# **“4Cs” Antibiotic Audit: Cephalosporins, Co-amoxiclav, Fluoroquinolones and Clindamycin**

## Audit aims and rationale

Determine and reflect on:

1. When and why you prescribe broad-spectrum antibiotics: cephalosporins (e.g. cefalexin), co-amoxiclav, fluoroquinolones (e.g. ciprofloxacin, levofloxacin, moxifloxacin, ofloxacin) and clindamycin.
2. Whether 4Cs use is in line with national/local antimicrobial guidance.
3. An action plan to ensure appropriate prescribing of the 4Cs.

## Why should you be interested in the “4Cs”?

* 4Cs do not improve outcomes compared to narrow-spectrum antibiotics if the bacteria are susceptible (NICE Guidance[[1]](#endnote-2) [NG84], [NG79], [NG109]).
* 4Cs increase the risk of antibiotic resistance for that patient and their community[[2]](#endnote-3).
* *Escherichia coli (E. coli)* resistance to co-amoxiclav in UTIs nationally is about 20% (lab samples).
* Resistance has contributed toincrease in *E. coli* blood stream infections (BSIs).
* Co-amoxiclav is no longer a first line empirical choice for pyelonephritis as over 40% of *E.coli* BSIs are resistant to it[[3]](#endnote-4).
* Ciprofloxacin and quinolone use increases multi resistant infections due to MRSA and Extended Spectrum Beta-Lactamase (ESBL) producing coliforms.

Safety:

* Ciprofloxacin is currently only recommended for a few infections (usually second choice).
* In [January 2024](https://www.gov.uk/drug-safety-update/fluoroquinolone-antibiotics-must-now-only-be-prescribed-when-other-commonly-recommended-antibiotics-are-inappropriate) the Medicines and Healthcare Products Regulatory Agency (MHRA) highlighted safety issues with fluoroquinolones stating that they *must now only be prescribed when other commonly recommended antibiotics are inappropriate.* Because of this, guidance recommendations related to Fluoroquinolones in this audit are under review, awaiting changes related to this safety update.
* Fluoroquinolones for patients: 60+ years, with renal impairment, solid-organ transplants, or when co-prescribed with a corticosteroid are at a higher risk of tendon injury. MHRA have also linked fluroquinolones to potential psychiatric side effects, including suicidal thoughts.
* It is important to consider the recommendation on [advice healthcare professionals can give to patients and caregivers](https://www.gov.uk/drug-safety-update/fluoroquinolone-antibiotics-must-now-only-be-prescribed-when-other-commonly-recommended-antibiotics-are-inappropriate" \l "advice-for-healthcare-professionals-to-give-to-patients-and-caregivers) as part of shared decision making if a fluroquinolone antibiotic needs to be prescribed.

Clostridium difficile:

* 4Cs are more likely to change the gut flora, encouraging *Clostridium difficile* infection.
* Older age, immunocompromise or multiple antibiotic courses increase *C.difficile* risk[[4]](#endnote-5).

National measures:

* The UK AMR ambition by 2024 is to reduce antimicrobial use in humans by 15%[[5]](#endnote-6),[[6]](#endnote-7).
* The AMR NHS Oversight Framework 2020/21 AMR Indicators aim to improve.

appropriate prescribing of primary care antibiotics (107a) including the 4Cs (107b).

* Benchmarking data is available at [PrescQipp](https://www.prescqipp.info/our-resources/webkits/antimicrobial-stewardship/).

