PrescQIPP Community Interest Company

System recovery post COVID-19

This bulletin focuses on areas of prescribing and particular medicines which have seen a significant increase in prescribing as a result of the COVID-19 pandemic. It includes recommendations and offers guidance on how to review and manage the increase in prescribing in these therapeutic areas and the system post pandemic.

Recommendations

Broad-spectrum antibiotics

- Review prescribing of co-amoxiclav, cephalosporins and quinolones to ascertain if prescribing is in-line with local and national antibiotic guidelines. Provide feedback to PCNs, practices and individual prescribers as appropriate and agree a change in practice or process.
- Develop an Antimicrobial Stewardship programme to promote and support antimicrobial use to prescribers and patients using resources available in the PrescQIPP Antimicrobial Stewardship hub and the TARGET antibiotic toolkit.
- Manage patient expectations around the prescribing of antibiotics by encouraging the use of Self Care Forum fact sheets, posters and videos for patient waiting areas.
- Promote the use of delayed antibiotic prescribing and encourage the use of the TARGET treating your infection patient information leaflets during consultations to increase the patient's confidence to self-care.

Direct Oral Anticoagulants (DOACs)

Patients newly initiated on DOACs or switched to a DOAC since March 2020 should be reviewed to assess:

- If a DOAC is still appropriate, for example:
  - » can the DOAC be stopped in patients with prior deep vein thrombosis or pulmonary embolism for whom the risk of recurrence is now considered low?
  - » patients switched from warfarin to a DOAC that should not have been considered for a switch (see list in DOAC section).
- To ensure the patient's DOAC dose is in-line with the licensed dose for the indication.
- To ensure the appropriate DOAC monitoring is in place.
  - » Annual review of renal profile if creatinine clearance (CrCl) above 60ml/min with full blood count (FBC) and liver function tests (LFTs).
  - » Renal profile six-monthly if aged over 75 years and/or frail.
  - » If CrCl is below 60ml/min, divide the value by 10 for testing frequency, e.g. if CrCl is 20ml/min, increase frequency to every two months.
- To ensure warfarin has been stopped if the patient was switched to a DOAC.

Recommendations

Oral Nutritional Supplements (ONS)

- ONS are only available on an NHS prescription if the specific criteria from the Advisory Committee on Borderline Substances (ACBS) are met. Patients who do not meet any of the relevant ACBS criteria should be advised to purchase ONS over the counter or prepare homemade nourishing foods and drinks. Products not listed as ACBS should not be prescribed.
- COVID-19 is not listed as an ACBS criteria, but disease-related malnutrition is included. Therefore, patients suffering or recovering from COVID-19 should only be prescribed an ONS if they have a MUST score of more than two and also meet the ACBS criteria for prescribing. Review patients not meeting these criteria.
- Where possible, if ONS is still indicated, switch suitable patients to a more cost-effective alternative ONS in-line with local formularies/guidance.

Vitamin B12 – oral cyanocobalamin

- Review patients with diet-related vitamin B12 deficiency:
  - » Give dietary advice about foods that are a good source of vitamin B12 or taking an over the counter supplement where appropriate.
  - » Patients suspected of having, or likely to have, diet-related vitamin B12 deficiency should be advised to purchase vitamin B12 supplements over-the-counter.
  - » If the patient has symptoms despite taking oral B12 supplements, reassess serum B12 levels.
  - » If patients do not have adequate levels, commence intramuscular (IM) hydroxocobalamin twice-yearly.
  - » Continued need for prescribing should be reviewed on a regular basis e.g. at annual review.
- Review patients with non-diet-related vitamin B12 deficiency prescribed oral cyanocobalamin 1mg tablets:
  - » Recommence patients on IM hydroxocobalamin given at intervals of up to two to three months.
  - » If administration of IM hydroxocobalamin is not tolerated, or not possible, ensure the licensed oral cyanocobalamin1mg tablet (Orobalin®) is prescribed.

Background

At the start of the COVID-19 pandemic NHS England and NHS Improvement wrote a series of letters to general practice regarding the emerging COVID-19 situation.[1,2] The NHS declared a level 4 National Incident on 30th January 2020. By March 2020 the outbreak intensified and evidence from other countries and the advice from the Scientific Advisory Group for Emergencies (SAGE) and the Chief Medical Officer was that at the peak of the outbreak, the NHS would come under intense pressure.[2]

The letters contained important actions for every part of the NHS to put in place the following measures, including:[2]

- Free-up the maximum possible inpatient and critical care capacity.
- Prepare for, and respond to, the anticipated large numbers of COVID-19 patients who will need respiratory support.
- Support staff, and maximise their availability.

Advice relating to primary care included, considering how staff who were at higher risk of severe illness from COVID-19 could work from home and continue to contribute remotely. How clinical staff could support older and vulnerable people who were shielding at home by rolling out remote consultations using video, telephone, email and text message services. Face-to-face appointments were only to take place when absolutely necessary.[2] Patients were strongly encouraged to use online services for repeat prescription ordering and practices must use the Electronic Prescription Service (EPS). Practices should move patients to electronic repeat dispensing unless there was a clinical reason not to do so. There should be no move to increase the duration of prescriptions.[1]

The Royal College of General Practitioners (RCGP) and the British Medical Association (BMA) developed guidance for clinicians working in general practice in the UK. This considered which work was essential to maintain public health and which work was unlikely to cause harm if delayed for a short number of months. The guidance recognised that general practice had a huge role to play in maintaining the underlying health of the population. Experience had shown that patients would die from non-COVID-19 related illnesses in addition to COVID-19 itself if all the health care resources were diverted towards treating it. The guidance is not an exhaustive list of general practice workload and it did not intend to replace clinical judgement for individual patient cases. It stratified the workload to ensure that those at greatest need are prioritised. To do this they colour coded workload as red, amber and green:[3]

- Green category
  - Aim to continue regardless of the prevalence of COVID-19 for the duration of the pandemic.
- Amber category
  - Continue if time/resources allow and appropriate for your patient population regardless of the prevalence of COVID-19 for the duration of the pandemic.
- Red category
  - Lower priority routine work which could be postponed in the event of a high prevalence of COVID-19 in your patient population, aiming to revisit once the pandemic ends, ensuring recall dates are updated where possible.

As the NHS slowly starts to recover post pandemic, practices are advised to review areas of prescribing that have increased significantly during the pandemic. This is to ensure there is quality prescribing which is safe and cost effective. These areas include, but are not limited to, oral cyanocobalamin, DOACs, broad-spectrum antibiotics and ONS.

