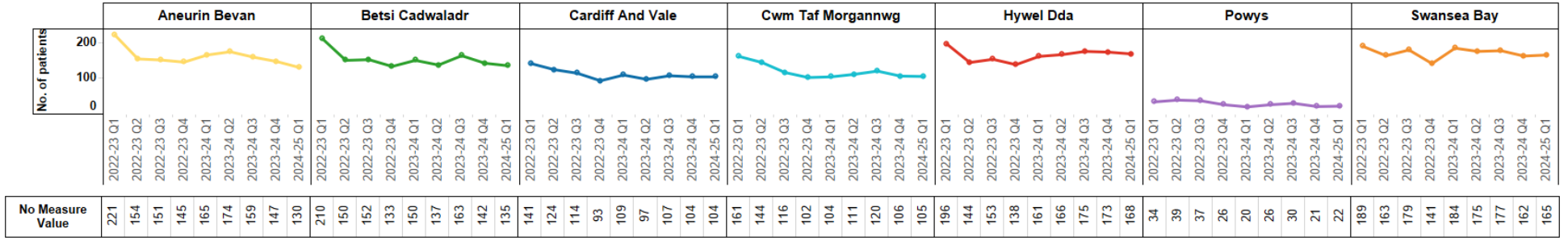
No Measure Value	2022-23 Q1	2022-23 Q2	2022-23 Q3	2022-23 Q4	2023-24 Q1	2023-24 Q2	2023-24 Q3	2023-24 Q4	2024-25 Q1
Aneurin Bevan	450	430	447	465	468	508	477	507	496
Betsi Cadwaladr	439	445	434	430	479	518	502	516	539
Cardiff And Vale	196	203	187	178	188	191	204	184	213
Cwm Taf Morgannwg	393	363	358	349	368	372	365	330	380
Hywel Dda	373	359	323	329	357	367	366	359	365
Powys	119	118	116	116	109	127	129	132	126
Swansea Bay	369	392	396	395	416	439	433	445	409

03. Number of patients with concurrent prescriptions of an NSAID, renin-angiotensin system (RAS) drug and a diuretic.



No Measure Value	2022-23 Q1	2022-23 Q2	2022-23 Q3	2022-23 Q4	2023-24 Q1	2023-24 Q2	2023-24 Q3	2023-24 Q4	2024-25 Q1
Aneurin Bevan	933	891	792	826	913	904	800	871	831
Betsi Cadwaladr	882	854	796	740	848	778	710	784	727
Cardiff And Vale	538	528	473	513	549	543	507	519	514
Cwm Taf Morgannwg	759	765	696	663	704	698	654	661	645
Hywel Dda	698	645	546	583	600	589	546	531	570
Powys	191	195	190	202	201	209	200	198	199
Swansea Bay	673	589	558	578	594	600	604	594	566

04. Number of patients aged 75 years and over with a current prescription for an ACE Inhibitor or loop diuretic without a check of renal function and electrolytes in the previous 15 months.



No Measure Value									
Aneurin Bevan	221	154	151	145	165	174	159	147	130
Betsi Cadwaladr	210	150	152	133	150	137	163	142	135
Cardiff And Vale	141	124	114	93	109	97	107	104	104
Cwm Taf Morgannwg	161	144	116	102	104	111	120	106	105
Hywel Dda	196	144	153	138	161	166	175	173	168
Powys	34	39	37	26	20	26	30	21	22
Swansea Bay	189	163	179	141	184	175	177	162	165

Prescribing Safety Indicators related to antimicrobial stewardship

05. Number of patients with recurrent prescriptions for nitrofurantoin, with an eGFR of < 45 ml/min.

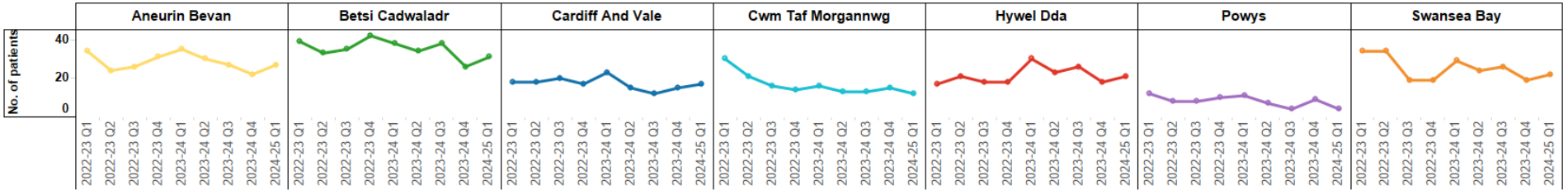
Unable to include graph due to the future withdrawal of Audit+

06. Number of trimethoprim items prescribed to patients aged ≥ 65 years, per 1,000 patient list size aged ≥ 65 years.

Unable to include graph due to the future withdrawal of Audit+

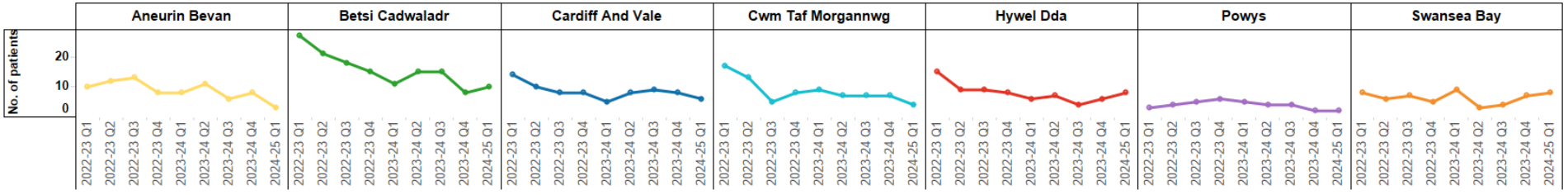
Prescribing Safety Indicators related to bleeds

07. Number of patients with a peptic ulcer who have been prescribed NSAIDs without a PPI.



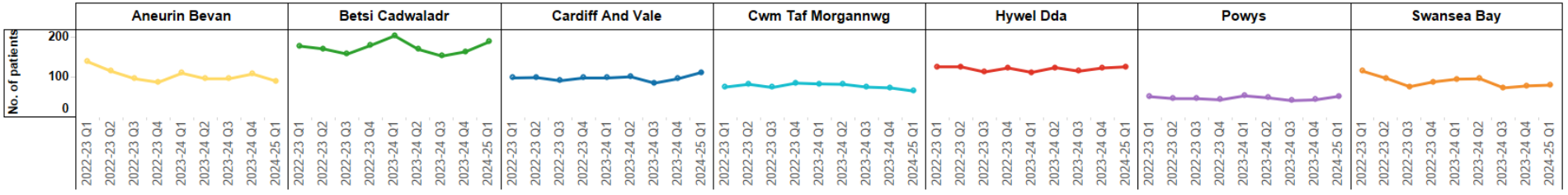
No Measure Value	2022-23 Q1	2022-23 Q2	2022-23 Q3	2022-23 Q4	2023-24 Q1	2023-24 Q2	2023-24 Q3	2023-24 Q4	2024-25 Q1
Aneurin Bevan	34	24	26	31	35	30	27	22	27
Betsi Cadwaladr	39	33	35	42	38	34	38	26	31
Cardiff And Vale	18	18	20	17	23	15	12	15	17
Cwm Taf Morgannwg	30	21	16	14	16	13	13	15	12
Hywel Dda	17	21	18	18	30	23	26	18	21
Powys	12	8	8	10	11	7	4	9	4
Swansea Bay	34	34	19	19	29	24	26	19	22

08. Number of patients with concurrent prescriptions of warfarin and an oral NSAID.



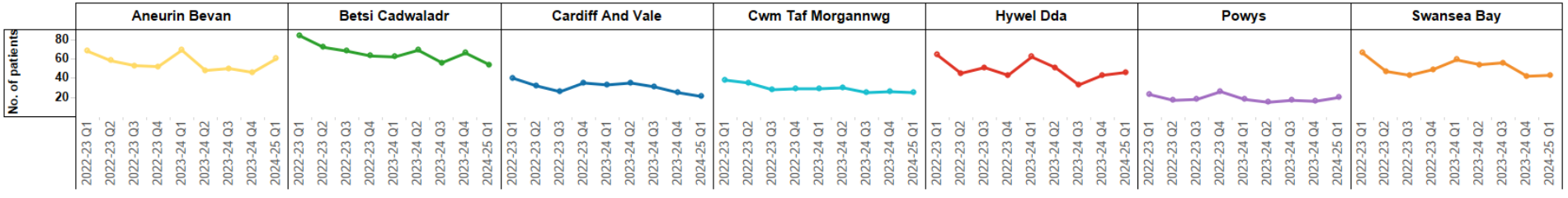
No Measure Value	2022-23 Q1	2022-23 Q2	2022-23 Q3	2022-23 Q4	2023-24 Q1	2023-24 Q2	2023-24 Q3	2023-24 Q4	2024-25 Q1
Aneurin Bevan	10	12	13	8	8	11	6	8	3
Betsi Cadwaladr	27	21	18	15	11	15	15	8	10
Cardiff And Vale	14	10	8	8	5	8	9	8	6
Cwm Taf Morgannwg	17	13	5	8	9	7	7	7	4
Hywel Dda	15	9	9	8	6	7	4	6	8
Powys	3	4	5	6	5	4	4	2	2
Swansea Bay	8	6	7	5	9	3	4	7	8

