NICE National Institute for Health and Care Excellence

NICE guidance

Faecal microbiota transplant for recurrent Clostridioides difficile infection

HealthTech guidance

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Your responsibility

This guidance represents the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take this guidance fully into account, and specifically any special arrangements relating to the introduction of new interventional procedures. The guidance 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.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties. Providers should ensure that governance structures are in place to review, authorise and monitor the introduction of new devices and procedures.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

This guidance replaces MTG71.

1 Recommendations

1.1 Faecal microbiota transplant (FMT) is recommended as an option to treat recurrent Clostridioides difficile infection in adults who have had 2 or more previous confirmed episodes.

1.2 FMT treatment is cheaper than almost all treatment options with antibiotics. It is not cost saving compared with vancomycin taper pulse if it's given using an enema. However, FMT via enema would only be an option for the minority of people who cannot have FMT by another route.

Why the committee made these recommendations

Clinical trial evidence shows that FMT treatment is significantly better than antibiotics alone at resolving a C. difficile infection in people who have had 2 or more previous infections.

Modelling shows that FMT treatment is cheaper than almost all treatment options with antibiotics. It is cost saving by £769 compared with vancomycin taper pulse (VTP) if it's given using colonoscopy, and by £8,297 compared with vancomycin if it's given using an oral capsule. This assumes FMT costs £1,300 for 50 ml, and that a quarter of people having antibiotics alone are treated in the community (that is, outside hospital). FMT is not cost saving compared with VTP if it's given using an enema – this costs £1,287 per person more.

2 The technology

Technology

2.1 Faecal microbiota transplant (FMT) aims to restore a healthy gut microbiome in people who have recurrent or refractory Clostridioides difficile infections. It involves transferring intestinal bacteria and other microorganisms from healthy donor faeces into the gut of the recipient.

2.2 FMT can be used as a fresh or frozen preparation or in capsule form. It can be given via a lower gastrointestinal route (rectal enema, colonoscopy or flexible sigmoidoscopy), upper gastrointestinal route (using a nasogastric tube, nasoduodenal tube or nasojejunal tube) or via oral capsules. British Society of Gastroenterology and Healthcare Infection Society guidelines recommend a short course of antibiotics before transplantation, with a minimum washout period of 24 hours between the last dose of antibiotic and treatment with FMT. Bowel lavage is also recommended before FMT if it's given via lower gastrointestinal routes.

2.3 FMT must be manufactured in accordance with Medicines and Healthcare products Regulatory Agency (MHRA) guidance for human medicines regulation. When FMT is supplied on a named patient basis, within a single organisation, a pharmacy exemption may be used, subject to ensuring proper governance and traceability. Before establishing an FMT service, NHS centres are legally required to seek advice from the MHRA and, if necessary, obtain licences to process, distribute and carry out FMT. A strict donor screening programme should also be in place for FMT in line with the British Society of Gastroenterology and Healthcare Infection Society guidelines. An FMT service should be delivered by a multidisciplinary team.

Care pathway

2.4 First-line treatment for a C. difficile infection involves rehydration and antibiotic

treatment. Some people have recurrent, relapsing, or refractory C. difficile infections and need further courses of antibiotics. NICE's guideline on antimicrobial prescribing for C. difficile infection recommends antibiotics for first and further C. difficile infections, and provides guidelines on antibiotic, dosage and course length. It also recommends considering FMT for a recurrent episode of C. difficile infection in adults who have had 2 or more previous episodes. NICE's interventional procedures guidance on FMT for recurrent C. difficile infection says that current evidence on the efficacy and safety of FMT for recurrent C. difficile infection is adequate to support the use of this procedure provided normal arrangements are in place for clinical governance, consent and audit. It also says that clinicians should ensure that a confidential record is kept of the donor and recipient of each FMT.

Innovative aspects

2.5 The aim of the procedure is to treat the infection with transplanted gut microbiota instead of prescribing further courses of antibiotics.

Costs

2.6 The cost of frozen FMT material is £850 per 50 ml or £1,700 for 150 ml. Including transportation and MHRA licensing, the cost is up to £1,300 per 50 ml (£2,600 for 150 ml). Oral capsules are likely to cost between £500 and £600, based on expert opinion. Additional costs include staff time, procedural costs, additional drugs given as part of the procedure and pretreatment short-course antibiotics.