Broad-spectrum antibiotics

Antibiotics have saved millions of lives, but with no new classes of antibiotics discovered since the 1980s, and the increased and inappropriate use of the drugs, means we are heading rapidly towards a world where antibiotics no longer work. Antimicrobial resistance (AMR) is a global problem that impacts all countries and all people, regardless of their wealth or status. The scale of the AMR threat, and the need to contain and control it, is widely acknowledged.[4]

The Department of Health and Social Care has set out a five year national action plan for the UK from 2019–2024 to tackle AMR. The plan has been designed to ensure progress towards the 20-year vision on AMR, in which resistance is effectively contained and controlled. It focuses on three key ways of tackling AMR:[4]

- Reducing need for, and unintentional exposure to, antimicrobials.
- Optimising use of antimicrobials.
- Investing in innovation, supply and access.

Broad-spectrum antibiotics are drugs effective against a wide range of bacteria. Their use needs to be limited to resistant infections because they tend to increase the risk of resistance in other bacteria.[4]

Compared with narrow-spectrum antibiotics, broad-spectrum antibiotics are more likely to significantly change the gut flora, potentially allowing other bacteria, such as Clostridioides difficile (C. difficile) to become established.[5] Inappropriate prescribing is defined by the Department of Health and Social Care as:[4]

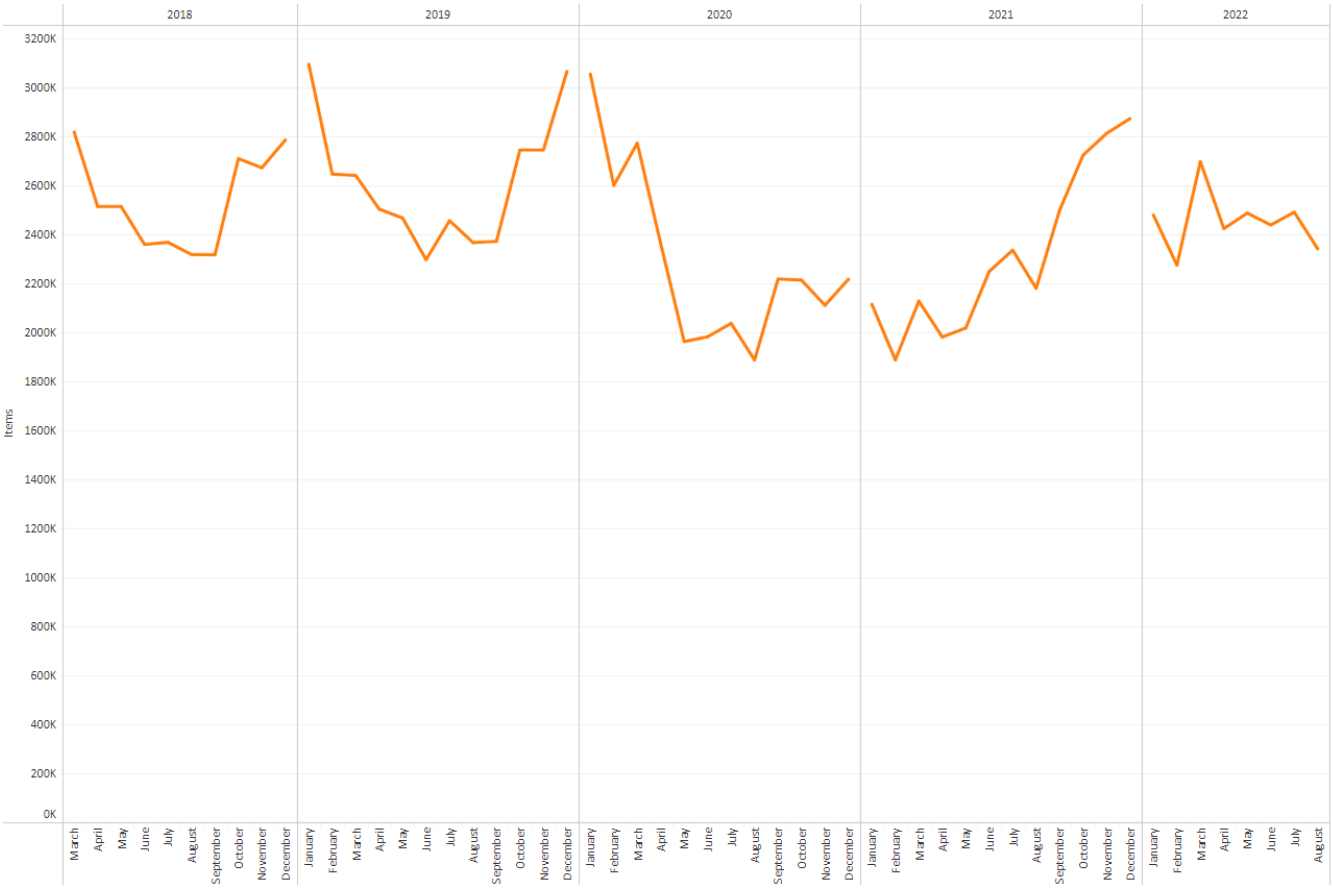
- Prescribing an antibiotic for a patient in the absence of (documented) evidence of bacterial infection.
- Prescribing a critical broad-spectrum antibiotic (piperacillin-tazobactam or carbapenems in secondary care; co-amoxiclav, cephalosporins and quinolones in primary care) to patients in the absence of a (documented) rationale.
- Continuing an antibiotic prescription beyond the course length recommended in local or national guidelines, in the absence of a (documented) rationale.

