Leicester, Leicestershire and Rutland
Area Prescribing Committee

Clinical management of Clostridioides (*Clostridium) difficile* infection (CDI) in the community

Guidance for the treatment of adult patients with either suspected or confirmed CDI

DAY 1

Patient having diarrhoea with clinical suspicion of *C.difficile infection*

1. Rule out alternative causes of diarrhoea as listed in general principles
2. Send **stool sample** for *C.difficile* toxin (CDT) **that same day**
3. Take **blood samples immediately** for WCC, urea, creatinine and albumin to allow assessment of severity
4. If in care home setting **isolate immediately** and inform infection control team

REVIEW MEDICINES

STOP:

Antibiotics - consult microbiology if antibiotic therapy is still needed for treatment of underlying infection

Proton Pump Inhibitors (PPIs) - consider alternatives if acid suppression required

Laxatives and prokinetic agents eg. metoclopramide

Anti-motility agents eg. loperamide

Where possible STOP:

Immunosuppressant therapy/steroids

Opioids

Review medicines that may cause problems in dehydration:

DAMN – diuretics, ACEI, ARBs, metformin, NSAIDs

Ensure **REGULAR ASSESSMENT** - refer to Appendix 1

- Temperature - is it raised?
- Bloated abdomen
- Abdomen pain
- Increased frequency and change of stool type - use Appendix 3 Bristol Stool Chart and record frequency/stool type
- Hydration status and electrolyte balance – consider if drinking enough fluids/requirement of oral rehydration salts

Assess severity of *C.difficile* infection. Take into account individual factors eg. age, frailty, comorbidities that may increase risk of complications or recurrence.

Mild: No increase in white cell count (WCC), less than 3 loose stools per day

Moderate: Increased WCC, although <15 x10^9/L, 3 to 5 loose stools per day

Severe. Irrespective of stool frequency: Clinical: temp >38.5°C, severe colitis (abdo pain/distention). Laboratory: WCC >15 x10^9/L, acutely increased serum creatinine (50% above baseline), albumin < 25g/L

Life-threatening: Hypotension Partial/complete ileus Toxic megacolon

Initiate **metronidazole 400mg TDS whilst awaiting CDT result.** Provide patient with C.diff factsheet – Appendix 4

Life-threatening, severely unwell or at risk of complications: **Refer to hospital**

DAY 2 - 3

Day 2-3 - GP/nursing staff to check lab and CDT results and continue regular assessment as above.
Clinical deterioration – consider admission to acute hospital if not in community hospital

Strong **clinical suspicion** of CDI despite **negative** CDT result - continue metronidazole and resend stool sample after 72 hrs

CDT result **negative** and **symptoms resolved** → Stop treatment

CDT result **positive** and **symptoms resolved/improving** → Continue **metronidazole 400mg TDS for total 10 days**

CDT result **positive** and **symptoms not improving** → Stop metronidazole. Initiate **vancomycin* 125mg QDS for 10 days**

4 - 9

Day 4-9 - Continue **regular assessment** as above (Appendix 1)**.** No clinical deterioration – continue course of antibiotics**.** Clinical deterioration – consider admission to acute hospital.

DAY 10

Day 10 of treatment

Diarrhoea may take 1 to 2 weeks to resolve. If **stools continue** to be type 5-7 on Bristol stool chart (Appendix 3), **reconsider diagnosis** and **adherence to antibiotic treatment**. If strong suspicion of *C.diff* with **no response to initial treatment** AND continue to be **clinically unwell**:

If initial treatment was with metronidazole – initiate **vancomycin* 125mg QDS for 10 days**.
If initial treatment was with vancomycin* - contact UHL CDI team (Appendix 2) as may be suitable for **fidaxomicin* 200mg BD for 10 days** (GP can initiate following specialist recommendation only).

Note: Isolation no longer required for **community hospital/care home** patients if no diarrhoea for 48 hours and passing normal stools (for them).

Clearance specimens are NEVER required

If diarrhoea persists despite 20 days treatment but the patient is stable and the daily number of type 5–7 motions has decreased, the WCC is normal, and there is no abdominal pain or distension, the persistent diarrhoea may be due to post-infective irritable bowel syndrome, and therefore may not be due to on-going CDI. Consider if the patient may need referral to gastroenterology.