3 Evidence

NICE commissioned an external assessment centre (EAC) to review the evidence. This section summarises that review. Full details of all the evidence are in the project documents on the NICE website.

Clinical evidence

The clinical evidence includes 5 randomised controlled trials

3.1 The EAC did a systematic review to identify randomised controlled trials (RCTs) comparing faecal microbiota transplant (FMT), by any route of delivery, with NICE-recommended comparators, to treat a Clostridioides difficile infection in people who have had at least 2 previous episodes. It identified and assessed 5 eligible RCTs including 274 adults in total. These trials compared FMT, given via different routes of administration and with a preceding course of antibiotics, with antibiotic treatment. For full details of the clinical evidence, see section 3 of the assessment report.

More C. difficile infections were resolved with FMT than antibiotic treatment in 4 RCTs; there was no difference in 1 RCT

3.2 FMT (with pretreatment antibiotics) was significantly better at resolving a C. difficile infection than:

- vancomycin in 4 RCTs (Cammarota et al. 2015, Hvas et al. 2019, Rode et al. 2021 and van Nood et al. 2013)
- fidaxomicin in 1 RCT (Hvas et al. 2019).

C. difficile infection was resolved in 57% (Rode et al. 2021) to 94% (van Nood et al. 2013) of people having FMT (when any number of infusions was considered). In comparison, C. difficile infection was resolved in 19% (Hvas et al. 2019; vancomycin) to 46% (Rode et al. 2021; vancomycin taper pulse

[VTP]) of people having antibiotic therapy in these RCTs. However, Hota et al. (2017) showed less C. difficile infection resolution in the FMT group (given via enema; 43.8%) compared with VTP (58.3%), although the study did not report statistical significance.

Recurrence rate is comparable to or lower than antibiotic treatment

3.3 Three trials found lower C. difficile infection recurrence in the FMT group (range 6% to 10%) compared with the antibiotic group (vancomycin range 62% to 69%, fidaxomicin 46%; Cammarota et al. 2015, Hvas et al. 2019 and van Nood et al. 2013). Hota et al. (2017) reported comparable C. difficile infection recurrence after FMT by enema (56.2%) and VTP (41.7%). However, none of the trials reported statistical significance.

Gastrointestinal side effects can occur in the short term after FMT treatment

3.4 Short-term gastrointestinal side effects were reported in 4 RCTs (Cammarota et al. 2015, Hota et al. 2017, Hvas et al. 2019 and van Nood et al. 2013). The most common effects included diarrhoea, bloating, abdominal pain or cramps. These symptoms lasted (when reported) between 3 hours (van Nood et al. 2013) and 12 hours (Cammarota et al. 2015), or were described as 'transient' (Hvas et al. 2019).

Small sample sizes and the relevance of the population to the NHS limit the evidence

3.5 The included studies had relatively small sample sizes, with a median of 39 and a range of 27 (Rode et al. 2021) to 64 adults (Hvas et al. 2019). This was partly because 4 of the trials stopped early; only 1 completed after recruiting the target number of people (Hvas et al. 2019). The evidence is also limited by not being done in the UK and the trial populations having fewer comorbidities and a lower

chance of being hospitalised than the eligible UK population.

Heterogeneous study characteristics may limit the evidence

3.6 The included studies used different FMT administration routes:

- 2 used an enema (Hota et al. 2017 and Rode et al. 2021)
- 1 used colonoscopy (Cammarota et al. 2015)
- 1 used a nasoduodenal tube (NDT; van Nood et al. 2013)
- 1 used mixed routes (colonoscopy or nasojejunal tube; Hvas et al. 2019).

None of the included trials evaluated FMT delivered via capsule, nasogastric tube (NGT) or flexible sigmoidoscopy. The number of times FMT was given also varied, from 1 to 4 infusions. In 3 of the trials a proportion of people taking part were being treated for a first recurrence of C. difficile infection (Cammarota et al. 2015, Hota et al. 2017 and van Nood et al. 2013). However, this was only a minority of cases.

