

Additional file 2: Study characteristics

The table includes the general study characteristics of the health economic evaluations included in the study. QALYs = quality-adjusted life years. rCDI = recurrent *Clostridioides difficile* infection. FMT= faecal microbiota transplantation.

| Author and year | Konijeti et al., 2014 [1] | Varier et al., 2015 [2] | Lapointe-Shaw et al., 2016 [3] | Merlo et al., 2016 [4] | Baro et al., 2017 [5] | Luo et al., 2020 [6] | Abdali et al., 2020 [7] |
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| Setting/country | United States | United States | Canada | Australia | France | United States | United Kingdom |
| Analytic method | Decision-tree | Decision-tree | Markov, 6-weeks cycle | Markov, 10-days cycle | Decision-tree | Decision-tree | Markov, 2-months cycle |
| Time horizon | 1 year, up to 2 additional recurrences | 90 days, up to 1 additional recurrence | 18 weeks for costs, lifetime for effects, up to 2 additional recurrences | Not reported - presumably lifetime, number of additional recurrences not reported | 78 days, up to 1 additional recurrence | 6 months, up to 2 additional recurrences | 1 year, up to 2 additional recurrences |
| Perspective | Societal | Third-party payer | Healthcare system | Not reported - presumably societal | Societal | Modified third-party payer | Healthcare system |
| Outcome measure | QALYs | QALYs | QALYs | QALYs, life years | QALYs | QALYs | QALYs |
| Patient population at inclusion | First rCDI, outpatient, mild-to-moderate | Third rCDI, outpatient, severity not reported | First rCDI, severity not reported | ≥1 rCDI, severity not reported | Second rCDI, outpatient, mild-to-moderate | First rCDI, outpatient, mild-to-moderate, | ≥1 rCDI, hospitalised, severity not reported |
| Intervention | FMT colonoscopy, enema or duodenal infusion. | FMT colonoscopy | FMT colonoscopy, enema, or nasogastric tube | FMT colonoscopy or nasoduodenal tube | FMT colonoscopy, enema, or duodenal infusion | FMT colonoscopy or capsules | FMT colonoscopy or nasogastric tube |
| Preceding treatment | Oral vancomycin 500mg qid x 4d | Not reported | Oral vancomycin 125xmg qid x 14d | Oral vancomycin 125mg qid x 4-5d and bowel lavage | Oral vancomycin 500mg qid x 4d | Oral vancomycin 125mg qid x 10d | Not reported |
| Treatment in case of additional recurrences | FMT similar delivery method (second recurrence), oral pulse-taper vancomycin 125 mg qid x 10d + 125 mg every third day x 10 doses (third recurrence) | Oral vancomycin 250 mg qid x 14d + 6 weeks oral vancomycin taper | FMT similar delivery method | FMT similar delivery method (first subsequent recurrence), oral vancomycin 125mg qid x 10d (additional recurrences) | FMT similar delivery method (mild-to-moderate or severe uncomplicated rCDI), oral vancomycin 500mg qid x10d plus intravenous metronidazole 500mg tid x10d (severe complicated rCDI) | FMT similar delivery method | FMT similar delivery method (first subsequent recurrence), oral vancomycin 6-weeks taper pulse starting with 250mg (second subsequent recurrence) |