The PrescQIPP AMS visual analytics to support NHS antimicrobial stewardship activity during COVID-19 pandemic allows primary care clinicians in England to monitor antibiotic prescribing trends. The data can alert clinicians to where further investigation of antibiotic use may be required to optimise safe and effective management of suspected infection. A webinar and presentation slides explaining the data and making the best use of it locally are available to view. The webinar suggests some actions to support antimicrobial stewardship and recovery post COVID:

- In suspected UTI ensure a urine sample is sent for culture before prescribing antibiotics. This may not have been possible during the COVID pandemic where face to face consultations were restricted but should now be re-introduced into the pathway for system recovery.
- The TARGET Treating Your Infection – Respiratory Tract Infection (TYI-RTI) advises patients to seek symptom relief advice from their local community pharmacist.
- Doxycycline should not be used to treat COVID-19 in the community https://www.nice.org.uk/guidance/ng191

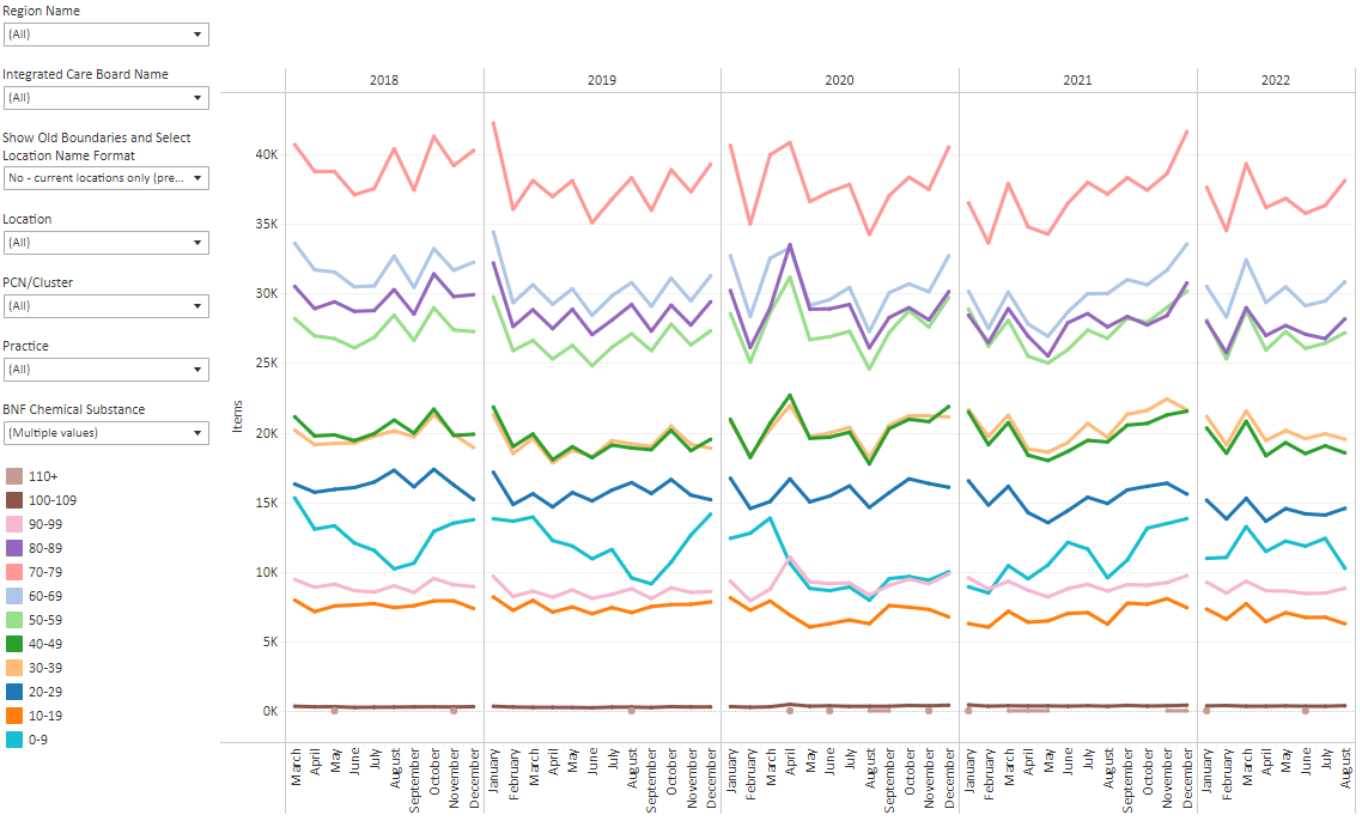
Graph 1 below from the PrescQIPP AMS Visual Analytics to support NHS antimicrobial stewardship activity during COVID-19 pandemic demonstrates a spike in the number of all antibiotics items in March 2020 at the beginning of the COVID-19 pandemic compared with March 2019. After this spike, levels reduced rapidly to lower-than-normal summer levels during the first lockdown, with levels starting to rise again as lockdown eased over the summer and schools returned in September.[6]

Graph 1: Number of antibiotic items prescribed by month in England[6]



Graph 2 shows a similar pattern to the all antibiotic items prescribed data, as broad spectrum antibiotics peaked across the majority of age ranges in April 2020 and then reduced to below seasonal levels.

Graph 2: Number of dispensed prescribed broad spectrum antibiotic items for England by month by 10yrs age band[6]



In England, Scotland and Wales there were 7.6 million co-amoxiclav, cephalosporins and quinolones items prescribed March to May 2020 compared to 8.5 million items June to August 2022 (NHSBSA and Public Health Scotland).

This increase in the prescribing of broad-spectrum antibiotics could be due to a number of factors, including the shielding programme and reduced face to face GP appointments. It could also be due to increased rates of other infections post COVID. A systematic review, primarily of the National Center for Biotechnology Information (NCBI) database, identified relevant literature for the period between November 1, 2019 and December 19, 2020 to evaluate antibiotic prescribing during the COVID-19 pandemic.[7] Of 28,093 patients included in the combined studies, 58.7% received antibiotics (16,490/28,093). Antibiotics coverage was less in children (57%) than in adults with comorbidities (75%). Broad-spectrum antibiotics were prescribed presumptively without pathogen identification.[7]

Use resources available in the PrescQIPP Antimicrobial Stewardship webkit and the TARGET antibiotic toolkit to promote and support antimicrobial stewardship to prescribers and patients. Resources include leaflets for patients, videos for waiting areas, prescribing data, visual analytics, audits, a self-assessment checklist to measure antibiotic prescribing practice against others and information on Antibiotic Guardians and European Antibiotic Awareness Day.

Review prescribing of co-amoxiclav, cephalosporins and quinolones to ascertain if prescribing is in-line with national and local antibiotic guidelines. Provide feedback to PCNs, practices and individual prescribers and agree a change in practice or process. An audit to assess if high risk broad-spectrum antibiotic (e.g. co-amoxiclav, quinolones, cephalosporins and clindamycin) prescribing is in-line with local antibiotic guidelines is available as a supporting resource with PrescQIPP Bulletin 177: Antimicrobial stewardship.