09. Number of patients with concurrent prescriptions for a DOAC and an oral NSAID.



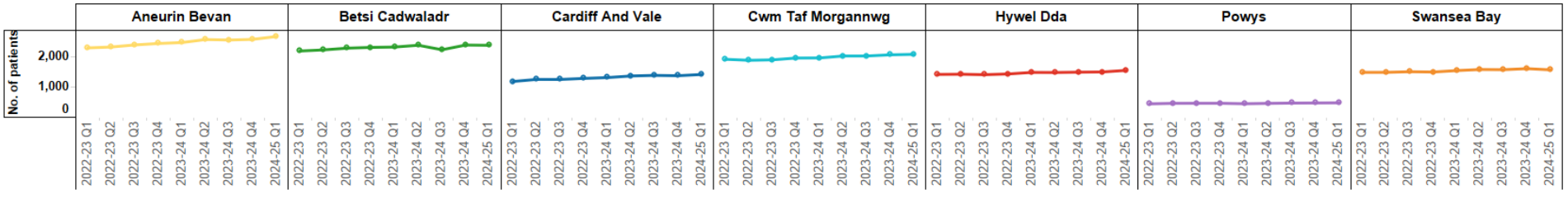
No Measure Value	2022-23 Q1	2022-23 Q2	2022-23 Q3	2022-23 Q4	2023-24 Q1	2023-24 Q2	2023-24 Q3	2023-24 Q4	2024-25 Q1
Aneurin Bevan	139	115	96	87	110	96	96	108	90
Betsi Cadwaladr	178	171	158	180	204	170	153	164	189
Cardiff And Vale	98	99	91	98	98	101	85	96	112
Cwm Taf Morgannwg	75	82	74	85	83	82	75	73	65
Hywel Dda	126	126	113	123	112	124	115	123	126
Powys	51	46	46	43	53	48	41	43	52
Swansea Bay	115	97	76	88	95	96	73	78	80

10. Number of patients aged 65 years or over prescribed an NSAID plus aspirin and/or clopidogrel but without gastroprotection (PPI or H_2 receptor antagonist).



	2022-23 Q1	2022-23 Q2	2022-23 Q3	2022-23 Q4	2023-24 Q1	2023-24 Q2	2023-24 Q3	2023-24 Q4	2024-25 Q1
Aneurin Bevan	68	58	53	52	69	48	50	46	60
Betsi Cadwaladr	84	72	68	63	62	69	56	66	54
Cardiff And Vale	40	32	26	35	33	35	31	25	21
Cwm Taf Morgannwg	38	35	28	29	29	30	25	26	25
Hywel Dda	64	45	51	43	62	51	33	43	46
Powys	23	17	18	26	18	15	17	16	20
Swansea Bay	66	47	43	49	59	54	56	42	43

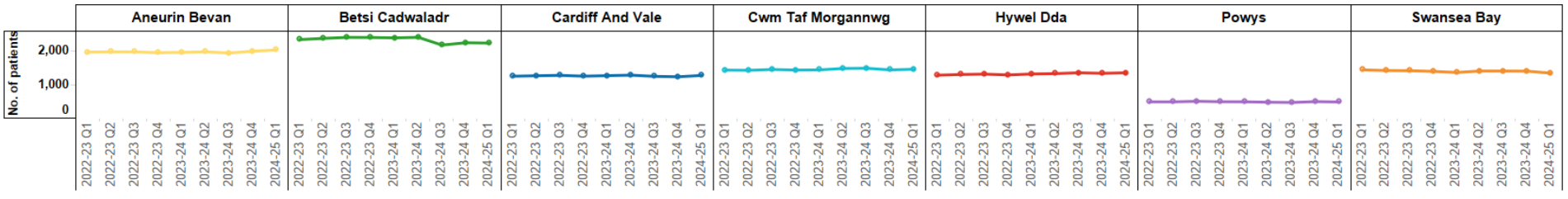
11. Number of patients with concurrent prescriptions of an oral anticoagulant (warfarin or DOAC) and an SSRI.



	2022-23 Q1	2022-23 Q2	2022-23 Q3	2022-23 Q4	2023-24 Q1	2023-24 Q2	2023-24 Q3	2023-24 Q4	2024-25 Q1
Aneurin Bevan	2,298	2,327	2,396	2,444	2,475	2,575	2,558	2,580	2,675
Betsi Cadwaladr	2,195	2,232	2,289	2,315	2,326	2,385	2,236	2,392	2,384
Cardiff And Vale	1,186	1,254	1,253	1,287	1,315	1,368	1,388	1,377	1,418
Cwm Taf Morgannwg	1,921	1,888	1,902	1,962	1,965	2,030	2,030	2,069	2,085
Hywel Dda	1,420	1,426	1,411	1,435	1,486	1,483	1,494	1,501	1,554
Powys	446	462	464	464	449	461	471	475	479
Swansea Bay	1,487	1,488	1,509	1,499	1,547	1,583	1,577	1,611	1,571

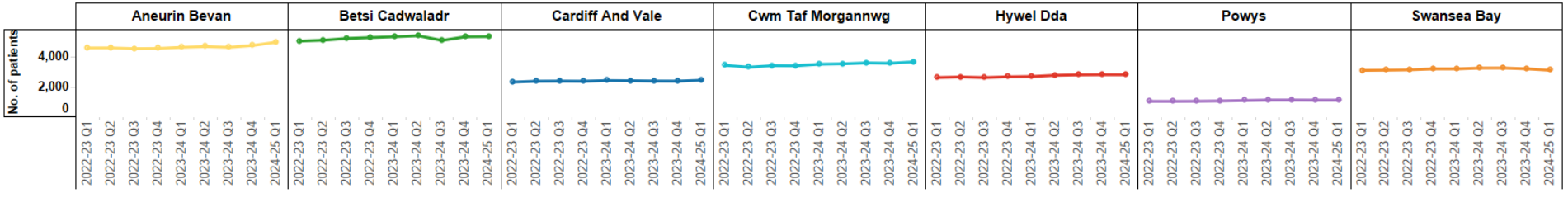
Prescribing Safety Indicators related to cognition

12. Number of patients aged 65 years or over prescribed an antipsychotic.



	2022-23 Q1	2022-23 Q2	2022-23 Q3	2022-23 Q4	2023-24 Q1	2023-24 Q2	2023-24 Q3	2023-24 Q4	2024-25 Q1
Aneurin Bevan	1,970	1,977	1,976	1,953	1,962	1,978	1,943	1,996	2,032
Betsi Cadwaladr	2,343	2,379	2,409	2,406	2,395	2,410	2,179	2,248	2,238
Cardiff And Vale	1,250	1,264	1,276	1,251	1,267	1,282	1,246	1,233	1,273
Cwm Taf Morgannwg	1,433	1,426	1,451	1,434	1,439	1,481	1,487	1,438	1,458
Hywel Dda	1,280	1,302	1,313	1,288	1,317	1,328	1,352	1,336	1,352
Powys	486	485	502	489	487	474	466	492	481
Swansea Bay	1,439	1,420	1,415	1,394	1,362	1,405	1,404	1,401	1,342

13. Number of patients aged 75 years and over with an Anticholinergic Effect on Cognition (AEC) score of 3 or more for items on active repeat.