Treatment of relapse/recurrence of CDI

RELAPSE: Further episode of CDI within 12 weeks of initial infection
Less than 28 days since first episode – do not send stool sample
28 days to 12 weeks since first episode – send stool sample for CDT toxin

Treat a recurrent episode as per table below:

Previous treatment	Choice for subsequent recurrent episode
Metronidazole	Vancomycin* 125mg QDS for 10 days
Vancomycin*	Contact UHL microbiology for fidaxomicin* 200mg BD for 10 days
Fidaxomicin*	Vancomycin* 125mg QDS for 10 days

RECURRENCE: Further episode of CDI 12 weeks after initial infection
Regardless of previous antibiotics used, treat as a new episode of CDI and start on CDI pathway at page 1

*Primary care supply of vancomycin and fidaxomicin

In hours – refer to regular community pharmacy to order in
Out of hours only for urgent supply – obtain from a LLR community pharmacy commissioned for urgent supply of specialised medicines – see list of community pharmacies here

General Principles

- **The parameters listed in Appendix 1 should be monitored regularly and can vary from daily assessment to once every 2–3 days depending on the clinical condition of the patient. Inform the GP or medical team (if in a community hospital) if parameters are abnormal and of concern. This is because elderly patients can deteriorate very quickly.**
- Consider *C.difficile* infection in any patient who has diarrhoea or clinical signs of CDI following or during antibiotic therapy, but **before sending stool samples for CDT testing ensure patient is reviewed to rule out alternative causes of diarrhoea** e.g. traveller's diarrhoea, enteral nutrition, laxatives, drug induced (e.g.metformin, metoclopramide, magnesium), constipation over-flow or exacerbation of an underlying medical condition (IBS, ischaemic colitis).
- Only unformed stools - types 5-7 Bristol stool chart (Appendix 3) - should be tested for CDT.
- A **medical review* of the patient must occur immediately** and blood samples taken for WCC, urea and creatinine to allow assessment of severity. For those with symptoms but no lab results, treatment should not be delayed. Those with symptoms and lab results should be assessed for markers of severe/life-threatening disease and placed on the appropriate treatment pathway.
- Where possible **STOP antibiotics** – contact UHL Microbiology Team for advice if antibiotic therapy is still needed for treatment of an underlying infection.
- Review to **STOP PPIs**. Acid-suppressing medications, in particular PPIs, may be a risk factor for CDI, therefore consider alternatives (eg H2 receptor antagonist or over-the-counter antacid) if acid suppression absolutely essential. Howell *et al* (2010) reported a correlation between the degree of acid suppression and risk of CDI (ie a 'dose response' effect), which ranged from lowest risk with no acid suppression, low risk with H2 receptor antagonist (ranitidine) and high risk with once daily PPI.
- **STOP laxatives and prokinetic agents** eg metoclopramide, domperidone and erythromycin. **Do not use anti-motility agents** eg loperamide – precipitates toxic megacolon by slowing the clearance of *C.difficile* from the intestine.
- Where possible stop immunosuppressant therapy/steroids and opioids.
- **No dose reductions are required for *C.difficile* treatment in renal impairment**. For information in liver impairment, contraindications, cautions, drug interactions and adverse effects, refer to the British National Formulary.
- **Prebiotics and probiotics are not recommended**.

*Medical review may also be conducted by an advanced nurse practitioner/independent prescriber competent in the area.

Reviewed July 2022. Version 7 approved by LLR APC September 2022
Reviewers: K Jones, AM Harrison

Appendix 1

Regular assessment: Can vary from daily assessment to once every 2-4 days depending on the clinical condition of the patient. Elderly patients can deteriorate very quickly.

A. **Community hospitals:** Must carry out a **DAILY** assessment of the following and inform the clinician (doctor/advanced nurse practitioner) responsible for the patient if any parameters are abnormal from day 1 until completion of treatment.

B. **Nursing and Care Home settings**: Must carry out a **DAILY** assessment of the following and inform patient's GP if any parameters are abnormal from day 1 until completion of treatment.

C. **Patients in their own home**: Arrangements need to be in place (eg patient/family member, carer, GP practice) to carry out **REGULAR** assessment which can vary from daily assessment to once every 2-3 days depending on the clinical condition of the patient, to identify and report worsening symptoms to alert the GP. **Severe CDI requires daily assessment, medical and nursing review therefore would require a hospital setting after discussing with patient and obtaining consent.**

- Temperature (is it raised?)
- Bloated abdomen
- Abdominal pain
- Increased frequency and change of stool type - use Bristol Stool Chart (Appendix 3) and record frequency and stool type including the normal stool type for that patient)
- Hydration status and electrolyte balance – consider if drinking enough fluids and requirement of oral rehydration salts
- Nutritional state
- Monitor blood pressure - is it low? (Nursing or care home setting/community hospitals only)
- Check for pressure ulcers (Nursing or care home setting/community hospitals only)

Infection prevention and control in care home settings

- Isolate individuals to own room with own toilet facilities until free of symptoms for 48 hours and stools normal for them
- Strict adherence to hand decontamination with liquid soap and water BEFORE and AFTER patient contact (staff and family members) and to remind patients of the importance of washing their own hands after using the toilet and before eating. Alcohol hand sanitiser on its own is not effective again *C.difficle*
- Staff to wear appropriate personal protection equipment (PPE) prior to patient contact (disposable gloves, single use plastic apron) and when handling soiled equipment from infected patient. These should be single use only
- De-clutter patient's environment to reduce equipment to minimum to facilitate cleaning
- Soiled waste must be disposed into clinical waste bag and soiled laundry should be placed separately in red dissolvable bags
- Ensure thorough cleaning of environment using a chlorine-based solution at least once daily (eg Chlorclean or Milton) on all surfaces including toilet, flush handles, taps, toilet doors etc.

