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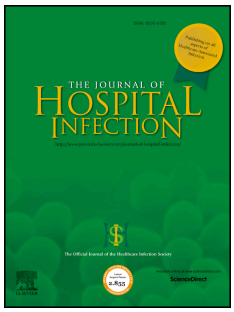

National survey of practice of faecal microbiota transplantation for *Clostridium difficile* infection in the United Kingdom

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Running title: UK survey of FMT for CDI

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Sir

We read with interest the recent editorial on faecal microbiota transplantation for recurrent or refractory *Clostridium difficile* infection (CDI) in which Dr Goldberg summarizes the efficacy of this treatment but also the obstacles in the way of undertaking this treatment.[1] Indeed although the National Institute of Health and Care Excellence advocate the use of faecal microbiota transplantation (FMT) for recurrent or refractory *Clostridium difficile* infection (CDI) when antibiotics fail, our perception is that it has not been widely adopted in the UK. Although the Medicines and Healthcare products Regulatory Agency (MHRA) recently announced that FMT falls within the definition of a medicinal product in the context of clinical trials, this is not the case for CDI treatment and in this context the practice of FMT has not yet been standardised or regulated in the UK.[2] We conducted a national survey to explore current experience with FMT and challenges faced by hospitals in setting up this service. We invited gastroenterologists, microbiologists and infectious disease physicians in the UK to take part in national survey by completing an online questionnaire in 2015.

A total of 255 responses were obtained, of which 204 were included from 120 microbiologists and infectious disease physicians and 84 gastroenterologists following exclusion of incomplete and invalid responses. The survey covered 130 independent sites including 112 acute hospital NHS Trusts in England, 9 in Scotland and 9 in Wales. We found that of these 130 sites only 28% (36/130) had ever performed FMT for refractory or recurrent CDI (Table 1). Furthermore, although 21 of these 36 sites reported having had experience of providing FMT for over one year, only seven sites had treated at least 10 patients. Of the sites that delivered this treatment 24 made the product up on site while 12 obtained FMT from other sites to administer at their hospital. A map of sites currently performing FMT or not is shown in Figure 1. One site performed FMT for refractory ulcerative colitis in a single patient. There were no other indications for its use.

Our survey showed that 94 independent sites did not perform FMT and of these 27 (29%) had referred their refractory or recurrent CDI patients elsewhere for FMT; primarily to Glasgow (in Scotland), Birmingham (in the English midlands) and Exeter (in south-west England). Of sites that were not undertaking FMT, 66 (70%) were keen to have support in setting up an FMT service for CDI locally. On surveying reasons for lack of local provision for FMT at these non-FMT sites, 42 (45%) believed that they were unable to do it due to lack of facilities and 36 (38%) did not know where to start. However only five (5%) felt reluctant to do it because of its perceived unpleasantness. Only a few physicians commented that they were not convinced with the evidence of its efficacy and safety, therefore would not recommend it for their patients.

Our survey provides the most comprehensive representation of FMT service and delivery in UK to date and these findings uncover a surprising lack of uptake for a highly effective, cheap and safe treatment for refractory or recurrent CDI.[3] With just over a quarter of sites in the UK performing FMT and less than one-third referring patients to other hospitals, it is clear that this geographical inconsistency in treatment availability needs to be urgently addressed. Consistent with a survey conducted three years ago,[4] logistical hurdles, costs and local expertise continue to be the primary barriers in set up this service in hospitals in the UK. Despite the MHRA's reasonably permissive approach on FMT as a treatment for CDI, there are considerable challenges and implications in setting up a safe, efficient and regulated FMT

service. This is especially with regard to donor screening (which can be laborious and expensive to perform) and preparation of stool prior to transplantation. The lack of protocols and guidelines for safe and regulated FMT preparation and delivery means it is likely there are significant differences in levels of governance amongst sites that perform FMT nationally.

It was clear from the survey that despite these significant challenges faced by hospitals, most would welcome support in providing FMT. Similar to the OpenBiome service established in Boston which caters to over 500 hospitals in USA,[5] a central or regional quality controlled and regulated FMT preparation, delivery and support service for the UK may be an appropriate and safe strategy.[6] There needs to be agreed national guidelines and protocols for patient and donor selection and screening as well as FMT preparation and delivery based on current evidence for efficacy and safety. Indeed a joint working group involving the Hospital Infection Society and the British Society of Gastroenterology are working on such guidelines. Additionally, there is an urgent need to establish a national registry of patients treated with FMT, in order to review long term outcome and safety data and improve our understanding of disease and treatment mechanisms.

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Table 1: Results of survey of practice of faecal microbiota transplantation for *Clostridium difficile* infection in the United Kingdom

	England	Scotland	Wales
Total sites responding to survey	112	9	9
Sites FMT performed in	32	1	3
Sites performing FMT for > 1 year	17	1	3
Sites performing FMT for < 1 year	15	0	0
Sites that delivered FMT in ≥ 10 patients	5	0	2
Sites that delivered FMT in < 10 patients	27	1	1

Figure 1: Map of sites of hospitals responding to the of survey of practice of faecal microbiota transplantation for *Clostridium difficile* infection in the United Kingdom


Don't perform FMT
Perform FMT
United Kingdom
Isle of Man
WALES
ENGLAND
Edinburgh
Glasgow
Paisley
Dumfries
Newcastle upon Tyne
Durham
Middlesbrough
Scarborough
Hull
York
Liverpool
Sheffield
Peterborough
Norwich
Cambridge
Ipswich
Colchester
Oxford
Swansea
Cardiff
Bath
Exeter
Plymouth
Torquay
Brighton
Peak District National Park
Yorkshire Dales National Park
North York Moors National Park
Lake District National Park
North Pennines AONB
The Cotswolds AONB
Snowdonia National Park