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| Control treatment | Oral metronidazole 500mg tid x 10d, oral vancomycin 125mg qid x 10d, or oral fidaxomicin 200mg bid x 10d | Oral vancomycin 250 mg qid x 14d + 6 weeks oral vancomycin taper | Oral metronidazole 500mg tid x 14d, oral vancomycin 125mg qid x 14d, or oral fidaxomicin 200mg bid x 10d | Oral vancomycin 125mg qid x 14d | Pulsed-tapered vancomycin 125mg qid x 10d + 500mg qod x 21d, or fidaxomicin 200mg tid x 10d | Tapered vancomycin 125 mg qid x 14d + 125 mg bid x 7d + 125 mg qd x 7d + 125 mg qod x 7d + 125 mg every third day x 7d, fidaxomicin 200mg bid x10d, or a combination of bezlotoxumab 10mg/kg one-time infusion and oral vancomycin 125mg qid x 10d | Oral vancomycin 250 or 500mg qid x 10d or oral fidaxomicin 200mg x 10d |
| Treatment in case of additional recurrences | Patients treated with metronidazole: oral vancomycin (second recurrence) or pulse-taper vancomycin (third recurrence) Patients treated with vancomycin or fidaxomicin: pulse-taper vancomycin (second recurrence) or FMT by colonoscopy (third recurrence) | Oral vancomycin 250 mg qid x 14d + 6 weeks oral vancomycin taper | 6 weeks taper-pulse oral vancomycin: 125 mg qid x 14d + 125 mg bid x 7d + 125mg qd x 7d + 125 mg qod x 7d + 125 mg every third day x 7d | Oral vancomycin 125mg qid x 10d | Similar treatment (mild-to-moderate or severe uncomplicated rCDI) or oral vancomycin plus intravenous metronidazole (severe complicated rCDI) | Not reported (second recurrence), FMT by colonoscopy (third recurrence). | Similar treatment for vancomycin (first subsequent recurrence), oral vancomycin 6-weeks taper pulse starting with 250mg (second subsequent recurrence) |
| WTP threshold (2019-level GBP) | 37,860 GBP (50,000 USD, 2012-level) | Not reported | 30,923 GBP (50,000 CAN, 2014-level) | Not reported | 30913 GBP (32,000 EUR, 2016-level) | 68,000 GBP (100,000 USD, 2019-level) | 20,340 GBP (20,000 GBP, 2018-level) |
| Cost-effective alternative (2019-level GBP) | FMT colonoscopy more effective and costlier than vancomycin, ICER 12,884 GBP/QALY (17,106 USD, 2012-level) | FMT colonoscopy more effective and less costly (dominant) than vancomycin. | FMT colonoscopy more effective and less costly (dominant) than vancomycin | FMT nasoduodenal tube and FMT colonoscopy more effective and less costly (dominant) than vancomycin ^a . | FMT enema more effective and costlier than pulsed-tapered vancomycin, ICER 17,478 GBP/QALY (18,092 EUR, 2016-level) | FMT colonoscopy and FMT capsules more (or equally) effective and less costly (dominant) than all other alternatives ^b . | FMT nasogastric tube (dominant compared with antibiotics). FMT colonoscopy more effective and costlier than FMT nasogastric tube ICER 246,642 GBP/QALY (242,524 GBP, 2018-level) |

^aFMT by nasoduodenal tube is reported as being equally effective but less costly than FMT by colonoscopy. FMT by nasoduodenal tube is therefore considered the most cost-effective alternative by the authors of the present systematic review.

^bFMT by colonoscopy is reported as being more effective and less costly than all other alternatives (Table 3 in Luo et al.). FMT by colonoscopy is therefore considered the most cost-effective alternative by the authors of the present systematic review.

References

1. Konijeti GG, Sauk J, Shrimel MG, Gupta M, Ananthakrishnan AN. Cost-effectiveness of competing strategies for management of recurrent clostridium difficile infection: A decision analysis. *Clinical Infectious Diseases*. 2014;58(11):1507-1514.
2. Varier RU, Biltaji E, Smith KJ, et al. Cost-Effectiveness Analysis of Fecal Microbiota Transplantation for Recurrent Clostridium difficile Infection. *Infection Control and Hospital Epidemiology*. 2015;36(4):438-444.
3. Lapointe-Shaw L, Tran KL, Coyte PC, et al. Cost-Effectiveness Analysis of Six Strategies to Treat Recurrent Clostridium difficile Infection. *PloS one*. 2016;11(2):e0149521.
4. Merlo G, Graves N, Brain D, Connelly LB. Economic evaluation of fecal microbiota transplantation for the treatment of recurrent Clostridium difficile infection in Australia. *Journal of gastroenterology and hepatology*. 2016;31(12):1927-1932.
5. Baro E, Galperine T, Denies F, et al. Cost-Effectiveness Analysis of Five Competing Strategies for the Management of Multiple Recurrent Community-Onset Clostridium difficile Infection in France. *PloS one*. 2017;12(1):e0170258.
6. Luo Y, Lucas AL, Grinspan AM. Fecal Transplants by Colonoscopy and Capsules Are Cost-Effective Strategies for Treating Recurrent Clostridioides difficile Infection. *Digestive diseases and sciences*. 2020;65(4):1125-1133.
7. Abdali ZI, Roberts TE, Barton P, Hawkey PM. Economic evaluation of Faecal microbiota transplantation compared to antibiotics for the treatment of recurrent Clostridioides difficile infection. *EClinicalMedicine*. 2020;24:100420.