Appendix 2

UHL CDI Team Contact:
During normal working hours (8am to 4pm Monday – Friday)
Please contact Infection Prevention team office on 0116 258 5448 (ask for *C.difficile* nurse) with patient's clinical details. The nurse will make contact with Dr D Jenkins or Dr D Bell to call GP back to discuss any cases or confirm authorisation of Fidaxomicin in line with pathway.

UHL Microbiology Contact for any urgent advice out of hours:
Use the LRI switchboard to contact Duty microbiologist

GP Practice / CCG Infection Prevention and Control Advice:
Head of Infection Control: 07917 000617 or 07432 063161

The Local Authority Infection Prevention and Control Service:
0116 305 1525 or infection@leics.gov.uk
The service covers the community and primary care setting outside the NHS

For infection control advice in community hospital setting contact:
LPT Infection Prevention and Control Team: 0116 295 1668

References

- Public Health England, May 2013.Updated guidance on the management and treatment of *Clostridium difficile* infection.
- Antimicrobial Guidelines for the management of Adults with *Clostridium difficile* infection, University Hospitals of Leicester.
- Howell MD, Novack V,Grgurich P, Soullaiard D, Novac L, Pencina M, Talmor D (2010).Iatrogenic gastric acid suppression and the risk of nosocomial Clostridium difficile infection*. Arch Intern Med* 170:784-90
- NICE, July 2021. NICE Guideline NG199 Clostridioides difficle infection: antimicrobial prescribing.

Appendix 3

Bristol Stool Chart

Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on the surface
Type 4		Like a sausage or snake, smooth and soft
Type 5		Soft blobs with clear-cut edges
Type 6		Fluffy pieces with ragged edges, a mushy stool
Type 7		Watery, no solid pieces. **Entirely Liquid**

Appendix 4

Clostridioides (Clostridium) difficile: Patient Information Factsheet

What is Clostridioides (Clostridium) difficile?

Clostridioides (Clostridium) difficile (also known as C.difficile or C.diff) is a bacteria that can live harmlessly in the gut, however sometimes it may cause infection, leading to diarrhoea.

Why does C.diff cause infection?

C.diff harmlessly lives alongside 'good bacteria' in the bowel of approximately 3% of healthy adults. The 'good bacteria' in the gut keeps C.diff under control, preventing harm from being caused. However if this balance is disrupted and the number of 'good bacteria' reduces, for example due to a recent course of antibiotics, C.diff bacteria may multiply and produce toxins, leading to bowel inflammation and diarrhoea.

What are the symptoms of C.diff?

- Diarrhoea several times a day
- High temperature
- Loss of appetite
- Feeling sick
- Stomach pain

Who is most at risk of C.diff infection?

C.diff mostly affects those who:

- Are taking or have had a recent course of antibiotics or are on long-term antibiotics
- Are or have had a long hospital or care home admission
- Are over 65 years old
- Have an immune system that is not working correctly
- Have had recent bowel surgery
- Have an underlying condition, eg. inflammatory bowel disease

How is C.diff diagnosed?

- Diarrhoea can be a symptom of many different conditions and a side effect of many medicines. Therefore, to establish whether diarrhoea is caused by C.diff, your doctor will take a sample of your faeces to send off to a lab to be tested for C.diff toxin.

Can C.diff be treated?

Yes, C.diff can be successfully treated with antibiotics prescribed by your doctor. It is important that the whole course of antibiotics is completed to ensure that symptoms do not re-occur. C.diff normally responds well to treatment, and most people will make a full recovery within 2 weeks. Also make sure you:

- Drink plenty of fluids to prevent dehydration
- Eat plain foods such as pasta, rice, soup and bread if you feel hungry
- Take paracetamol for stomach ache or a high temperature
- Do not take anti-diarrhoea medicines, as this can stop the infection being cleared from your body

In approximately 20% of cases, C.diff symptoms re-occur. If this happens, treatment with antibiotics may need to be repeated.

Can I spread C.diff?