No Measure Value	Aneurin Bevan								
	4,631	4,633	4,587	4,599	4,676	4,723	4,674	4,795	5,021

No Measure Value	Betsi Cadwaladr								
	5,096	5,152	5,273	5,330	5,387	5,452	5,136	5,385	5,396

No Measure Value	Cardiff And Vale								
	2,333	2,394	2,401	2,392	2,436	2,423	2,404	2,399	2,459

No Measure Value	Cwm Taf Morgannwg								
	3,464	3,337	3,438	3,428	3,538	3,565	3,626	3,602	3,696

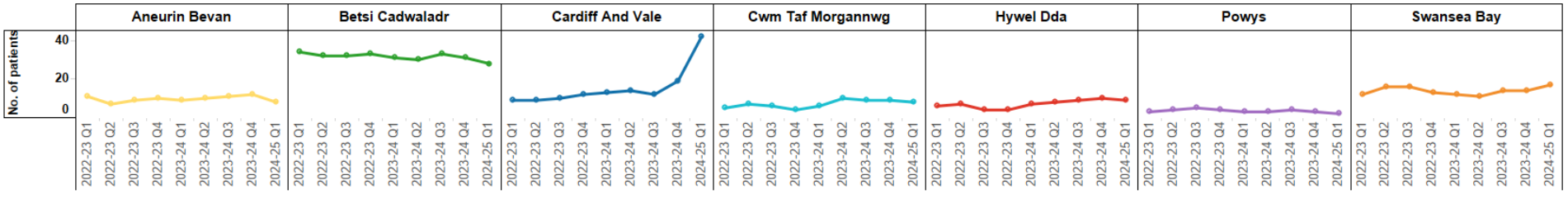
No Measure Value	Hywel Dda								
	2,641	2,678	2,638	2,689	2,710	2,791	2,821	2,831	2,827

No Measure Value	Powys								
	1,039	1,037	1,045	1,063	1,094	1,125	1,125	1,118	1,117

No Measure Value	Swansea Bay								
	3,123	3,138	3,160	3,221	3,220	3,280	3,283	3,225	3,128

Prescribing Safety Indicators specific to females

14. Number of female patients with a past medical history of venous or arterial thrombosis who have been prescribed combined hormonal contraceptives.



No Measure Value	Aneurin Bevan								
	11	7	9	10	9	10	11	12	8

No Measure Value	Betsi Cadwaladr								
	34	32	32	33	31	30	33	31	28

No Measure Value	Cardiff And Vale								
	9	9	10	12	13	14	12	19	42

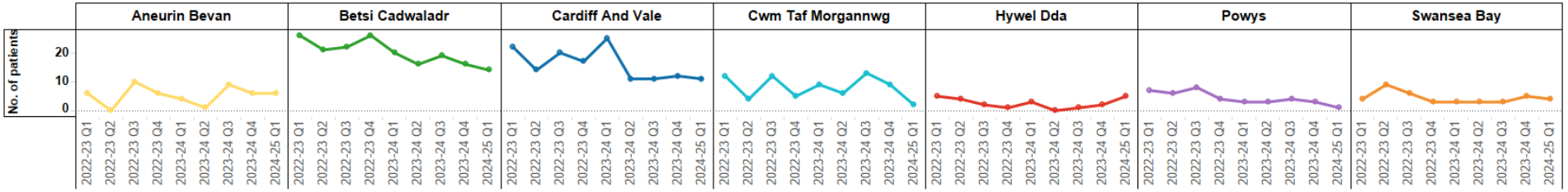
No Measure Value	Cwm Taf Morgannwg								
	5	7	6	4	6	10	9	9	8

No Measure Value	Hywel Dda								
	6	7	4	4	7	8	9	10	9

No Measure Value	Powys								
	3	4	5	4	3	3	4	3	2

No Measure Value	Swansea Bay								
	12	16	16	13	12	11	14	14	17

15. Number of female patients aged 14–55 years with a prescription for oral retinoids.



No Measure Value	Aneurin Bevan								
	6	0	10	6	4	1	9	6	6

No Measure Value	Betsi Cadwaladr								
	26	21	22	26	20	16	19	16	14

No Measure Value	Cardiff And Vale								
	22	14	20	17	25	11	11	12	11

No Measure Value	Cwm Taf Morgannwg								
	12	4	12	5	9	6	13	9	2

No Measure Value	Hywel Dda								
	5	4	2	1	3	0	1	2	5

No Measure Value	Powys								
	7	6	8	4	3	3	4	3	1

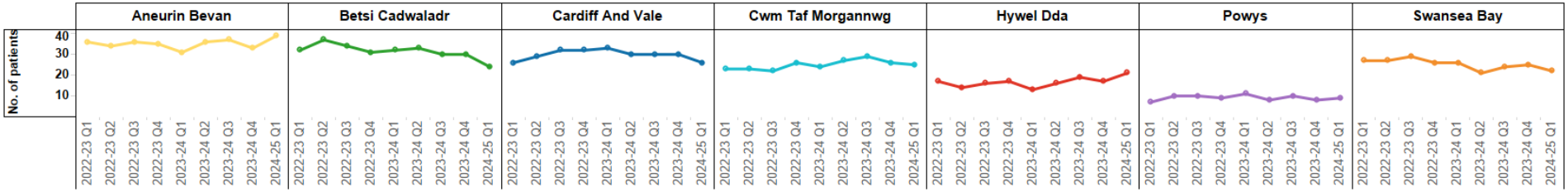
No Measure Value	Swansea Bay								
	4	9	6	3	3	3	3	5	4

16. Number of female patients aged 14–55 years with a prescription for topiramate.

Unable to include graph due to the future withdrawal of Audit+

Prescribing Safety Indicators related to 'other'

17. Number of patients aged under 16 years with a current prescription of aspirin.

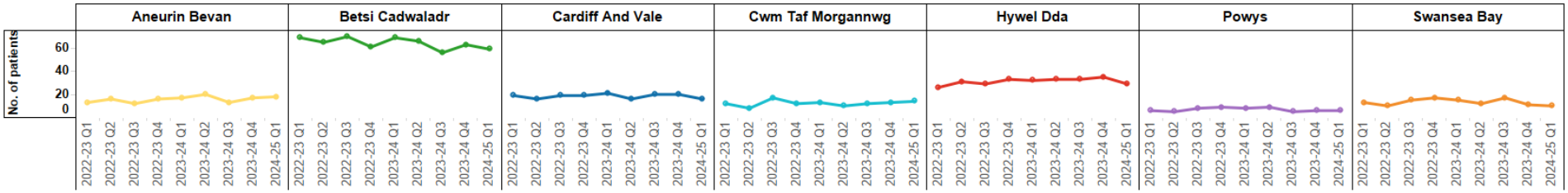


	2022-23 Q1	2022-23 Q2	2022-23 Q3	2022-23 Q4	2023-24 Q1	2023-24 Q2	2023-24 Q3	2023-24 Q4	2024-25 Q1
Aneurin Bevan	36	34	36	35	31	36	37	33	39
Betsi Cadwaladr	32	37	34	31	32	33	30	30	24
Cardiff And Vale	26	29	32	32	33	30	30	30	26
Cwm Taf Morgannwg	23	23	22	26	24	27	29	26	25
Hywel Dda	17	14	16	17	13	16	19	17	21
Powys	7	10	10	9	11	8	10	8	9
Swansea Bay	27	27	29	26	26	21	24	25	22

18. Number of patients with asthma who have been prescribed a non-cardioselective beta-blocker.

Unable to include graph due to the future withdrawal of Audit+

19. Number of patients with concurrent prescriptions of verapamil and a beta-blocker.



	2022-23 Q1	2022-23 Q2	2022-23 Q3	2022-23 Q4	2023-24 Q1	2023-24 Q2	2023-24 Q3	2023-24 Q4	2024-25 Q1
Aneurin Bevan	13	16	12	16	17	20	13	17	18
Betsi Cadwaladr	69	65	70	61	69	66	56	63	59
Cardiff And Vale	19	16	19	19	21	16	20	20	16
Cwm Taf Morgannwg	12	8	17	12	13	10	12	13	14
Hywel Dda	26	31	29	33	32	33	33	35	29
Powys	6	5	8	9	8	9	5	6	6
Swansea Bay	13	10	15	17	15	12	17	11	10

20. Number of female patients aged ≤ 55 years with a prescription for sodium valproate.

Unable to include graph due to the future withdrawal of Audit+

21. Number of male patients with a prescription for sodium valproate.

Unable to include graph due to the future withdrawal of Audit+

Background and evidence
As adverse drug reactions can often be predictable, a system to identify patients at risk can enable potential problems to be identified and addressed before actual patient harm occurs[123]. Prescribing Safety Indicators (PSIs) identify groups of patients within the GP practice, enabling intervention and avoidance of harm. Patients identified via the PSIs should be reviewed and/or monitored as appropriate.

These indicators support the third WHO Global Patient Safety Challenge, *Medication Without Harm*, launched in 2017, which aims to reduce severe avoidable medication-related harm by 50% globally, within 5 years[124].

PSIs related to Acute Kidney Injury (AKI)
AKI is a term covering a range of injury to the kidneys, resulting from a number of different causes. It is characterised by a decline in renal excretory function over hours or days that can result in failure to maintain fluid, electrolyte and acid based homeostasis[125].