Another area of antimicrobial prescribing that may require reviewing post COVID-19 is the prescribing of antibiotics that patients keep at home, known as 'rescue packs' as part of their exacerbation of COPD action plan.

DOACs

In England, Scotland and Wales March to May 2020 there were 3.7 million DOAC items prescribed compared to 4.5 million items June to August 2022 (NHSBSA and Public Health Scotland).

At the start of the COVID-19 pandemic NHS England published a guideline on the management of anticoagulation services to ensure that patients prescribed anticoagulants were kept as safe as possible and that anticoagulant care continued with minimum burden on the NHS.[8] The guideline contained recommendations for i) patients already prescribed DOACs, ii) patients requiring the initiation of an oral anticoagulant and iii) patients prescribed warfarin.

For patients already receiving DOACs the guideline recommended that appropriate primary care-based monitoring should be in place. It advised that telephone triage, instead of face-to-face consultations, should be in place to support patients, for example for those experiencing bleeding symptoms in primary care.[8] Monitoring renal function is important to avoid overdose and/or toxicity as DOACs are renally excreted:

- At least annual review of renal profile if CrCl above 60ml/min with FBC and LFTs.[8,9]
  - » Renal profile six monthly if aged over 75 years and/or frail.
  - » If CrCl is below 60ml/min, divide the value by 10 for testing frequency, e.g. if CrCl is 20ml/min, increase frequency to every two months.
- Check for side effects/bleeding issues and patient adherence at each routine appointment.[8,9]

Patients that required the initiation of an oral anticoagulation during COVID-19 should where possible have had a DOAC initiated, instead of warfarin to minimise the monitoring burden and the need for regular INR (International Normalised Ratio) monitoring.[8] NICE guidance recommends offering

anticoagulation with a DOAC to people with atrial fibrillation (AF) and a CHA_2DS_2-VASc score of 2 or above, or men with AF and a CHA_2DS_2-VASc score of 1 or above taking into account the risk of bleeding.[10] NICE recommends that prescribing apixaban, dabigatran, edoxaban and rivaroxaban are all options, but NHS England's commissioning recommendations for national procurement for DOACs recommends clinicians should use edoxaban where this is clinically appropriate.[10,11] If edoxaban is contraindicated or not clinically appropriate for the specific patient then, subject to the criteria specified in the relevant NICE technology appraisal guidance, clinicians should then consider rivaroxaban first, then apixaban or dabigatran.[11]

Anticoagulation services should consider if patients on warfarin can be switched to a DOAC. DOACs require blood tests to assess renal function throughout treatment, the monitoring is less rigorous than INR testing with warfarin and routinely carried out in primary care. Patients should only be switched from warfarin to a DOAC by clinicians in primary or secondary care with experience in managing anticoagulation. A switch from warfarin to a DOAC should not be considered for patients:[8]

- With a prosthetic mechanical valve.
- With moderate-to-severe mitral stenosis.
- With antiphospholipid antibodies.
- Who are pregnant, breastfeeding or planning a pregnancy.
- Requiring a higher than standard INR range of 2.0–3.0.
- With severe renal impairment (CrCl less than 15ml/min).
- With active malignancy/chemotherapy (unless advised by a specialist).
- Prescribed some HIV antiretrovirals and hepatitis antivirals.
- On phenytoin, carbamazepine, phenobarbitone or rifampicin; these patients are likely to have low DOAC levels so should be discussed with an anticoagulation specialist.
- There is little data on DOACs for patients with venous thrombosis at unusual sites and they should be discussed with an anticoagulation specialist.
- On triple therapy (dual antiplatelet plus warfarin); switching these patients should be discussed with an anticoagulation specialist or cardiologist.

The British Society for Haematology guidance – INR testing for out-patients on warfarin during COVID-19 restrictions, also recommends assessing patients on warfarin for a switch to a DOAC.[12]

The Medicines and Healthcare products Regulatory Agency (MHRA) published guidance on monitoring of patients on warfarin and other anticoagulants during the COVID-19 pandemic. This guidance highlighted to healthcare professionals that DOACs including apixaban (Eliquis), edoxaban (Lixiana), dabigatran (Pradaxa) or rivaroxaban (Xarelto) interact with several medicines. This includes interactions between oral anticoagulants (i.e. vitamin K antagonists (VKA) or DOACs) and certain antibiotics and antivirals which may be used to treat patients with COVID-19.[13,14] The BNF and the individual Summary of Product Characteristics (SPC) should be checked for more information about drug interactions.

The MHRA advised that they were aware of a small number of patients in whom warfarin treatment was continued in error after starting treatment with DOACs. They advised that to reduce the risk of over-anticoagulation and bleeding, healthcare professionals should ensure that warfarin treatment is stopped before DOACs are started.[13]

Patients newly initiated or switched to a DOAC should be prescribed a dosage regime in-line with the therapeutic indication, patient age, actual bodyweight, renal function (calculated through CrCl), drug interactions and patient preference/lifestyle.[8] Table 1 has guidance on DOAC prescribing for non-valvular AF and DVT/PE. Ensure that the indication for the DOAC is accurately coded on the clinical system in addition to the indication and duration of treatment for the DOAC.

The PrescQIPP bulletin 282: Anticoagulation supports DOAC initiation, review and switching with accompanying attachments including: an AF prescriber decision aid, patient information and AF decision aid, patient DOAC leaflets, table of anticoagulant comparisons, venous thromboembolism (VTE) flow chart, edoxaban commissioning position statement, VKA information and a presentation based on the resources.

The PrescQIPP Bulletin 288: Medicines safety includes an audit tool (attachment 13) to assess if DOACs for the prophylaxis of stroke and systemic embolism in patients with non-valvular atrial fibrillation are prescribed and monitored appropriately (e.g. monitoring is up to date and dosing is correct and in-line with product licences).