### Table 1. Summary of indications for “4Cs” in NICE and BASHH ‘Managing Common Infections Guidelines’. *See a comprehensive list* [*here*](https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/antimicrobial-prescribing-guidelines)

|  |  |  |
| --- | --- | --- |
| **“4C” antimicrobial** | **First choice indications for 4Cs**  with their conditions of use.  *[Alternative first choice options for adults]* | **Second choice or alternative indications for 4Cs** with their conditions of use.  *[Alternative first choice option for adults]* |
| Cephalosporins: cefalexin  (other cephalosporins are not recommended) | **RENAL**   * **Acute pyelonephritis,** **complicated UTI, catheter UTI** **with upper UTI symptoms,**   *[Co-amoxiclav OR trimethoprim both only if culture results available and susceptible,*  *OR ciprofloxacin (consider safety issues)]*   * **Pregnancy related asymptomatic bacteriuria**   *[Nitrofurantoin,*  *OR amoxicillin if culture results available and susceptible].* | **RENAL**   * **Pregnancy lower UTI,** if no improvement in symptoms on first choice taken for at least 48 hours or when first choice not suitable   *[Nitrofurantoin if eGFR ≥45 ml/min (avoid at term)]*   * **Lower UTI in children,** worsening lower UTI symptoms on first choice taken for at least 48 hours or when first choice not suitable   *[Nitrofurantoin if eGFR ≥45 ml/min, trimethoprim if low risk of resistance]*   * **Recurrent UTI (prophylaxis)**   *[Trimethoprim,*  *OR nitrofurantoin if eGFR ≥45 ml/min]*  **GUT**   * **Acute diverticulitis (uncomplicated)**,  |  | | --- | | if Penicillin allergy or co-amoxiclav unsuitablecefalexin (caution in penicillin allergy) **AND** metronidazole |   *[Co-amoxiclav*  *OR in penicillin allergy trimethoprim WITH metronidazole]* |
| **Co-amoxiclav** | **RESPIRATORY AND ENT**   * **Community-acquired pneumonia,** high severity CRB65 score 3-4 use co-amoxiclav PLUS clarithromycin OR erythromycin in pregnancy   **RENAL**   * **Acute pyelonephritis,** **complicated UTI, catheter UTI** **with upper UTI symptoms**, excluding pregnant women and only if culture results available & susceptible   *[Cefalexin,*  *OR trimethoprim only if culture results available and susceptible, OR ciprofloxacin (consider safety issues)]*  **SKIN**   * **Bites** (human and animal), prophylaxis/ treatment. * **Cellulitis and erysipelas** if infection near eyes or nose or severe.   *[Clarithromycin WITH metronidazole]*  **GUT**   * **Acute diverticulitis**   *[Cefalexin WITH metronidazole,*  *OR trimethoprim WITH metronidazole if penicillin allergy]* | **RESPIRATORY AND ENT**   * **Sinusitis, if systemically very unwell** or high risk of complications or if worsening symptoms on first choice * **Acute otitis media, worsening symptoms** in children on first choice taken for at least 2 to 3 days. * **Acute exacerbation of COPD or bronchiectasis**, **and person at higher risk of treatment failure** and guided by microbiology results   *[Amoxicillin, OR doxycycline, OR clarithromycin]*  **SKIN**   * **Leg ulcer infection,** guided by microbiological results.   *[Flucloxacillin.*  *If penicillin allergy or flucloxacillin unsuitable: Doxycycline OR clarithromycin (erythromycin in pregnancy)]* |
| **Fluoroquinolones:** levofloxacin,  ciprofloxacin, ofloxacin, moxifloxacin  (Adults)  Fluoroquinolone antibiotics: In January 2024, the MHRA published a Drug Safety Update on fluoroquinolone antibiotics. These must now only be prescribed when other commonly recommended antibiotics are inappropriate. NICE is assessing the impact of this warning on recommendations in this audit. **Please check the relevant guidance for any updates.** | *Consider safety issues*  **No first choice indications for levofloxacin**  **RENAL**   * **Acute pyelonephritis,** **complicated UTI, catheter UTI** **with upper UTI symptoms**, Ciprofloxacin. Excluding pregnant women and guided by microbiology results,   *[Cefalexin,*  *OR co-amoxiclav OR trimethoprim both only if culture results available and susceptible]*   * **Acute prostatitis** guided by susceptibilities when available   *[Ciprofloxacin OR ofloxacin*  *OR trimethoprim if fluoroquinolone not appropriate]*  **GENITAL**   * **Gonorrhoea,** Ciprofloxacin only if known to be sensitive.   *[IM ceftriaxone if susceptibilities not known]* | *Consider safety issues*  **RESPIRATORY**   * **Acute exacerbation of COPD or bronchiectasis, if person at higher risk of treatment failure,** use Levofloxacin with specialist advice if co-amoxiclav or co-trimoxazole cannot be used * **Community-acquired pneumonia, high severity CRB65 3-4,** Levofloxacin if co-amoxiclav with clarithromycin cannot be used   **RENAL**   * **Acute prostatitis,** Levofloxacin after discussion with a specialist.   *[First choice Ciprofloxacin OR ofloxacin (considering safety issues)*  *OR trimethoprim if fluoroquinolone not appropriate with specialist advice]*  **GENITAL**   * **Pelvic inflammatory disease,** Metronidazole PLUS ofloxacin OR moxifloxacin alone. See local guidelines and [BASHH](https://www.bashh.org).   *[IM ceftriaxone PLUS metronidazole PLUS doxycycline]*   * **Epididymitis,**   *[Ofloxacin PLUS IM ceftriaxone if probably due to chlamydia or non-gonococcal organisms*  *sexually transmitted and gonorrhoea and enteric organisms*  *Ofloxacin if probably due to chlamydia or non-gonococcal organisms*  *OR ofloxacin OR levofloxacin if probably due to enteric organisms]* |
| **Clindamycin** | No indications for oral clindamycin in 2022 NICE guidance. | No indications for oral clindamycin in 2022 NICE guidance. |