One of the most common causes of AKI is reduced perfusion of the kidneys leading to decreased GFR. This can be caused by drugs that reduce blood pressure, circulating volume or renal blood flow, for example ACE inhibitors, ARBs, NSAIDs and loop diuretics[125]. Groups of patients most at risk of developing AKI include those aged over 65 years; patients with CKD; use of nephrotoxic drugs within the last week and people with a history of AKI[125]. NICE guidance, *Chronic kidney disease: assessment and management,* highlights that in patients with CKD, the long-term use of NSAIDs may be associated with disease progression while acute use is associated with a reversible decrease in GFR. The guideline recommends caution and monitoring of the effects on GFR, when using NSAIDs in people with CKD over prolonged periods of time[115,126].

Processes for regular review of the ongoing need for treatment with drugs that may contribute to AKI, in addition to ensuring systems are in place for regular monitoring of renal function as well as reassessment of the risk versus benefit is appropriate.

PSIs related to antimicrobial stewardship

Nitrofurantoin when eGFR of < 45 ml/min
Nitrofurantoin is a broad-spectrum antibacterial agent used to treat or prevent acute or recurring UTIs[127,128]. As its efficacy is dependent on its renal secretion into the urinary tract, it is not recommended in patients with an eGFR of < 45 ml/min as it is likely to be ineffective. For this reason, it can also increase risk of harm to the patient due to adverse effects while driving antimicrobial resistance.

Trimethoprim in the elderly
Trimethoprim is an antibacterial agent primarily used to treat or prevent UTIs[129]. Due to high resistance levels (in Wales its resistance to *E. coli* was found to be 38.1%), it should only be prescribed if a lower risk of resistance is likely[68]. For this reason, its use in patients older than 65 years of age is not recommended as first line treatment (unless recent mid-stream sample of urine shows sensitivity) and as such is likely to be ineffective and increase the risk of harm due to treatment failure while driving antimicrobial resistance[129].

PSIs related to bleeds
NSAIDs have been shown to be the medicine group most likely to cause an adverse drug reaction requiring hospital admission due to events such as gastrointestinal bleeding and peptic ulceration[123]. A proton pump inhibitor (PPI) can be considered for gastroprotection

in patients at high risk of gastrointestinal complications with an NSAID[14]. NSAIDs can reduce platelet aggregation which can worsen any bleeding event in patients on an anticoagulant[14]. Wherever possible, patients taking anticoagulants should avoid concomitant use of NSAIDs[130].

Hospital admission due to gastrointestinal bleeding has been associated with aspirin and clopidogrel, as well as NSAIDs[123]. The harmful consequences of bleeds due to antiplatelet therapy increase with age[131] and PPIs are recommended in older patients undergoing antiplatelet treatment[131,132]. PPIs are the preferred option to reduce GI adverse effects in people taking low dose aspirin, as the level of suppression provided by traditional doses of H_2-receptor antagonists may not prevent NSAID related ulcers[133].

SSRIs are associated with increased risk of bleeding, especially in the elderly, or those taking drugs which damage the GI mucosa/interfere with clotting such as aspirin, NSAIDs and warfarin[134]. Anticoagulants are likely to increase the risk of bleeding events used in conjunction with SSRIs[14].

PSIs related to cognition

Use of antipsychotics in patients with dementia have a significant risk of harm, with only a limited benefit in treating behavioural and psychological symptoms of dementia[135]. The Welsh Government *Dementia Action Plan for Wales 2018–2022* called for health boards to demonstrate a reduction in the percentage of people with a diagnosis of dementia prescribed an antipsychotic medication, and a reduction in the duration of treatment[136].

The harms associated with antipsychotic use in patients with dementia include a clear increased risk of stroke and a small increase in risk of death[137]; falls; gait disturbances; dehydration; chest infection and cognitive decline[134]. Antipsychotics should be avoided in patients with dementia unless the person is at risk of harming themselves or others, or experiencing agitation, hallucinations or delusions that are causing them severe distress[138]. Completion of the AWMSG National Audit *Antipsychotics in Dementia* can help to ensure appropriate prescribing.

An increasing number of studies report that medicines with anticholinergic effects are associated with an increased risk of cognitive impairment, dementia and falls in older people, with research also suggesting a link to increased mortality with the number and potency of anticholinergic agents prescribed. Anticholinergic medicines are used for a variety of conditions, including Parkinson's disease, overactive bladder, COPD and depression. Risk of adverse clinical outcomes in older people prescribed anticholinergic medications increases with increasing anticholinergic exposure[139], and a number of rating scales are available to asses overall anticholinergic burden. The Anticholinergic Effect on Cognition (AEC)[140] scale is used for this indicator and it is good practice, where possible, to use drugs with AEC scores of zero and to avoid those scored 1, 2 or 3 (Appendix 3)[141]. Encouraging timely review to reduce the anticholinergic burden in older people by avoiding or reducing doses and deprescribing medicines with anticholinergic activity where clinically possible will help minimise potential medication-related risks.

PSIs specific to females

Combined hormonal contraceptives in thrombosis patients

There is an increased risk of venous thromboembolic disease and a slight increase in the risk of arterial thromboembolism in people using combined hormonal contraceptives[14]. Any

patients with a history of venous or arterial thrombosis who have been prescribed combined hormonal contraceptives are therefore at an increased risk[14].

Oral retinoids in females of child bearing age
Oral retinoids are highly teratogenic and there is an extremely high risk that foetal exposure to isotretinoin will result in life-threatening congenital abnormalities. Any use of oral acitretin, alitretinoin, and isotretinoin in women and girls of childbearing potential must be in accordance with the conditions of a Pregnancy Prevention Programme[142].

Topiramate in females of child bearing age
Topiramate is associated with an increased risk of congenital malformations, low birth weight and a potential increased risk of intellectual disability if used during pregnancy. The use of topiramate is contraindicated in females of childbearing potential unless the conditions of a Pregnancy Prevention Programme are fulfilled[143].

PSIs related to 'other'

Aspirin in under 16s
Reye's syndrome is a very rare disorder that can cause serious liver and brain damage. If it is not treated promptly, it may lead to permanent brain injury or death. Reye's syndrome mainly affects children and young adults under 20 years of age[144]. Owing to an association with Reye's syndrome, aspirin should not be given to children under the age of 16, unless specifically indicated e.g. for Kawasaki disease[14,145].

Non-cardioselective beta-blockers in asthma patients
Beta-blockers should be avoided in patients with asthma due to the potential to precipitate bronchospasm[14]. Non-cardioselective beta-blockers have been associated with a significantly increased risk of asthma exacerbations[146,147]. If the benefits of using a beta-blocker in an asthma patient are justified (e.g. for heart failure following myocardial infarction), then a cardioselective beta-blocker should be selected and the patient should be monitored closely.

Verapamil in combination with beta-blockers
Beta-blockers are associated with adverse drug reactions such as bradycardia and atrio-ventricular conduction disturbances[14]. A co-prescription of a calcium channel blocker, such as verapamil, with a beta-blocker is generally not recommended due to an increased negative effect on heart function compared with beta-blocker therapy alone[14].

Sodium valproate
The MHRA January 2024 Drug Safety update highlighted sodium valproate must not be started in new patients (male or female) under the age of 55 years, unless two specialists independently consider and document that there is no other effective or tolerated treatment, or unless there are compelling reasons that the reproductive risks do not apply[148]. The measures apply to people under the age of 55 because this is the age-group evidence suggests is most likely to be affected by the risks of valproate when taken during pregnancy and the possible risk of impaired fertility in males, which is thought to be reversible upon dose reduction or discontinuation[149]. A further update in September 2024 informed prescribers of a potentially increased risk of neurodevelopmental disorders in children fathered to men taking valproate around the time of conception[150]. Sodium valproate use in pregnancy carries significant risk of harm to the unborn child and must no longer be used in any girls and women of child bearing potential unless a pregnancy

prevention programme is in place to ensure that patients are fully aware of the risks and the need to avoid becoming pregnant[149,151]. An annual risk acknowledgement form is available to support the valproate Pregnancy Prevention Programme[152].

Useful resources

- AWMSG (2024) Primary care antimicrobial guidelines
- AWMSG (2023) Polypharmacy in older people: A guide for healthcare professionals
- AWMSG (2018) CEPP National Audit: antipsychotics in dementia
- AWMSG (2017) CEPP National Audit: Medicines Management for CKD
- AWMSG (2015) CEPP All Wales Audit: Towards Appropriate NSAID Prescribing
- MHRA (2022) Antipsychotics e-learning module
- PrescQIPP (2020) Bulletin 253: Anticholinergic burden (log in required)
- Sanofi (2020) Guide for healthcare professionals: Information on the risks of valproate▼ use in girls (of any age) and women of childbearing potential
- South London and Maudsley NHS Foundation Trust (2017) Medichec: The Anticholinergic Effect on Cognition Tool (Android and iOS Medichec apps available)

2.1.2 Hypnotics and anxiolytics

Purpose:
To encourage a reduction in the inappropriate prescribing of hypnotics and anxiolytics in primary care.
Unit of measure:
Hypnotic and anxiolytic UDG ADQs per 1,000 STAR-PUs.
Target for 2025–2028:
Maintain performance levels within the lower quartile, or show a reduction towards the quartile below.