Table 1: Guidance on DOAC prescribing for non-valvular AF and DVT/PE[8]

DOAC	Apixaban	Edoxaban	Rivaroxaban	Dabigatran
Baseline checks	Renal function (CrCl) – serum creatinine (Cr) and bodyweight, full blood count (FBC), liver function tests (LFTs). Use results from last three months if stable. If for AF: CHA_2DS_2-VASc and HASBLED scores.			
Dosing in non-valvular AF (lifelong unless risk:benefit of anticoagulation therapy changes)	Prescribe apixaban 5mg twice daily. Reduce dose to 2.5mg twice daily if at least 2 of the following characteristics: age 80 years or older, body weight 60 kg or less, or serum creatinine 133 micromol/l or more, or if exclusive criteria of CrCl 15 to 29 ml/min.	Prescribe edoxaban 60mg once daily. Reduce dose to 30mg once daily if: body weight under 61kg, or CrCl under 50ml/min, or co-prescribed with ciclosporin, dronedarone, erythromycin or ketoconazole.	Prescribe rivaroxaban 20mg once daily. Reduce dose to 15mg once daily if CrCl under 50ml/min in NVAF patients only.	Prescribe dabigatran 150mg twice daily if aged under 75 years, CrCl over 50ml/min, low risk of bleeding (weight under 50kg with close clinical surveillance). Reduce dose to 110mg twice daily if aged over 80 years or prescribed verapamil. Consider 110mg twice daily based on individual assessment of thrombotic risk and the risk of bleeding in patients aged between 75 and 80 years or with CrCl under 50ml/min or with increased risk of bleeding (including gastritis, oesophagitis, gastro-oesophageal reflux).
Dosing in patients with DVT / PE (loading doses are not required if patient has been stabilised on warfarin)	Dose is 5mg twice daily (use with caution if CrCl under 30ml/min). Check intended duration of therapy. For long term prevention of recurrence 2.5mg twice daily (after six months' treatment dose).	Dosing as above. Check intended duration of therapy.	Dose is 20mg daily (consider 15mg dose if CrCl under 50ml/min and bleeding risk outweighs VTE risk). Check intended duration of therapy. For long term prevention of recurrence 10mg daily could be considered.	Dosing as above. Check intended duration of therapy.

DOAC	Apixaban	Edoxaban	Rivaroxaban	Dabigatran
Duration of therapy for DVT/PE	For a provoked DVT/PE: 3 months treatment if provoking factors have been addressed. For unprovoked DVT/PE or recurrent DVT/PE: At least six months treatment dose followed by prophylaxis dosing as indicated/ advised.			
Contraindications	CrCl <15ml/min.	CrCl <15ml/min.	CrCl <15ml/min.	CrCl <30ml/min.
Cautions See also individual SPCSs		CrCl above 95ml/min.	CrCl under 30ml/min. Take with or after food (15mg and 20mg doses).	Do not use in a standard medication compliance aid (MCA).
Interactions Check BNF and SPC	Ketoconazole, itraconazole, voriconazole, posaconazole, ritonavir – not recommended (see SPC for full details) Rifampicin, phenytoin, carbamazepine, phenobarbital, St. John's wort – use with caution. Do not use apixaban with patients on strong enzyme inducers for acute VTE treatment.	Rifampicin, phenytoin, carbamazepine, phenobarbital or St. John's wort – use with caution. Ciclosporin, dronedarone, erythromycin, ketoconazole – reduce dose as above. (See BNF and SPC for edoxaban for further information.)	Ketoconazole, itraconazole, voriconazole, posaconazole, ritonavir, dronedarone – not recommended (see SPC for full details) Rifampicin, phenytoin, carbamazepine, phenobarbital, St. John's wort – should be avoided	Ketoconazole, ciclosporin, itraconazole, tacrolimus, dronedarone – contraindicated (See SPC for full details). Rifampicin, St John's wort, carbamazepine, phenytoin –should be avoided. Amiodarone, quinidine, ticagrelor, posaconazole – use with caution. Verapamil (use reduced dose). Antidepressants: SSRIs and SNRIs – increased bleeding risk.

ONS

NICE guidance defines malnutrition as a state in which a deficiency of nutrients such as energy, protein, vitamins and minerals causes measurable adverse effects on body composition, function or clinical outcome. Malnutrition is both a cause and a consequence of ill health. It is common and increases a patient's vulnerability to disease. One of the methods to improve or maintain nutritional intake is oral nutrition support – for example, fortified food, additional snacks and/or sip feeds also known as ONS.[15] NICE guidance suggests that the Malnutrition Universal Screening Tool (MUST) may be used to screen for malnutrition.[15] The Patients Association Nutrition Checklist was developed to address a gap that existed for self-screening tools that were simple and easy to use. The checklist helps patients and staff working in health and social care to identify the potential risk of undernutrition in adults, aiming to encourage conversations and raise awareness of the potential for undernutrition. The Patients Association Nutrition Checklist has been validated against MUST and may help to identify clinical concern.[16]

ONS should be prescribed in-line with local guidance, or in the absence of any local guidance, ONS may be suitable for the following patients:

- MUST score of two or more – high risk, treatment indicated.[17]
- Patient meets relevant ACBS criteria to be eligible for an NHS prescription for ONS products.[18]
- Dietary advice and food fortification have been followed appropriately and adequately for at least four weeks and there has been no progress towards the goal set.[19]

Different approved ACBS conditions may apply to different products. Requirements should be checked for a particular ONS product(s) prescribed to ensure the patient is eligible to receive them on an NHS prescription.[18] Patients who do not meet ACBS prescribing criteria should be offered advice on how to prepare homemade nourishing foods and drinks and purchase nutritional supplements over the counter if they wish to do so. COVID-19 is not listed as an ACBS criteria, but disease-related malnutrition is included. Therefore, patients suffering or recovering from COVID-19 should only be prescribed an ONS if they have a MUST score of more than two and also meet the ACBS criteria, such as disease-related malnutrition.

A 'food first' approach, rather than ONS, should be tried first for patients with a 'MUST' score of one, with regular review prior to prescribing ONS on the NHS.[19] 'Food first' involves dietary advice, eating additional snacks and fortifying foods – by adding extra energy, protein and other nutrients to them.[20]

In England, Scotland and Wales between March to May 2020 there were 944,000 items of ONS prescribed in primary care compared to 1.1 million items June to August 2022 (NHSBSA and Public Health Scotland). Prescribing of ONS has increased during the COVID-19 pandemic despite COVID-19 not being listed as an ACBS criteria. There may be many reasons for this increase in prescribing, such as a lack of access to NHS services, deteriorating comorbidities and as a direct result of COVID-19. Patients prescribed ONS should be reviewed and screened using the MUST tool or The Patients Association Nutrition Checklist to assess if there is a clinical need to continue prescribing or discontinue treatment when it is no longer indicated. If continued prescribing is clinically indicated, patients should switched, if appropriate to a more cost-effective alternative ONS in-line with local formularies/ guidance.