Cost evidence

Of 8 economic studies found, 1 used an NHS perspective

3.7 The EAC did a systematic review to find economic evaluations comparing FMT, by any route of delivery, with NICE-recommended comparators, to treat a C. difficile infection in people who have had at least 2 previous episodes. It assessed 8 economic evaluation studies relevant to the decision problem. Abdali et al. (2020) was a UK-based cost–utility analysis comparing 4 treatments for recurrent C. difficile infection (FMT via NGT, FMT via colonoscopy, oral fidaxomicin, and oral vancomycin). The analysis used a Markov model with 4 health states (relapsed, recovered, recurrent C. difficile infection and dead) and had a cycle length of 2 months and time horizon of 1 year. The analysis found that fidaxomicin and vancomycin were dominated by FMT via NGT and FMT via

colonoscopy (that is, FMT was cost saving and more effective).

For full details of the cost evidence, see section 4 of the assessment report and the assessment report appendix.

A Markov model compared FMT with antibiotic treatment

3.8 The EAC created a cohort Markov model that included adults with recurrent C. difficile infection who have had 2 or more previous episodes. It had a time horizon of 6 months and cycle length of 2 months. The model included 4 routes of FMT administration (colonoscopy, enema, NDT and oral capsules) and 3 antibiotic comparators (vancomycin, fidaxomicin and VTP). It had 4 health states:

- recurrent C. difficile infection (starting state)
- persistent C. difficile infection (recurrent, relapsed or refractory C. difficile infection)
- recovered
- dead.

The quality of the clinical evidence limits the economic model

3.9 The quality of the clinical evidence leads to uncertainty in the clinical parameters used in the economic model. No eligible RCTs were identified comparing FMT oral capsules with antibiotics in people with 2 or more previous episodes of C. difficile infection. However, because 2 studies found oral capsules were comparable to FMT colonoscopy (Kao et al. 2017, Ramai et al. 2020) the EAC assumed the transition probabilities to be the same. FMT via NGT and flexible sigmoidoscopy were excluded from the economic model because of a lack of RCT-level data from the clinical evidence review.

The economic model used a number of clinical assumptions

3.10 The economic model used the following clinical assumptions:

- people are treated with the same treatment again if the first treatment does not work
- there are constant treatment response and recurrence rates in each cycle
- pretreatment with antibiotics is only used for the first FMT treatment
- for anyone in the recovered group there is the same risk of death as the general population
- initial treatment includes 5 days of hospital stay for FMT and 10 days for antibiotics
- costs of tests and follow up are assumed to be the same between groups and so are excluded from the model.

  After talking to clinical experts, the assumptions around hospital stay and pretreatment antibiotics were amended in the base case, as discussed in section 4.9 and section 4.10.

FMT by all administration routes evaluated was cost saving in the base case

3.11 The EAC's base case analysis found that all 4 routes of FMT were associated with increased health benefits and reduced costs against all 3 antibiotic comparators, with savings ranging from £3,369 (FMT enema compared with VTP) to £13,134 (FMT oral capsule compared with vancomycin). Health benefits ranged from a quality-adjusted life year (QALY) gain of 0.17 (FMT enema compared with VTP) to 0.66 (FMT via NDT compared with vancomycin).

FMT via NGT could also be cost saving, although there is no RCT-level evidence

3.12 The EAC identified a meta-analysis by Ramai et al. (2020), which suggested an overall cure rate of 78.1% when FMT is given via NGT. The cost of delivering FMT via NGT is estimated to be £740 (Abdali et al. 2020). Because the cure rate is estimated to be higher for FMT via NGT than via enema, and costs less, FMT via NGT is likely to be cost saving for recurrent C. difficile infections, against all 3 comparators considered.

FMT remained cost saving in the sensitivity and scenario analyses

3.13 The EAC did deterministic and probabilistic sensitivity analyses, and scenario analyses. The deterministic sensitivity analysis compared FMT via enema (the least cost saving FMT route) with VTP (the comparator with the second lowest cost and highest health benefit). It found that the largest cost drivers were the resolution probability for FMT via enema and VTP, followed by the hospital stay for any cases of C. difficile infection in subsequent cycles. The results of the probabilistic sensitivity analysis showed that FMT is estimated to be cost saving 96% to 100% of the time compared with antibiotic treatment. The EAC also did 5 scenario analyses. FMT remained cost saving in all of them:

- Pretreatment antibiotics for all FMT treatments, not just the index treatment (FMT was compared with the VTP treatment group only).
- Subsequent treatment with VTP for all treatment arms for people in the persistent C. difficile infection state.
- Threshold analysis on fidaxomicin cost discounting.
- Extending the time horizon from 6 months to 1 year.
- All treatment arms having a 1-day hospital stay for the index treatment instead of 5 or 10 days' stay in the FMT and antibiotic groups, respectively.