Figure 24. Trend in hypnotic and anxiolytic ADQs per 1,000 STAR-PUs to quarter ending June 2024

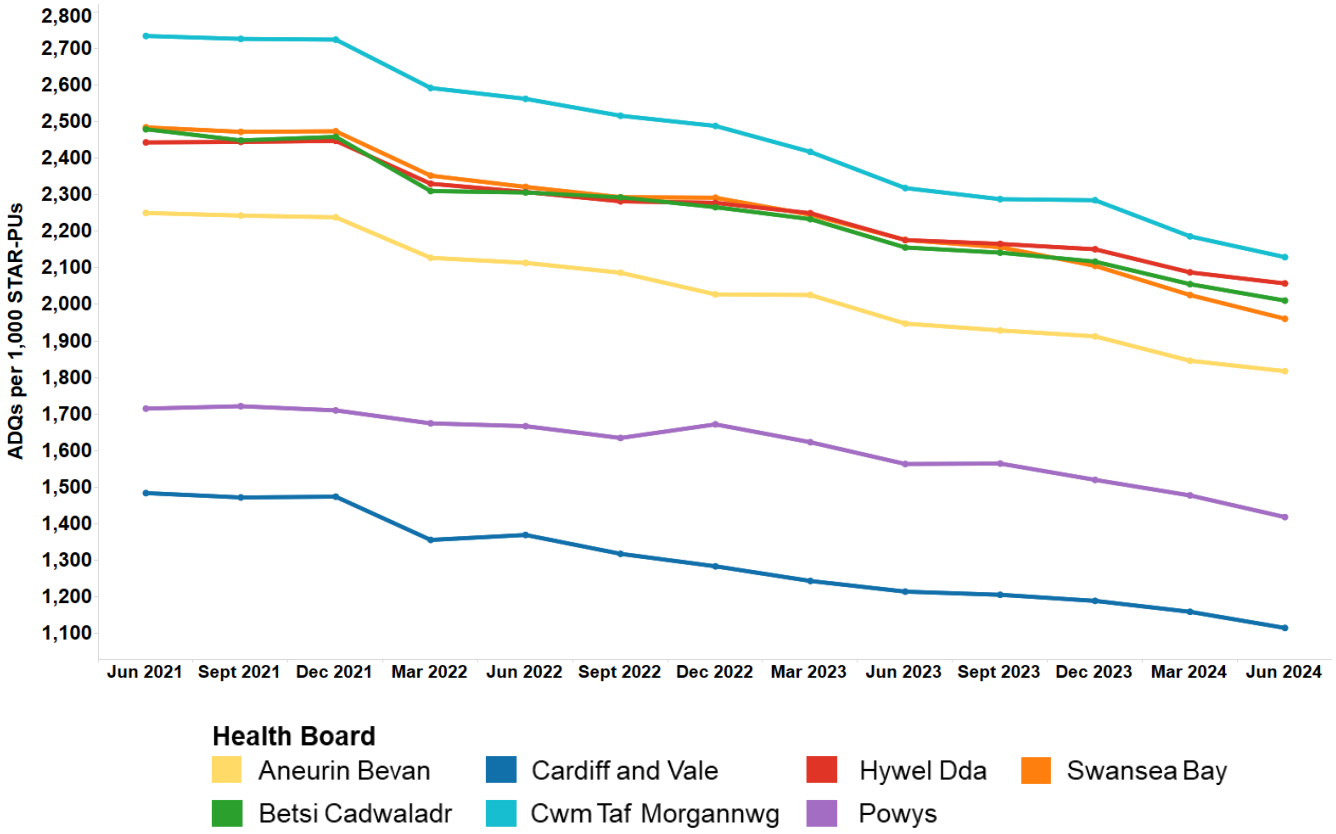
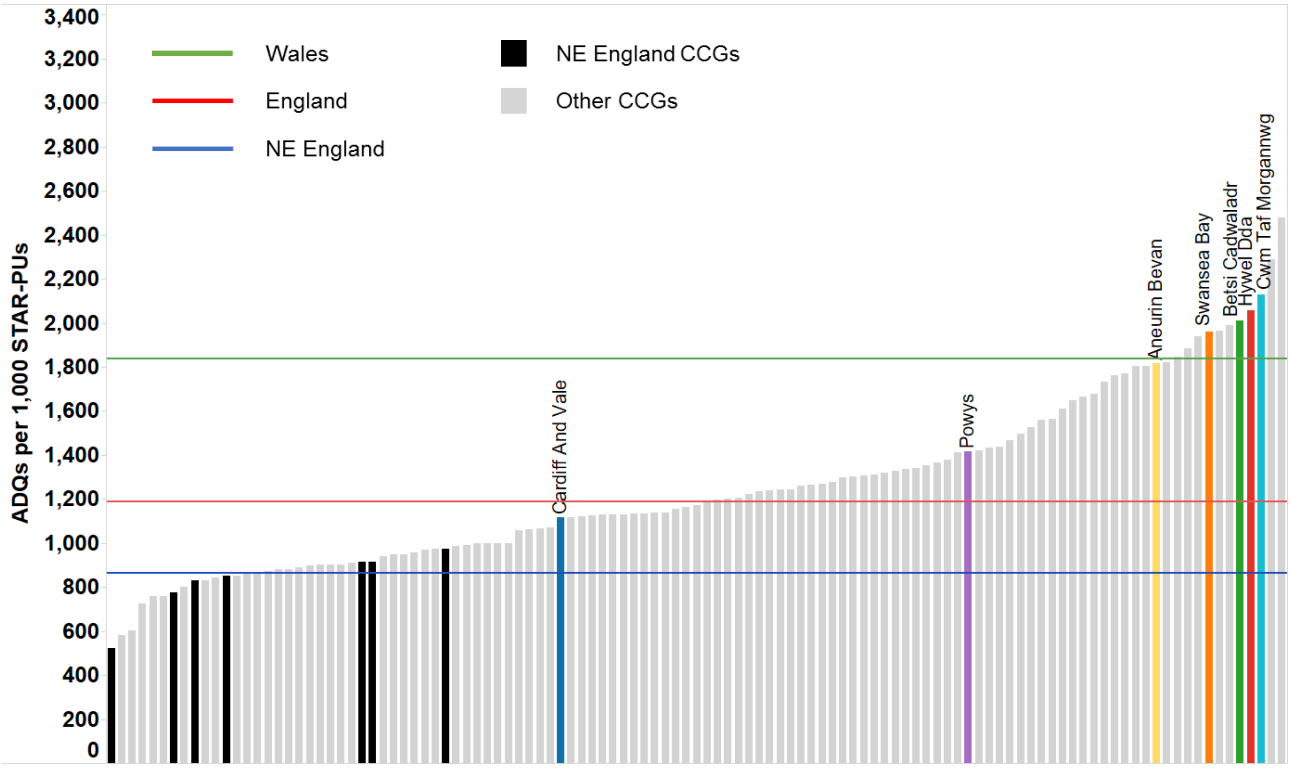


Figure 25. Hypnotic and anxiolytic ADQs per 1,000 STAR-PUs in Welsh health boards and English CCGs – Quarter ending June 2024



Background and evidence

There has been concern with regard to the high level of hypnotic and anxiolytic prescribing in NHS Wales, with the substance misuse strategy of the Welsh Government, *Working together to reduce harm*, calling for the reduction of inappropriately prescribed benzodiazepines[153]. Although the prescribing volume of hypnotics and anxiolytics in Wales has declined over recent years, there is considerable variation in prescribing rates across health boards and between GP practices. Prescribing in Wales is still high in comparison to England, with five out of seven health boards in Wales within the highest prescribing quartile when compared with CCGs in England[37,38]. Across Wales, 53 deaths were recorded where any benzodiazepine was mentioned on the death certificate in 2022, a decrease from 61 deaths the year prior[20]. In England, 452 deaths were recorded in 2022, a decrease from 476 deaths the year prior[20].