PrescQIPP Bulletin 261: Oral Nutritional Supplements and supporting resources cover the prescribing of ONS and provides useful advice on initiating treatment, monitoring progress and prescribing in malnutrition associated with special conditions, such as palliative care or drug misuse. It includes advice on self-care, reducing inappropriate prescribing and waste. Supporting resources include an audit to ensure that NHS prescribing is in-line with current guidance in terms of choice, review, duration of supply and eligibility.

Vitamin B12 – oral cyanocobalamin

Hydroxocobalamin and cyanocobalamin are both manufactured versions of vitamin B12.[21,22]

The body requires vitamin B12 to make red blood cells and is obtained from food or supplements.[22] Vitamin B12 deficiency can be diet-related (e.g. malnutrition, vegan diet) or non-diet-related (e.g. pernicious anaemia, inflammatory bowel disease, gastrectomy, drug related). The most common cause of severe non-diet-related vitamin B12 deficiency in the UK is pernicious anaemia, an autoimmune disorder causing reduced production of intrinsic factor (IF) in the stomach; IF is essential for absorption of dietary vitamin B12. Prescribers should consider the cause of their patient's vitamin B12 deficiency before deciding on the appropriate dose of oral cyanocobalamin.[23,24]

Diet-related vitamin 12 deficiency (e.g. malnutrition, vegan diet)

Patients with diet-related deficiency require much lower doses of cyanocobalamin (50-150micrograms daily).[23] In vegans, treatment may need to be life-long, whereas in other people with dietary deficiency replacement treatment can be stopped if they have received vitamin B12 supplementation for up to a year and their diet has improved.[23,24] Dietary advice about foods that are a good source of vitamin B12 should be given. Good sources of vitamin B12 include:[24]

- Eggs
- Foods which have been fortified with vitamin B12 (for example some soy products, and some breakfast cereals and breads) are good alternative sources to meat, eggs, and dairy products
- Meat
- Milk and other dairy products
- Salmon and cod.

Recommendations for prescribing cyanocobalamin for patients who are vegan and/or have dietary deficiency are set out in table 2 and discussed below. The NHS England and NHS Clinical Commissioners guidance for CCGs about "Conditions for which over the counter items should not routinely be prescribed in primary care" recommend that vitamins and minerals should not be routinely prescribed due to limited evidence of clinical effectiveness. The exceptions are patients with 'medically diagnosed deficiency', including for those patients who may have a lifelong or chronic condition or have undergone surgery that results in malabsorption.[25] Therefore, low-dose oral cyanocobalamin should not routinely be prescribed for patients suspected of having or likely to have diet-related vitamin B12 deficiency unless it has been medically diagnosed (e.g. non-diet-related cause); such patients should be advised to purchase a supply instead.[23]

In Wales, cyanocobalamin tablets can be prescribed for patients who are vegan or have a proven vitamin B12 deficiency of dietary origin only for treatment or prevention of vitamin B12 deficiency as specified under the 'Selected List Scheme' (SLS) in part XVIIIB of the Drug Tariff, and the prescriber must endorse the prescription with 'SLS'. This is not applicable to prescriptions for cyanocobalamin tablets in England, Northern Ireland or Scotland, or when prescribing cyanocobalamin tablets for non-diet-related vitamin B12 deficiency in any of the countries.[18,23] Cyanocobalamin 50-150 microgram tablets are available as Pharmacy only medicines (cyanocobalamin 50microgram tablets) or as food supplements which can be purchased from pharmacies, supermarkets and health food shops.[22,23]

Table 1: Recommendations for prescribing cyanocobalamin for patients who are vegan and/or have dietary deficiency

	Recommendations
Wales	• Cyanocobalamin tablets can be prescribed for patients who are vegan or who has a proven vitamin B12 deficiency of dietary origin.[18] • Vitamin B12 tablets, cyanocobalamin solution (any strength), Cytacon tablets and Cytacon liquid are included in Part XVIIIA the "Blacklist" and cannot be prescribed on the NHS.[18] Prescriptions must be written as "cyanocobalamin tablets" for dispensing by a UK community pharmacy.[23]
England	• Should not be routinely prescribed in primary care.[25] • Prescribing is not recommended for patients who are vegan,[23] only for patients with medically diagnosed deficiency, (e.g. non-diet-related cause), including for those who may have a lifelong or chronic condition or have undergone surgery that results in malabsorption.[25] • Vitamin B12 tablets, cyanocobalamin solution (any strength), Cytacon tablets and Cytacon liquid are included in Part XVIIIA the "Blacklist" and cannot be prescribed on the NHS.[18]
Scotland	• Prescribing is not recommended for patients who are vegan.[23]
Northern Ireland	• Prescribing is not recommended for patients who are vegan.[23]

Non-diet-related vitamin B12 deficiency

Non-dietary vitamin B12 deficiency can occur with pernicious anaemia, prior gastrectomy, bariatric surgery, achlorhydria, pancreatic insufficiency, short bowel syndrome, bacterial overgrowth, inflammatory bowel disease. It can also rarely be drug related and caused by drugs such as colchicine, metformin, nitrous oxide, protein pump inhibitors and H2-receptor antagonists.[24,26]

In June 2022, the MHRA issued a Drug Safety Update advising that metformin can commonly reduce vitamin B12 levels in patients leading to B12 deficiency. This risk is greater with higher doses of metformin, longer treatment duration and in patients with other risk factors. Vitamin B12 levels should be tested if deficiency is suspected and corrective treatment given in line with local guidelines.[27]

NICE CKS recommends: administer hydroxocobalamin 1mg intramuscularly every two to three months for life.[24]

Intramuscular (IM) hydroxocobalamin is the preferred method of treatment as it is retained in the body longer than cyanocobalamin, allowing maintenance therapy to be given at intervals of up to three months.[23]

The BNF states that cyanocobalamin injection is less suitable for prescribing.[14] However, where administration of IM hydroxocobalamin is not tolerated, or not possible (e.g. during a pandemic), oral cyanocobalamin may be considered as an alternative, provided sufficient doses are taken (much higher than the doses used for diet-related deficiency, at least 1mg) and there is good compliance with treatment.[23] Cyanocobalamin 1mg tablets are available as a food supplement (immediate-release, modified-release or sublingual tablets), a prescription-only medicine that is unlicensed in the UK but can be imported; and a licensed 1mg tablet (Orobalin®).[14,23]

Neurological involvement

Oral vitamin B12 should not be prescribed for patients presenting with neurological involvement. In these cases, seek urgent advice from a haematologist. IM hydroxocobalamin should be given if this advice is not immediately available. Patients prescribed high-dose oral cyanocobalamin should be advised to monitor their symptoms carefully and contact their GP if they begin to experience neurological or neuropsychiatric symptoms, such as pins and needles, numbness, problems with memory or concentration, or irritability.[23]

The COVID-19 workload prioritisation guidance categorised vitamin B12 injections as:[3]

- **Amber category (Medium priority): Vitamin B12 injections for post bariatric surgery patients** – consider teaching appropriate patients to self-administer and ensure frequency is not more than 12-weekly. Review whether oral supplementation would be appropriate.
- **Red category (Lower priority): Vitamin B12 injections** – consider teaching appropriate patients to self-administer and ensure frequency is not more than 12-weekly. Review whether oral supplementation would be appropriate if asymptomatic with a dietary deficiency.