For full details see assessment report appendix 1 in the supporting documents for this guidance.

4 Committee discussion

Clinical-effectiveness overview

FMT is an effective treatment for recurrent C. difficile infection for people who have had 2 or more previous episodes

4.1 The randomised controlled trial (RCT) evidence showed that faecal microbiota transplant (FMT) after pretreatment antibiotics was significantly better at resolving a recurrent Clostridioides difficile infection than vancomycin in 4 RCTs, and better than fidaxomicin in 1 RCT. Only 1 RCT found no statistical difference in the efficacy of FMT compared with antibiotics. The committee acknowledged that there are limitations to the evidence base. However, it considered that, because there is an unmet need in this population, FMT is likely to be an effective alternative to continued antibiotic use. It also acknowledged that FMT is already being used in the NHS for recurrent C. difficile infections and is recommended in NICE's guideline on antimicrobial prescribing for C. difficile infection. Therefore, the committee agreed that FMT should be recommended to treat a recurrent episode of C. difficile infection if people have had 2 or more previous episodes.

The use of FMT for refractory C. difficile infections is uncertain because the definition of refractory is not clear

4.2 The external assessment centre (EAC) did not identify any in-scope RCTs comparing FMT with antibiotics for refractory C. difficile infections. The clinical experts said that there is no consensus on the definition of refractory C. difficile infection, meaning that there is less available evidence. The committee acknowledged that FMT could benefit this population, but there was too much uncertainty about the definition of a refractory infection to make a recommendation in this population.

FMT via enema is likely to be less effective but is a clinically

appropriate option in some cases

4.3 The clinical evidence presented showed that FMT given via enema is likely to be less effective than the other administration routes evaluated. However, the included studies were not designed to compare FMT administration routes with each other. Clinical experts said that FMT is usually done by NGT or colonoscopy, depending on patient preference and suitability of the procedure. They said that enema would only be an option for people who could not have FMT via other routes, and would be based on discussions with the patient. They said that the challenge of administering FMT via enema is around the FMT sample being retained for long enough for the treatment to be successful. The EAC's economic model showed that FMT via enema was less likely to be a cost saving route of FMT administration and could be cost incurring in some instances, as discussed in section 4.10. The committee concluded that, although enema may be a less effective route of administration, it could be available as an option for the minority of people who cannot have FMT by another route.

There is no evidence in scope comparing FMT via oral capsules and antibiotics

4.4 The EAC did not identify any RCTs comparing FMT given in oral capsules with antibiotics in people who have had 2 or more previous episodes of C. difficile infection. As a result, no evidence was presented for the clinical efficacy of oral capsules. However, the EAC did identify 2 studies for its economic evaluation (1 RCT and 1 systematic review and meta-analysis), which showed that oral capsules were comparable to FMT via colonoscopy. It also said there are 2 ongoing RCTs comparing the oral capsules with antibiotic treatment. Clinical experts said that, if oral capsules were more widely available, they would be preferred because of safety and patient acceptability, especially because newer capsules containing lyophilised FMT material can be given in fewer pills than older versions. The committee acknowledged that, although the comparative evidence presented was limited, oral capsules are a promising option for FMT treatment.

Safety

A strict donor screening programme should be followed

4.5 The British Society of Gastroenterology and Healthcare Infection Society guidelines say that donor screening should be done for all potential stool donors. This includes a questionnaire and personal interview, to establish risk factors for transmissible diseases and factors that could affect the gut microbiome. Blood and stool screening for transmissible disease must also be done. Clinical experts said that only a small proportion of donors pass screening, and they are generally young and healthy adults. The committee acknowledged that there is still a risk of disease transmission because screening tests are not 100% sensitive. However, it acknowledged that the strict donor screen programme currently used makes FMT relatively safe. The committee also acknowledged that there is a lack of long-term safety data on FMT treatment and thought that a registry to collect this information would be appropriate. It also recognised that NICE's interventional procedures guidance on FMT for recurrent C. difficile infection has reviewed the safety of FMT and concluded that there is adequate evidence to support the use of this procedure provided that normal arrangements are in place for clinical governance, consent and audit.