The problems associated with benzodiazepines (such as development of tolerance and dependence, and falls) are well known. It is recommended that benzodiazepines should not be used for more than two to four weeks for insomnia and anxiety, and only if it is severe, disabling, or subjecting the individual to unacceptable distress[154]. NICE guidance on the management of insomnia advises that if, after non-drug therapies have been explored, hypnotics are considered appropriate, they should be used in the lowest effective dose possible for the shortest duration possible in strict accordance with their licensed indications[155,156].

AWMSG has developed an educational pack, *Material to Support Appropriate Prescribing of Hypnotics and Anxiolytics across Wales*, which provides examples of practice protocols to allow clinicians to agree a consistent approach for the prescribing and review of hypnotics and anxiolytics. The pack also provides materials to support the review and discontinuation of hypnotic and anxiolytic treatment.

Useful resources

- AWMSG (2023) Polypharmacy in older people: A guide for healthcare professionals
- AWMSG (2021) Material to Support Appropriate Prescribing of Hypnotics and Anxiolytics across Wales
- Bruyère Research Institute (2019) Benzodiazepine & Z-Drug (BZRA) Deprescribing Algorithm

2.1.3 Yellow Cards

Purpose:

To encourage an increase in the number of Yellow Cards submitted in Wales.

Unit of measure:

- Number of Yellow Cards submitted, per GP practice, per health board and per hospital.
- Number of Yellow Cards submitted by community pharmacies, per health board.

Target for 2025–2028:

GP practices: Submit one Yellow Card per 2,000 practice population.
Health boards:

- Submit one Yellow Card per 2,000 health board population.
- Demonstrate a 10%, or greater, increase from baseline (previous financial year), for Yellow Cards submitted by secondary care.
- Demonstrate a 25%, or greater, increase from baseline (previous financial year), for Yellow Cards submitted by members of the public.

Community pharmacy: no target set.

Figure 26. Percentage of GP practices meeting the target of one Yellow Card per 2,000 practice population 2023–2024

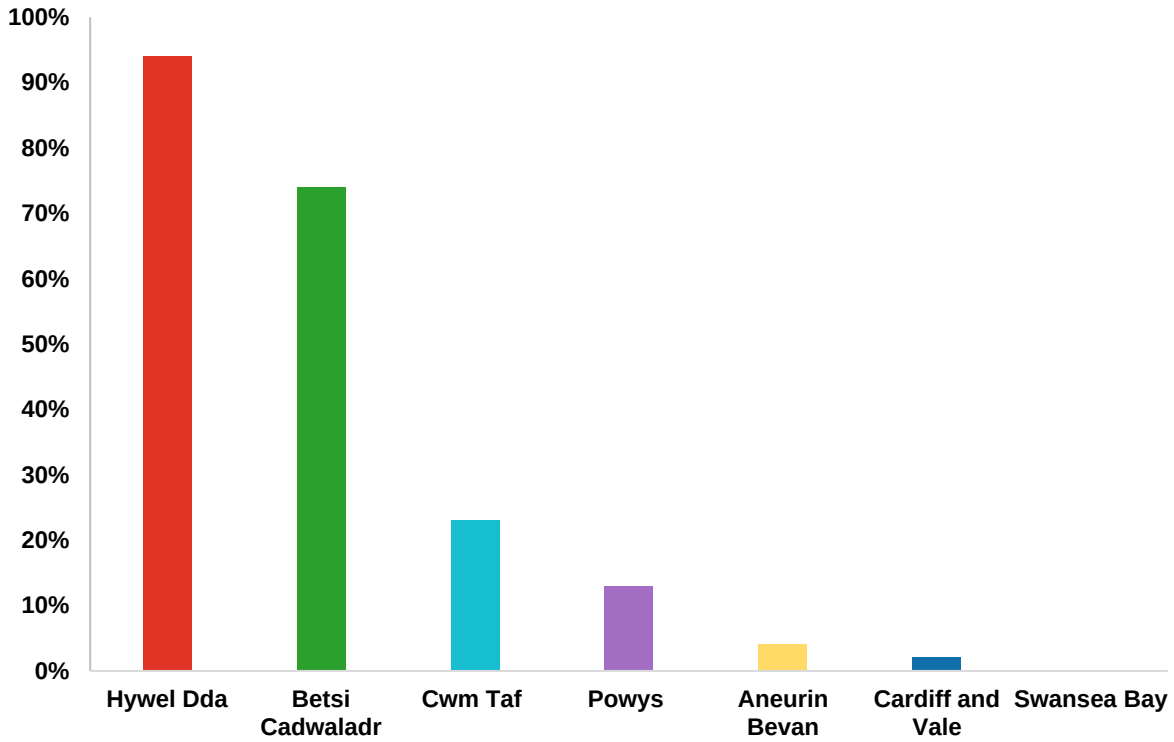


Table 4. Yellow Card data showing total number of reports, number of secondary care reports and number of member of public reports in 2023–2024

Health board/ NHS Trust	Total number of reports	General Practice reports	Secondary care reports	Member of public reports
Aneurin Bevan	407	41	104	231
Betsi Cadwaladr	1,528	930	179	352
Cardiff and Vale	387	56	87	205
Cwm Taf Morgannwg	410	120	88	173
Hywel Dda	451	253	50	136
Powys	121	13	1	100
Swansea Bay	221	20	42	132
Velindre	15	N/A	15	N/A

Background and evidence

Adverse drug reactions (ADRs) are a significant clinical problem, and can increase morbidity and mortality. Studies have shown that ADRs are the cause of up to around 16.5% of hospital admissions[123,157,158]. An ADR has been defined as *"*a response to a medicinal product that is noxious and unintended resulting not only from the authorised use of a medicinal product at normal doses but also from medication errors and uses outside the terms of the marketing authorisation, including the misuse and abuse of the medicinal product*"*[159]*.* The Yellow Card Scheme is vital in helping the MHRA monitor the safety of all healthcare products in the UK, to ensure they are acceptably safe for those that use them[160,161].

Prior to April 2013, the number of reports from GPs across Wales had been in decline. In April 2013, Yellow Card reporting was included as a Clinical Effectiveness Prescribing Programme (CEPP) Local Comparator and in April 2014 it became an NPI. In 2023–2024, the number of Yellow Cards submitted by GP practices in Wales decreased by 21% compared with the previous year, to 1,329. This NPI also monitors the number of Yellow Cards submitted by all reporters per health board population. In 2023–2024, the number of Yellow Cards submitted by health boards in Wales decreased compared with the previous year, to 3,540.

In 2023–2024, 566 Yellow Card reports were submitted across Wales from secondary care settings. This represents an 14% increase on the number reported in the previous year although is lower than that reported in 2020–2021 (597). The purpose of this measure is for health boards to compare how their secondary care sites are progressing each quarter, it is not intended to measure performance between health boards due to the varying size and nature of the services provided.

Yellow Cards submitted by patients have been shown to provide greater descriptions of reactions than those from healthcare professionals, and more often noted the effects of ADRs on their lives. Patient reporting of suspected ADRs has the potential to add value to pharmacovigilance by reporting types of drugs and reactions different from those reported by healthcare professionals, therefore generating new potential signals[162]. In 2023–2024, 1,329 Yellow Card reports were submitted across Wales by members of the public. Continued monitoring of the number of Yellow Cards submitted by patients, their carers and/or parents will aim to ensure that reporting continues to increase.

Community pharmacists are required to ask patients about ADRs as part of the essential (batch repeat dispensing) and discharge medicines review [DMR]) elements of the community pharmacy contract[163,164]. As a result, community pharmacists are ideally placed to make a significant contribution to the number of Yellow Cards submitted. In 2023–2024, a total of 73 Yellow Card reports were submitted from community pharmacies across Wales. This NPI will measure the total number of reports submitted from community pharmacies in each health board.