The British Society for Haematology (BSH) guidance on vitamin B12 replacement during the COVID-19 pandemic recommends:[26]

- **Diet-related vitamin B12 deficiency:** If patients are established on IM hydroxocobalamin, an alternative is to offer oral cyanocobalamin tablets, 50-150 micrograms, daily between meals. Reassess the serum B12 prior to recommencing IM hydroxocobalamin. Many of these patients may be vitamin B12 replete with adequate levels within the liver, and therefore may be able to safely stop taking vitamin B12 supplements possibly for up to a year. Give dietary advice to all patients. Patients on vegetarian and especially vegan diets should continue taking oral supplements.
- **Non-diet-related vitamin B12 deficiency:** The need for IM hydroxocobalamin should be discussed with each patient individually. Alternatives to attending the GP surgery, such as local pharmacies or home administration by district nurses should be explored. Oral cyanocobalamin can be offered at a dose of 1 mg per day until regular IM hydroxocobalamin can be resumed i.e. once GP surgeries are able to do so safely, aiming to have a shortest possible break from regular injections.

If the GP surgery is able to safely return to managing medium and lower priority workload then patients switched to oral cyanocobalamin from IM hydroxocobalamin due to the pandemic should be reviewed to identify the indication for prescribing – diet-related or non-diet-related vitamin B12 deficiency.

Review the identified patients that have diet-related vitamin B12 deficiency prescribed low dose oral cyanocobalamin at doses of 50-150 micrograms daily, check compliance with the patient. If patient is vitamin B12 replete with adequate levels within the liver, they may be able to safely stop taking vitamin B12 supplements possibly for up to a year.[26] If patient does not have adequate levels recommence IM hydroxocobalamin twice-yearly.[26] Continued need for prescribing should be reviewed on a regular basis, for example at an annual review.[25]

Review the identified patients that have non-diet-related vitamin B12 deficiency and recommence patients on IM hydroxocobalamin given at intervals of up to two to three months.[24]

The PrescQIPP bulletin 296: Vitamins and minerals and supporting resources may be used to support a review of vitamin B12.

In England, Scotland and Wales the number of items or oral cyanocobalamin prescribed March to May 2020 was 391,000, this increased to 530,000 items June to August 2022 (NHSBSA and Public Health Scotland).

Primary care prescribing trends during COVID-19

OpenPrescribing prescribing data for March 2020 demonstrated an increase of 8.5 million items (9.3%) in March 2020 and additional costs of £118 million (17.6%) compared to March 2019. In this month alone, prescribing of salbutamol inhalers increased by 53% and beclomethasone inhalers by 39%, which led to concerns for availability of inhalers due to the increased demand. Paracetamol also demonstrated a substantial increase in prescriptions, as well as the reported increase in over-the-counter purchases.[28]

An analysis of primary care prescription trends during the COVID-19 pandemic used the English Prescribing Dataset from January 2014 to November 2020. A total of 7,542,293,921 prescriptions were separated into pre-pandemic (January 2014–October 2019) and pandemic data sets (November 2019–November 2020). A Holt-Winters predictive model was used to forecast individual drug prescribing based on historic trends. This analysis demonstrated that prescribing and dispensing of a wide variety of medications was affected during the pandemic. Prescriptions of health-critical medications such as salbutamol, insulin aspart, tacrolimus, and end-of-life medications increased while others involving face-to-face visits were reduced. Some medications including those for type 2 diabetes, hypertension and mental health remained unchanged.[29]

The areas of increased prescribing could be prioritised for review, in addition to therapeutic areas identified by reviewing prescribing data for the Integrated Care Board (ICB)/Health Board(HB), PCN or practice from ePACT2, OpenPrescribing or PrescQIPP data and analysis.

Analysis of the dataset in the OpenPrescribing data found the prescribing of the following therapeutic areas increased.

Respiratory drugs

As demonstrated in the OpenPrescribing data, prescribing of inhaled bronchodilators increased overall by 41.5% (99% CI (31.3% to 53.5%)) compared with the Holt-Winters predictive forecast model for March 2020. Individual medications increased as follows:[29]

- Terbutaline sulfate: **64.3%** (99% CI 45.1% to 89.3%)
- Salbutamol: **53.0%** (99% CI 41.2% to 66.9%)
- Ipratropium bromide: **21.8%** (99% CI 4.1% to 46.8%)
- Formoterol fumarate: **15.2%** (99% CI 2.7% to 31.3%)
- Tiotropium bromide: **12.3%** (99% CI 0.3% to 27.6%)

Respiratory corticosteroid prescriptions were **39.8%** (99% CI 30.3% to 50.7%) above predicted for March 2020. Individual medications increased as follows:[29]

- Budesonide: **37.3%** (99% CI 25.7% to 51.4%)
- Beclometasone dipropionate: **39.3%** (99% CI 29.2% to 51.2%)
- Fluticasone propionate: **39.0%** (99% CI 21.6% to 62.4%)

Insulins and diabetic control

Increased prescribing of all types of insulin was seen during March 2020 compared with predictions. The biggest increase was with insulin aspart. Other items for diabetes control also increased:[29]

- Insulin aspart: **26.9%** (99% CI 18.5% to 36.6%)
- Glucose testing reagents: **11.6%** (99% CI 2.8% to 22.2%)
- Ketone testing strips: **39.0%** (99% CI 30.6% to 48.5%)
- Glucose: **18.7%** (99% CI 10.4% to 28.5%)
- Glucagon: **27.8%** (99% CI 10.7% to 51.1%)

Immunomodulators

Drugs used in the prevention of transplant rejection and disease-modifying antirheumatic drugs demonstrated increases from March 2020 predictions. Individual medications increased as follows:[29]