Other patient benefits or issues

People with a recurrent C. difficile infection need to be informed about FMT

4.6 Patient experts said that recurrent C. difficile infections reduce quality of life. Pain and diarrhoea mean people can need help with day to day living and may not be able to work, so lose income. Diarrhoea can also affect people's dignity, especially when it leads to incontinence or when the person is in a hospital or nursing home. The patient experts said patients and clinicians need to be made more aware that FMT is a treatment option for recurrent C. difficile infection. The committee also acknowledged there should be shared decision making with people with the condition, to help them understand their treatment options and

the role of FMT in the treatment pathway.

FMT may not be appropriate for some people

4.7 The committee acknowledged that FMT may not be appropriate for some people with an anaphylactic food allergy. It also recognised that the diet and alcohol consumption of potential donors may be a barrier to having FMT for people from some faith groups or people with dietary preferences. The clinical experts said they had not experienced problems relating to religious beliefs but acknowledged that this is a valid consideration. The committee also acknowledged that there are some people who FMT treatment may not be appropriate for, or who will need treating with additional caution, such as people who are immunosuppressed or immunocompromised and people who are pregnant.

Cost modelling overview

FMT is cost saving compared with antibiotics in the EAC's original economic model

4.8 The base case showed that FMT is likely to be cost saving by at least £3,300 per person, compared with antibiotics. The committee acknowledged that the clinical evidence was very heterogeneous. But the cost savings were robust enough to recommend FMT for recurrent C. difficile infections for people who have had 2 or more previous episodes.

The base case was updated to amend 4 assumptions used in the original model

4.9 After feedback from clinical experts, the EAC updated the original base case to amend 4 assumptions. This is because clinical experts said that a short course of antibiotics is used before most FMT treatments and that the length of stay for treatment with FMT or antibiotics is likely to be short. They also said that not everyone in the antibiotic group would need hospitalisation for treatment. The

unit cost in the EAC's original base case also did not take into account additional costs associated with sample transportation and of maintaining a Medicines and Healthcare products Regulatory Agency (MHRA) licence. The amended base case includes:

- the unit cost of FMT being £1,300 per 50 ml (£2,600 for 150 ml)
- a 1-day hospital stay for all groups
- pretreatment with antibiotics for all FMT rounds
- 25% of people having antibiotic treatment being treated in the community (calculated as the cost of 2 GP appointments and a microbiology stool test, in addition to the antibiotics).

FMT is cost saving compared with almost all antibiotic treatments

4.10 Almost all routes of FMT remained cost saving against all 3 comparators considered, with cost savings ranging from £769 (FMT via colonoscopy compared with VTP) to £8,297 (FMT via oral capsule compared with vancomycin). The exception was FMT via enema, which was cost incurring compared with VTP by £1,287 per person. Threshold analysis found that FMT remained cost saving compared with VTP until the unit cost of FMT is approximately £1,650 to £4,620 (FMT via colonoscopy and oral capsules, respectively). For FMT via enema compared with VTP, the unit cost would have to be reduced to £640 for FMT to be cost neutral. The EAC also did a threshold analysis of the proportion treated in hospital in the comparator arm, in which FMT was compared with VTP. FMT remained cost saving until the proportion treated in hospital was between 14% and 92% (FMT via oral capsule and enema, respectively). The committee concluded that FMT was highly likely to be cost saving even when the cost changes are taken into account.

Further data collection is welcome to address uncertainties in the evidence base

4.11 The committee recognised that there is not much data on the long-term outcomes of FMT treatment and encouraged establishing a registry to collect them. This would help identify long-term adverse events and reduce uncertainty in the economic modelling. The committee also acknowledged that more RCT evidence comparing capsulised FMT with antibiotic treatment would improve the evidence base for this treatment.

5 Committee members and NICE project team

Committee members

This topic was considered by NICE's medical technologies advisory committee, which is a standing advisory committee of NICE.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of the medical technologies advisory committee, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each medical technologies guidance topic is assigned to a team consisting of 1 or more health technology assessment analysts (who act as technical leads for the topic), a health technology assessment adviser and a project manager.

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Update information

Minor changes since publication

December 2025: Medical technologies guidance 71 has been migrated to HealthTech guidance 638. The recommendations and accompanying content remain unchanged.

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