Abbreviations: UTI (urinary tract infection); ENT (ears, nose and throat); COPD (chronic obstructive pulmonary disease); IM (intramuscular).

## How to use the audits

**Step 1: Familiarise yourself with the** [**NICE Managing Common Infection Guidance**](https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/antimicrobial%20guidance/summary-antimicrobial-prescribing-guidance.pdf)**, see** Table 1 **above.** Visit the [TARGET Antibiotics](http://www.rcgp.org.uk/TARGETantibiotics) or NICE [Antimicrobial Prescribing Guidelines](https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/antimicrobial-prescribing-guidelines) websites for more information and the rationale behind recommendations. You may wish to use your local primary care organisation’s guidance as an alternative.

**Step 2: Search and identify all patients prescribed oral 4Cs antibiotics in the 4 weeks prior to the search date.** Document the number of courses issued for each antibiotic. Save the search for reference. Consider setting audit to run automatically every 4 weeks so prescribing lead can report back to the whole practice about their ongoing “4C” prescribing.

**Step 3: Ideally audit *all* people identified by the search.** If large numbers of patients, ensure a minimum of 10 prescriptions (all if <10 prescriptions) from each 4Cs group. You may not get any results for clindamycin.

**Step 4: Complete the data collection table (Table 3) for each selected patient.** When completing the table use the numbers 1 and 0 where yes=1, no=0. It may be easier to complete compliance for each “4C” antibiotic in turn as each has different indications.

**Step 5: Assess prescribing against the guidance.** If first choice antibiotic is not used, clear rationale must be outlined in the data collection table to support reflection.

**Step 6:** Complete the ‘Conclusions and Reflection’ section of the audit to help identify action required going forward.

## Conclusions and reflection

|  |  |
| --- | --- |
| **Date of search:** |  |
| **Practice size:** |  |

Use these questions to reflect upon your own and your practice’s antimicrobial prescribing.

**Table 2. 4C prescribing and compliance with NICE guidance**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **During the “4C” audit** | **Co-amoxiclav** | | | **Cephalosporins** | | | **Fluoroquinolones** | | | **Clindamycin** | | |
|  | **n** | **% of total prescribed 4Cs** | **Your % target for good practice** | **n** | **% of total prescribed 4Cs** | **Your % target for good practice** | **n** | **% of total prescribed 4Cs** | **Your % target for good practice** | **n** | **% of total prescribed 4Cs** | **Your % target for good practice** |
| How many courses were issued? |  |  |  |  |  |  |  |  |  |  |  |  |
| What was the proportion of 4C prescriptions with an appropriate code in the clinical record? |  |  |  |  |  |  |  |  |  |  |  |  |
| Proportion of 4Cs use in line with NICE guidance? |  |  |  |  |  |  |  |  |  |  |  |  |