Useful resources

- Health Education and Improvement Wales (HEIW) e-Learning module on the Yellow Card Scheme
- MHRA website
- NHS Education for Scotland e-learning modules on ADRs
- Yellow Card champions are available in each health board to provide training. Contact YCCWales@wales.nhs.uk for more information
- Yellow Card reports can be completed online – Yellow Card website
- The Yellow Card scheme: guidance for healthcare professionals, patients and the public
- YCC Wales website

Download the Yellow Card App:

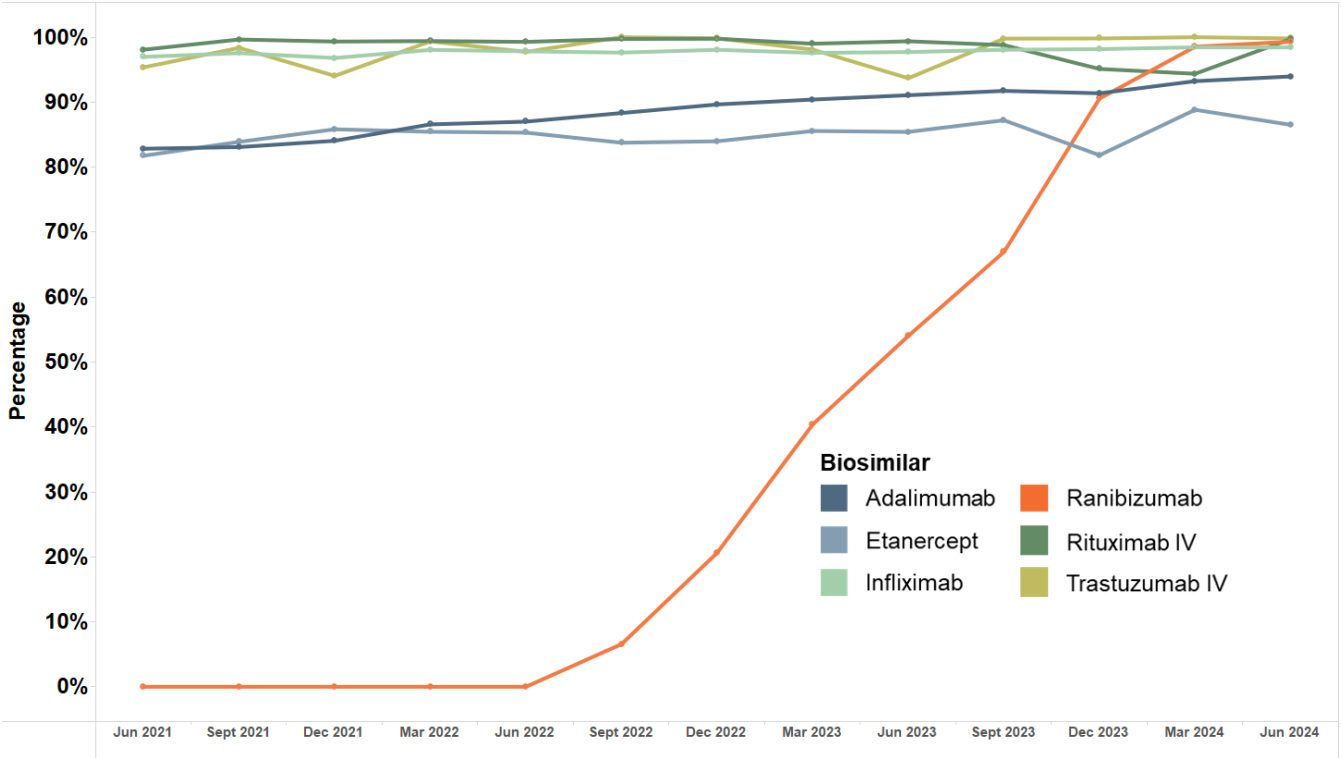
- Android
- Apple

2.2 Efficiencies

2.2.1 Best value biological medicines

Purpose:
To ensure prescribing of best value biological medicines supports cost-efficient prescribing in primary and secondary care in Wales.
Unit of measure:
Quantity of best value biological medicines prescribed as a percentage of total ‘biosimilar’ plus ‘reference’ product.
Target for 2025–2028:
Increase the appropriate use of cost-efficient biological medicines, including biosimilar medicines.

Figure 27. Trend in biosimilar percentage to quarter ending June 2024



Background and evidence

Biological medicines account for a significant expenditure within the NHS. Continuing development of biological medicines, including biosimilar medicines, creates increased choice for patients and clinicians, increased commercial competition and possible enhanced value propositions for individual medicines. This indicator supports the ongoing work within NHS Wales to increase the use of the best value intervention wherever possible within healthcare.

The list of biological medicines being reported on will be determined by the requirements of the service. For 2025–2028 this will be focused on the biological medicines where a

biosimilar version has recently become available however, monitoring of an overall basket of biological medicines will continue.

Within this efficiency indicator, ‘best value’ is primarily derived from cost data as any meaningful outcome data is not retrievable from within the current prescribing systems. Currently, for all of the biological medicines being reported on, the ‘best value’ option is a biosimilar version.

It is the responsibility of the clinician, in consultation with the patient, to make the decision about whether to prescribe a biological medicine and whether that should be the original reference medicine or a biosimilar medicine. Switching between a reference product and its biosimilar (and indeed amongst biosimilar medicines) should be managed at the discretion of the individual prescriber in partnership with the patient, and with appropriate monitoring in place. The NHS England publication *What is a biosimilar medicine?* provides supportive information for the use of biosimilar medicines[165].

Where AWMSG or NICE has already recommended the reference biological medicine, the same guidance will normally apply to any biosimilars[166,167]. However, where a review of the evidence for a biosimilar medicine is considered necessary, NICE will consider producing a further evidence summary[166].

Useful resources

- AWMSG (2023) Maximising the opportunity presented by biosimilar medicines – A national strategy for Wales
- AWTTC (2024) SPIRA – Biosimilar Efficiencies (NHS network connection required)
- NHS England (2023) What is a biosimilar medicine?
- SPS (2023) Understanding biological and biosimilar medicines
- NICE Position statement for biosimilar medicines
- MHRA (2014) Drug safety update. Biosimilar products

2.2.2 Low value for prescribing

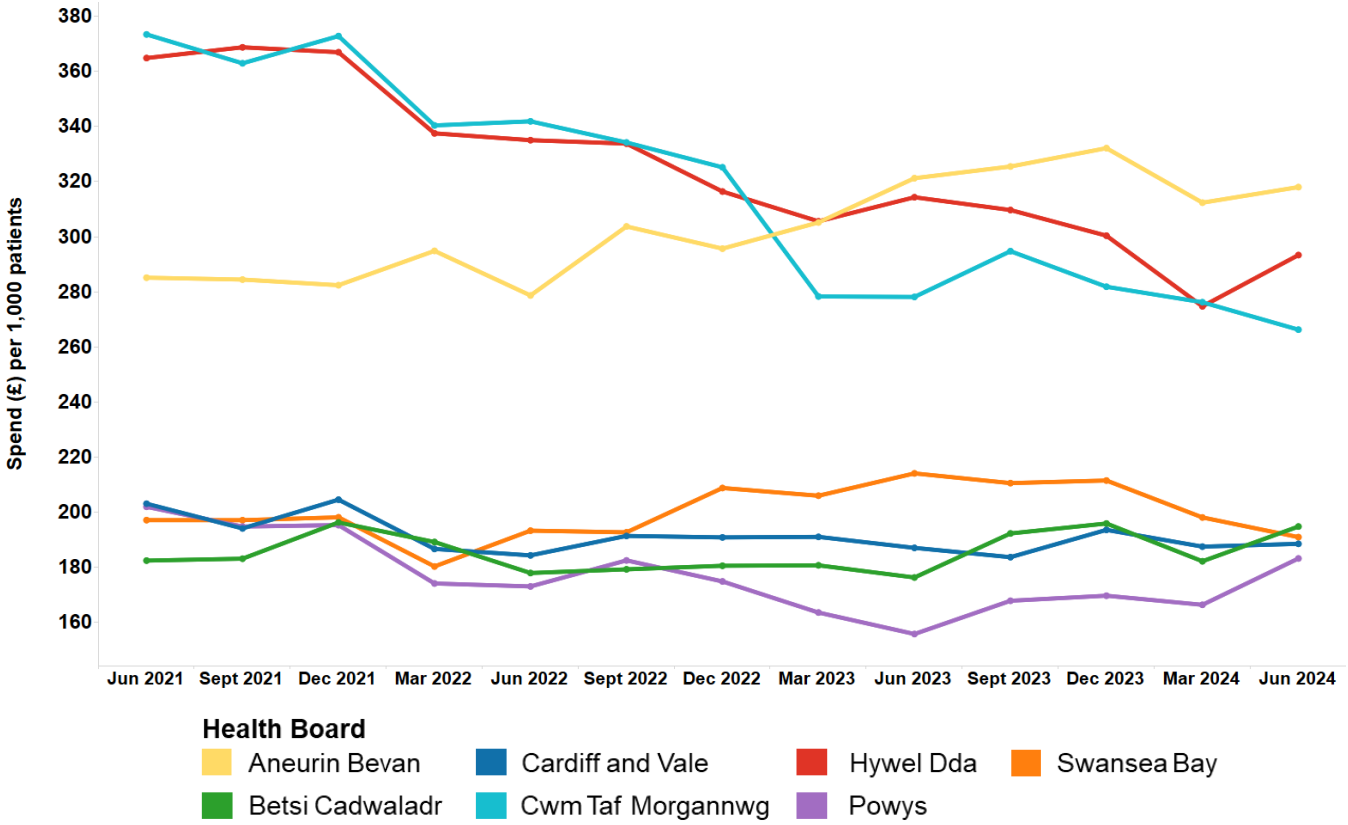
Purpose:
To drive a reduction in the prescribing of items considered as not suitable for routine prescribing in Wales.
Unit of measure:
Low value for prescribing UDG spend per 1,000 patients.
Target for 2025–2028:
Maintain performance levels within the lower quartile or show a reduction towards the quartile below.