Yes, C.diff can easily be spread between humans through infected diarrhoea. Once out of the body, C.diff turns into resistant cells called spores. Spores can survive on surfaces for long periods of time, including on hands, objects like toilets, and clothes.
To prevent the infection spreading:

- Regularly wash your hands with liquid soap and water, especially after going to the toilet and before eating
- Regularly clean contaminated surfaces eg. toilet, light switches and handles with a bleach-based cleaner after each use
- Do not share towels
- Wash contaminated clothes and sheets separately at the highest temperature
- Stay at home for 48 hours after your last episode of diarrhoea

When should I seek help during C.diff treatment?

Contact your GP without delay if you experience any of the following:

- If you are feeling worse despite treatment, for example have more frequent diarrhoea, blood in stools, tender, painful or swollen stomach, fever, rapid heartbeat
- If you are showing signs of dehydration, such as a dry mouth, dark coloured urine, thirst, tiredness, passing urine less often

Created August 2021. Author Katie Jones, Medicines Optimisation Team, Leicester, Leicestershire and Rutland CCG

Version Control

Date	Issue no	Reviewed by	Description of change (if any)
11.2012	2	Dr D Modha, Dr P Monk	Amendment to title and addition of wording to box 1 'A positive result for *C. difficile* may represent colonisation that does not need treating. If the patient's symptoms have now resolved, they do not require treatment for *C. difficile* infection. Those with symptoms should be assessed to decide whether they have mild or serious infection and should be placed on the appropriate pathway.'
11.2013	3	Dr D Modha, Mini Satheesh, Dr A Swann, Dr P Monk, Diane Worthington, Amanda Howell	Addition of Vancomycin treatment for patient who are symptomatic but non responsive to 10 day treatment of metronidazole. Addition of General principles and appendix 1, 2 and 3 (Image of Bristol Stool Chart). Review, reformatting and rewording including update of other information based onPublic Health England, May 2013 (Updated guidance on the management and treatment of *Clostridium difficile* infection)
11.2014	4	Dr P Monk, Mini Satheesh, Dr D Jenkins, Dr P Danaher, Dr D Bell, Kate Dawson,	Addition of Fidaxomicin as third line in treatment failure with metronidazole and Vancomycin. Addition of fidaxomicin in first recurrence in line with HPA guidance Guide table for recurrence treatment if within 30 days and guidance if more than 30 days UHL CDI team contact details and Care Home infection control nurse (local authority) contact details included
16.5.19	5	Mini Satheesh, Dr D Bell, Shazia Patel, Anne-Marie Harrison, Dr P Danaher, Dr D Jenkins	New nomenclature Clostridioides (Clostridium) difficile added In flow chart deleted the text : If CDT negative and symptomatic, clinical decision to be made to continue/stop treatment) In flow chart added text in line with secondary care CDT guidance and AWP advice: If CDT results are negative, treatment should be stopped. If there is a strong clinical suspicion of CDI, despite a negative result, continue treatment and resend a stool sample after 72 hours. Contact details of various service updated Page 3 specifics added "liquid soap" "disposable gloves" and " single use plastic apron"
August 2021	6	Mini Satheesh, Katie Jones, Anne-Marie Harrison, Dr P Danaher, Dr D Jenkins, Leslene Edwards, Zoe Green, Amanda Hemsley	Addition to review NSAIDS, ACEI, ARBs, diuretics NICE NG199 2021 Addition of markers of disease severity PHE 2013 Treatment pathway amended – same first line treatment recommended despite mild, moderate or severe disease; use of metronidazole until CDT results back Removal of statement - positive CDT but symptoms now resolved may represent colonisation and therefore no treatment needed Addition of advice to reconsider diagnosis and adherence to treatment if loose stools continue at day 10 Updated that on-going diarrhoea post 20 days may not be due to on-going CDI and to refer to gastroenterology if necessary Updated definition of recurrence to within 12 weeks of previous episode and relapse to 12 weeks after previous episode as per NICE NG199 2021 Updated treatment of recurrence to include all severities NICE

			NG199 2021 Addition to use vancomycin if previously used fidaxomicin for a recurrent episode Addition to send a stool sample for a recurrent episode if 28 days to 12 weeks Change to consider H2 receptor antagonist or over-the-counter antacid (previously ranitidine) if acid suppression is essential due to supply issues with H2 antagonists Addition of prebiotics and probiotics not recommended NICE NG199 2021 Amended appendix 1 community hospitals to include advanced nurse practitioners Appendix 1 removal of advice to use alcohol sanitizers after hand wash Updated telephone numbers for UHL IP nurse, CCG IPC advice and local authority contact Addition of patient information factsheet
May 2022	7	Katie Jones	Vancomycin/fidaxomicin added to specialised medicines CBS 22-23 – addition of section regarding supply in hours and out of hours