**Reflection / discussion with practice or Primary Care network**

1. What are the criteria that you perform best in?
2. What are the criteria that need discussion? Identify an area to focus on and create an action plan, consider:

* where you think you may be able to improve your 4Cs prescribing even further?
* has your practice responded to the MHRA safety alert to use less fluoroquinolones?
* alternatives to ciprofloxacin/quinolones particularly in patients 70 + years. Remember they are no longer supposed to be prescribed for [any group](https://www.gov.uk/drug-safety-update/fluoroquinolone-antibiotics-must-now-only-be-prescribed-when-other-commonly-recommended-antibiotics-are-inappropriate) when other commonly prescribed antibiotics are available. Check national and local prescribing guidance for updates.
* catheter UTI: First choice cefalexin, or if susceptible trimethoprim or co-amoxiclav.
* epididymitis: first choice doxycycline, ofloxacin
* which milder infections you could use alternatives to the 4Cs?
* patients or conditions where the management pathway needs review or referral e.g. recurrent infections? *See* [*Wales UTI Mini-Audit for urinary prophylaxis 2019/20*](https://phw.nhs.wales/services-and-teams/harp/urinary-tract-infection-uti-resources-and-tools/uti-downloads/wales-qi-uti-prophylaxis-3a/)

**Consider what you can do to increase ‘4C’ prescribing in line with guidelines:**

* identify condition or antibiotic that needs focused analysis or re-audit in 4-8 weeks.
* run the report every 4-8 weeks to identify whether there is a reduction in the volume of ‘4C’ broad spectrum antibiotics prescribed.
* consider a run chart to display ‘4C’ antibiotic use graphically (*Fig. 1)*. Data can be added monthly for prescribers to follow any changes in prescribing.
* Compare your practice 4C prescribing to the CCG and nationally by quarter or as a twelve-month rolling percentage using [PrescQipp](https://www.prescqipp.info/our-resources/webkits/antimicrobial-stewardship/) or [Fingertips](https://fingertips.phe.org.uk/amr-local-indicators#page/0/gid/1938132909/pat/46/par/E39000026/ati/165/are/E38000056/cid/4/tbm/1/page-options/ovw-do-0) website.