- Tacrolimus: **18.6%** (99% CI 8.3% to 31.1%)
- Sirolimus: **16.2%** (99% CI −0.59% to 51.9%)
- Ciclosporin: **14.0%** (99% CI −8.5% to 51.1%)
- Mycophenolate mofetil: **12.8%** (99% CI 4.8% to 22.2%)
- Azathioprine: **7.1%** (99% CI −0.2% to 15.6%)
- Hydroxychloroquine sulfate: **13.1%** (99% CI 3.8% to 24.1%)
- Methotrexate: **8.4%** (99% CI 0.8% to 17.2%)
- Leflunomide: **7.4%** (99% CI −0.7% to 17.0%)

Benzodiazepines, opioids and analgesics

Prescribing of drugs associated with end-of-life care also reached their highest recorded point during 2020, coinciding with the UK peak number of deaths from COVID-19 in April 2020. Compared to March 2020 predictions, individual medications increased as follows:[29]

- Levomepromazine hydrochloride: **94.7%** (99% CI 54.6% to 163.0%)
- Midazolam hydrochloride: **78.0%** (99% CI 53.1% to 112.4%)
- Cyclizine lactate: **75.7%** (99% CI 35.2% to 150.7%)
- Haloperidol: **36.5%** (99% CI 13.8% to 70.5%)
- Glycopyrronium bromide: **17.2%** (99% CI 0.1% to 41.4%)
- Morphine sulfate: **7.5%** (99% CI −0.7% to 17.1%)
- Oxycodone hydrochloride: **2.0%** (99% CI −5.3% to 10.5%)
- Paracetamol: **21.7%** (99% CI 8.6% to 38.5%) during March 2020.
- Lorazepam: **10.2%** (99% CI 1.9% to 19.9%)

Use of medications requiring face-to-face visits decreased, including the local anaesthetic bupivacaine hydrochloride which showed a reduction of 86.6% in April 2020. Drugs used in dementia (including donepezil, rivastigmine, memantine, and galantamine) exhibited a slight drop in absolute number of prescriptions dispensed during 2020. Anti-Parkinsonian medications exhibited a similar decline. Prescribing of ibuprofen, diazepam, clonazepam and temazepam remained unchanged.[29]

Primary care post COVID-19

Analysis of patient-level data (up to the end of June 2020) for the impact of COVID-19 on primary care activity in England found that the number of face-to-face consultations fell by 2.3 per person per year and remote consultations increased by 1 per person per year. After the first lockdown 50-60% of consultations were conducted remotely, this allowed vulnerable patients the chance to keep in touch with their GPs without the need to visit a practice and risk contraction or spreading of the disease. This was consistent with message at the time from NHS England that patients should be seen remotely first then face-to-face if necessary. This reduction in GP consultations since the start of the pandemic has been widely reported and has led to concerns about the care of non-COVID patients, people with long-term health conditions, and the potential for delayed diagnoses.[30] Professor Martin Marshall, Chair of the Royal College of General Practitioners (RCGP) in 2021, issued a statement in reply to the reports:[31]

"General practice is now making more patient consultations than before the pandemic, with well over half being face to face. It is also important to remember that we are still in a pandemic, and GP practices are high risk for disease transmission so it's vital we take measures to minimise this, to continue to keep patients as well as GPs and our teams safe. We understand patients' frustrations when they have to wait a long time for an appointment but GPs are currently working under intense workload and workforce pressures. There is a huge shortage of GPs and our workforce is simply not big enough to manage the needs of an ageing and growing patient population with increasingly complex needs. This was the case before the pandemic and it has only been further exacerbated by the events of the past year."

The RCGP have launched the General practice is open resources to support GPs in communicating how patients can best access services. The resources describe the way in which services are offered and how most appointments are currently carried out over the phone or via video in the first instance. They reiterate to patients that if a face-to-face appointment is needed, they will still be seen in person by a GP. Resources include posters and social media materials in both English and Welsh.[32] A report from the RCGP describes how general practice is re-thinking how to deliver it's Fit for the Future vision published in 2019. The vision itself has not changed as a result of the pandemic, it is about how it is realised whilst adapting to the new post-COVID-19 health landscape. Delivery of care that is holistic, person-centred and relationship-based remains at the heart of the vision for general practice. The report focuses on three key features of the COVID-19 response which, they believe, have the most potential for transforming general practice so that it is equipped to meet the health challenges of the 21st century:[33,34]

1. New ways of working enabled by digital technology.
2. Reducing workload by eliminating unnecessary contractual and regulatory compliance activities.
3. Developing the public/community health function of general practice.

Digital technology has not just enabled GPs to care for patients remotely during the pandemic, it has also facilitated better collaboration for practices across organisational boundaries. Video conferencing has helped GPs to build relationships and communicate with hospital consultants, for example, a hospital running video meetings between consultants and GPs, which has reduced referrals and improved communication, or the use of apps, such as Consultant Connect, Near Me and Pando, which allow GPs to communicate directly and confidentially with consultants. The RCGP has long strived to improve the interface between primary and secondary care, so it is vital that these new channels of communication across organisational boundaries are sustained after COVID-19 and developed further, for example, three-way video meetings between the GP, consultant and patient.[34]

NHS England and NHS Improvement published "Our plan for improving access for patients and supporting general practice" in October 2021. This document outlines further actions that will now be taken by the NHS, Government and partner organisations, to support general practice and improve access, including face-to-face appointments with GPs. They include steps to (a) increase and optimise capacity; (b) address variation and encourage good practice; and (c) improve communication with the public, including tackling abuse and violence against NHS staff.[35]

Summary

As the NHS slowly starts to recover post pandemic, and if capacity allows, practices are advised to review areas of prescribing that have increased significantly during the pandemic. This is to ensure quality prescribing which is safe and cost effective. Areas of increased prescribing could include, but are not limited to broad-spectrum antibiotics, oral cyanocobalamin, DOACS and ONS. Other therapeutic areas to prioritised for review in practice, across a PCN or ICBs/HBs can be identified from ePACT2, OpenPrescribing or PrescQIPP data and analysis.

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Additional PrescQIPP resources

Briefing	https://www.prescqipp.info/our-resources/bulletins/bulletin-304-system-recovery-post-covid/
Implementation tools	
Data pack	https://data.prescqipp.info/#/views/B304_SystemrecoverypostCOVID/FrontPage?:iid=1

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