The aim of the *Low Value for Prescribing in NHS Wales* initiative is to minimise the prescribing of items that offer a limited clinical benefit to patients and where more cost-effective treatments may be available. The first paper in the initiative, entitled *Medicines Identified as Low Priority for Funding in NHS Wales* was endorsed by AWMSG in 2017, and the second paper was endorsed in 2018[168,169]. Five items/item groups were identified for the purposes of the first phase of this initiative, with an additional four included in the second phase. The paper detailing the items included in the third phase of this initiative was endorsed and published in February 2020. These items were not considered within the 2022–2025 NPIs however some are included within the 2025–2028 NPIs namely: chloral hydrate, rubefacients and alimemazine.

Within 2023–2024 there has been a decrease achieved in the overall spend on the items/item groups included in phases 1 and 2 of the low value for prescribing initiative of £55,440. Although this cannot be taken as a direct overall saving to the NHS in Wales it does confirm a continuing decreased spend on the items identified as not suitable for routine prescribing.

Figure 28 illustrates the differences in spend between December 2020 and December 2023 for the nine items/item groups within phases 1 and 2 of the low value for prescribing initiative by health board.

Figure 28. Trend in low value for prescribing UDG spend per 1,000 patients to quarter ending June 2024



Useful resources

- AWMSG (2017) Medicines Identified as Low Priority for Funding in NHS Wales – paper 1
- AWMSG (2018) Medicines Identified as Low Priority for Funding in NHS Wales – paper 2
- AWMSG (2020) Items Identified as Low Value for Prescribing in NHS Wales – paper 3
- AWTTC (2024) SPIRA - Low Value for Prescribing Dashboard (NHS network connection required).

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Appendix 1. Examples of 2DRx NPIs

Prescribing Safety Indicators

- Number of patients prescribed a daily oral morphine equivalence of 120 mg or greater
- Number of patients prescribed multiple opioids:
  - Combination of opioids stratified to age group, deprivation quintile group
  - Combinations of opioids and gabapentinioids/benzodiazepines
- Number of patients over 65 prescribed medication with an anticholinergic effect on cognition score of 3 or greater
  - Breakdown by scores of 3 or more, 6 or more, 9 or more, 12 or more
- Number of patients prescribed sodium valproate in females aged 14-55 years
  - Also prescribed oral contraceptive

Respiratory

- Number of patients prescribed 3 or more Short-Acting Beta-Agonists (SABAs) in 12 months
- Number of patients on any inhaler with > 2 prescriptions for prednisolone in last 12 months
- Number of patients on SABA monotherapy
- Number of patients prescribed rescue packs: number of incidences in a period e.g. courses of steroids and antibiotics

Antimicrobial stewardship:

- Age banded data for 4Cs antimicrobials: co-amoxiclav, cephalosporins, fluoroquinolones and clindamycin
- Number of Care home patients prescribed X antibiotics in 12-month period

Antipsychotics

- The length of time over which a patient had been prescribed an antipsychotic.
- Care home patients: duration of prescribed antipsychotics e.g. for a period of three months or longer.

Diabetes

- Number of patients prescribed blood glucose testing strips with any non-insulin blood glucose lowering therapy and not prescribed insulin.
- Number of patients prescribed blood glucose testing strips with metformin but not insulin.

Appendix 2. Oral Morphine Equivalence (OME)

BNF Chemical Substance Name	Relative potency to oral morphine*†	References
Buprenorphine sublingual tablet	60	PCG
Buprenorphine transdermal patch	100	PCG
Butorphanol nasal spray	7	PME
Co-codamol (codeine phos/paracetamol) oral	0.1	PCG
Codeine phosphate oral	0.1	PCG
Co-dydramol oral	0.1	PCG
Dextromoramide tartrate	4	OPN
Dextropropoxyphene	0.1	OPN
Diamorphine hydrochloride oral	1	OPN
Dihydrocodeine tartrate oral	0.1	PCG
Dipipanone hydrochloride oral	0.5	CHF
Fentanyl oromucosal lozenge	130	PME
Fentanyl transdermal patch	100	BNF
Fentanyl oromucosal tablet	130	PME
Fentanyl intra-nasal spray	160	PME
Fentanyl oromucosal film	180	PME
Hydromorphone hydrochloride oral	5	BNF
Levorphanol tartrate oral	11	PME
Meptazinol hydrochloride oral	0.04	CHF
Methadone hydrochloride oral	4	CHF
Morphine hydrochloride oral	1	OPN
Morphine hydrochloride suppository	1	PCG
Morphine sulfate oral	1	PCG
Oxycodone hydrochloride oral	1.5	BNF
Papaveretum	1	OPN
Pentazocine hydrochloride oral	0.37	OPN
Pentazocine lactate	0.37	OPN
Pethidine hydrochloride oral	0.125	CHF
Phenazocine hydrobromide	4	OPN
Tapentadol hydrochloride oral	0.4	FPM
Tramadol hydrochloride oral	0.1	PCG
BNF: British National Formulary; CHF: Cheshire Formulary; FPM: Faculty of Pain Medicine of the Royal College of Anaesthetists; PME: Pain Management Education at UCSF; OPN: Open Prescribing; PCG: Palliative Care Guidelines (traditional)		

*Relative potency to oral morphine values have been discussed at Welsh Pharmacy Pain Group. This was set up by Emma Davies and Simon Gill and is an Analgesic Interest Network (PAIN in Wales) for NHS Wales Pharmacists and Pharmacy Technicians.

† There is no universal agreement, or national or internationally recognised consensus, for these values as there is no mechanism by which they can be determined. Values are based on national and international opinion and have been taken from what are believed to be the most robust sources, with an emphasis on UK sources reflective of UK practice where available.

Appendix 3. Anticholinergic effect on cognition (AEC) score[140]

Drugs with AEC score of 0		Drugs with AEC score of 1	Drugs with AEC score of 2	Drugs with AEC score of 3
Alprazolam	Lorazepam	Amiodarone	Amantadine	Alimemazine (trimeprazine)
Amlodipine	Losartan	Aripiprazole	Chlorphenamine	Amitriptyline
Amoxicillin	Lovastatin	Bromocriptine	Desipramine	Atropine
Aspirin	Lurasidone	Carbamazepine	Dicycloverine (dicyclomine)	Benztropine
Atenolol	Meloxicam	Citalopram	Dimenhydrinate	Chlorpromazine
Atorvastatin	Metoclopramide	Diazepam	Diphenhydramine	Clemastine
Bupropion	Metopralol	Domperidone	Disopyramide	Clomipramine
Cephalexin	Moclobemide	Fentanyl	Levomepromazine	Clozapine
Cetirizine	Morphine	Fluoxetine	Olanzapine	Cyproheptadine
Chlordiazepoxide	Naproxen	Fluphenazine	Paroxetine	Dothiepin (dosulepin)
Cimetidine	Omeprazole	Hydroxyzine	Pethidine	Doxepin
Ciprofloxacin	Paracetamol	Iloperidone	Pimozide	Hyoscine hydrobromide
Clopidogrel	Pantoprazole	Lithium	Prochlorperazine	Imipramine
Darifenacin	Pravastatin	Mirtazepine	Promazine	Lofepramine
Diclofenac	Propranolol	Perphenazine	Propantheline	Nortriptyline
Diltiazem	Rabeprazole	Prednisolone	Quetiapine	Orphenadrine
Enalapril	Ranitidine	Quinidine	Tolterodine	Oxybutynin
Entacapone	Risperidone	Sertindole	Trifluoperazine	Procyclidine
Fexofenadine	Rosiglitazone	Sertraline		Promethazine
Fluvoxamine	Simvastatin	Solifenacin		Trihexyphenidryl (benzhexol)
Furosemide	Theophylline	Temazepam		Trimipramine
Gabapentin	Thyroxine (levothyroxine)			
Gliclazide	Tramadol			
Haloperidol	Trazodone			
Ibuprofen	Trimethoprim			
Ketorolac	Trospium			
Lamotrigine	Venlafaxine			
Levadopa	Valproate			
Lisinopril	Warfarin			
Loperamide	Ziprasidone			
Loratadine	Zolpidem			

Score 3	Review and withdraw or switch
Score 2	Review and withdraw or switch
Score 1	Caution required
Score 0	Safe to use