## Table 3. “4Cs” audit data collection sheet: cephalosporins, co-amoxiclav, fluoroquinolones & clindamycin

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Patient** | | | | | | | | | |  |  |  |
|  | **Complete table using yes=1 and 0 = no, or additional follow instructions if needed** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | No. patients | **%** of total prescribed 4Cs | Your target % |
| A | Patient ID |  |  |  |  |  |  |  |  |  |  | N/A | N/A | N/A |
| B | Age |  |  |  |  |  |  |  |  |  |  | N/A | N/A | N/A |
| C | Sex |  |  |  |  |  |  |  |  |  |  | N/A | N/A | N/A |
| D | [Optional: clinician initials and role] |  |  |  |  |  |  |  |  |  |  | N/A | N/A | N/A |
| E | Indication with rationale [Use free-text] |  |  |  |  |  |  |  |  |  |  | N/A | N/A | N/A |
| F | **Degree of illness**   |  |  | | --- | --- | | 0 = temperature (temp.) normal | 1 = temp. abnormal (over 37.9°C OR 36°C or below) | | 2 = temp not known |  | |  |  |  |  |  |  |  |  |  |  | N/A | N/A | N/A |
| G | Other signs supporting use of antibiotics e.g. pulse, fevers/rigors. [Use free-text] |  |  |  |  |  |  |  |  |  |  | N/A | N/A | N/A |
| H | Was indication appropriately coded? |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | **Compliance with NICE/ local guidance – check if antibiotic is first, second or alternative choice in guidance and conditions met** (see Table 1) |  |  |  |  |  |  |  |  |  |  |  |  |  |
| I | **CO-AMOXICLAV PRESCRIBED** |  |  |  |  |  |  |  |  |  |  |  |  |  |
| J | **CO-AMOXICLAV** prescribed in line with guidance first choice   * **Community-acquired pneumonia,** high severity * **Bites**: prophylaxis/treatment all. * **Acute diverticulitis uncomplicated** * **Cellulitis and erysipelas** and infection near eyes or nose. * **Acute pyelonephritis, complicated UTI, catheter UTI with upper UTI symptoms.** |  |  |  |  |  |  |  |  |  |  |  |  |  |
| K | **CO-AMOXICLAV** prescribed in line with guidance second choice/alternative option. |  |  |  |  |  |  |  |  |  |  |  |  |  |
| L | **CEFALEXIN PRESCRIBED** |  |  |  |  |  |  |  |  |  |  |  |  |  |
| M | **CEFALEXIN** prescribed in line with guidance first choice   * **Acute pyelonephritis, complicated UTI, catheter UTI with upper UTI symptoms** * **Pregnancy associated asymptomatic bacteriuria** |  |  |  |  |  |  |  |  |  |  |  |  |  |
| N | **CEFALEXIN** prescribed in line with guidance second choice/alternative option. |  |  |  |  |  |  |  |  |  |  |  |  |  |
| O | **QUINOLONE prescribed** |  |  |  |  |  |  |  |  |  |  |  |  |  |
| P | **QUINOLONE** prescribed in line with guidance first choice. Consider safety issues   * **16+** **Acute pyelonephritis, complicated UTI, catheter UTI with upper UTI symptoms** * **Gonorrhoea,** only if known to be sensitive * **Acute prostatitis**: guided by microbiology results. |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Q | **QUINOLONE** prescribed in line with guidance second choice/alternative option. (Please ensure you have checked for guidance updates in accordance with |  |  |  |  |  |  |  |  |  |  |  |  |  |
| R | **CLINDAMYCIN prescribed** |  |  |  |  |  |  |  |  |  |  |  |  |  |
| S | No indications for oral clindamycin in 2022 NICE guidance: not a first or second line option. |  |  |  |  |  |  |  |  |  |  |  |  |  |
| T | **Compliance with NICE guidance** |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | **Notes indicating rationale for any deviation from guidance** |  |  |  |  |  |  |  |  |  |  |  |  |  |

1. NICE. (2020). *Antimicrobial prescribing guidance - managing common infections.* [www.nice.org.uk/](http://www.nice.org.uk/) [↑](#endnote-ref-2)
2. Costello *et al*. (2010). Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. *BMJ* 2010;340:c2096. [↑](#endnote-ref-3)
3. UK Health Security Agency. (2022). *English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) report 20121 to 2022.* [English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) report - GOV.UK (www.gov.uk)](https://www.gov.uk/government/publications/english-surveillance-programme-antimicrobial-utilisation-and-resistance-espaur-report) [↑](#endnote-ref-4)
4. Wilcox et al. (2008). A case-control study of community-associated *Clostridium difficile* infection. *J Antimicrob Chemother.* 62:388-396. [↑](#endnote-ref-5)
5. Department of Health and Social Care, (2019). [*UK 5-year action plan for antimicrobial resistance 2019 to 2024 - GOV.UK* (www.gov.uk)](https://www.gov.uk/government/publications/uk-5-year-action-plan-for-antimicrobial-resistance-2019-to-2024)

   Medicines and Healthcare Products Regulatory Agency (MHRA). (2024). *Fluoroquinolone antibiotics: must now only be prescribed when other commonly recommended antibiotics are inappropriate.* [Fluoroquinolone antibiotics: must now only be prescribed when other commonly recommended antibiotics are inappropriate - GOV.UK (www.gov.uk)](https://www.gov.uk/drug-safety-update/fluoroquinolone-antibiotics-must-now-only-be-prescribed-when-other-commonly-recommended-antibiotics-are-inappropriate) [↑](#endnote-ref-6)
6. [↑](#endnote-ref-7)