Cystic Fibrosis Trust

The University of Nottingham
UNITED KINGDOM · CHINA · MALAYSIA

cf

THE EVIDENCE BASED
CHILD HEALTH GROUP
University of Nottingham

# Working With The Patient And Clinical Community To Deliver Clinical Research In Cystic Fibrosis

## James Lind CF Phase II

## @question CF

**PROTOCOL [updated 8th February 2018]**

**AUTHORS:** S Smith*, NJ Rowbotham, AR Smyth

*Corresponding author

**ADDRESS:** Evidence Based Child Health Group, Division of Child Health, Obstetrics & Gynaecology, E Floor East Block, Queens Medical Centre, Nottingham NG7 2UH.

Email: sherie.smith@nottingham.ac.uk

**AFFILIATION:** Evidence Based Child Health Group, University of Nottingham, UK

**Abbreviations:**

JLA: James Lind Alliance

PSP: Priority Setting Partnership

MDT: Multi-disciplinary Team

PwCF: person with CF

## 1. Purpose of the advisory panel and background

The purpose of this protocol is to set out the aims, objectives and commitments of the second phase of the James Lind Alliance (JLA) Priority Setting Partnership (PSP).in Cystic Fibrosis (CF) and the basic roles and responsibilities of the partners therein.

The James Lind Alliance Priority Setting Partnership PSP (JLA PSP) in cystic fibrosis (CF) has used a robust and widely accepted methodology to develop the top 10 questions for clinical research in CF, through discussions with both the clinical and patient community[1]. The top ten priorities are available on the James Lind Alliance website[2].

We believe that this represents an important step towards "co-production" of clinical research, so that the conception, delivery and dissemination of research are each conducted in partnership with the patient community[3]. However, a number of the questions in the JLA PSP top 10 are very broad and do not lend themselves to being transformed into a testable hypothesis for a clinical trial or other clinical research study. Indeed, some of the top 10 questions may give rise to several clinical studies. We believe there is a need to have an ongoing conversation with the CF community (both lay and professional) in order to gain a deeper understanding of what JLA PSP participants understand by the top 10 research questions and to design the research studies which meet their needs. Four of the top 10 questions stand out as requiring further discussion.

***What are the effective ways of simplifying the treatment burden of people with Cystic Fibrosis? (Q1)***

***How can we relieve gastro-intestinal (GI) symptoms, such as stomach pain, bloating and nausea in people with Cystic Fibrosis? (Q2)***

***What effective ways of motivation, support and technologies help people with Cystic Fibrosis improve and sustain adherence to treatment? (Q6)***

***Can exercise replace chest physiotherapy for people with Cystic Fibrosis? (Q7)***

Other questions in the top 10 could be formulated into testable hypotheses more readily and a specific study design then explored with the patient community.

## 2. Aims and objectives

We aim to set up an advisory panel representative of the whole CF community (lay and professional) to allow us to explore the four questions above and develop them into a series of testable hypotheses for clinical research. Where the hypothesis will be tested in a clinical trial, we will develop a PICO question for each hypothesis (Population, Intervention, Comparator & Outcome).

The objectives of the @questionCF advisory panel are to:

- work with people with CF, their family and friends, and clinicians to gain a deeper understanding of what JLA PSP participants understand by four of the top 10 research questions
- produce testable hypotheses for research studies which meet the needs of the CF community.

## 3. The Steering Group

The @questionCF advisory panel will be led and managed by the following:

Patient representative/s:

- Zoe Elliott (Parent of children with CF)
- Oli Rayner (pwCF)
- Katie Gathercole (pwCF)

Clinical representative/s:

- Alan Smyth (Respiratory Paediatrician)
- Tracey Daniels (CF Physiotherapist)
- Ed Nash (adult respiratory physician)

- Alistair Duff (psychologist)
- Sarah Collins (dietician)
- Suja Chandran (social worker)
- Patrick Wilson (pharmacist)
- Matt Hurley (consultant respiratory paediatrician)
- Michelle Tabberner (CF Nurse)

The project will be supported and guided by:

- University of Nottingham
    - Sherie Smith (Project coordinator)
    - Nicola Rowbotham (Academic Clinical Fellow)
    - Paul Leighton (Qualitative Researcher)
- Sophie Herbert (F1 junior doctor with interest in research)
- CF Trust
    - Keith Brownlee (Director of Impact)
    - Lorna Allen (Patient and Public Involvement Co-ordinator)

The Steering Group includes representation from lay and professional groups. The Steering Group will agree the resources, including time and expertise that they will be able to contribute to each stage of the process.

## 4. The wider Contributors

Organisations and individuals will be invited to be involved with this phase of the project as contributors. Contributors are groups or individuals who agree to take part in the online surveys and who will then be invited to participate more fully by joining our advisory panel as members. Advisory panel members will be involved in the design of and participation in the focus groups for more detailed analysis of the priorities. Contributors represent the following groups:

- people who have CF
- family and friends of people who have CF
- medical doctors, nurses and professionals allied to medicine with clinical experience of treating CF.

We will work with others who are undertaking activity in this field – both identifying research priorities, with the patient community and disseminating research findings to the community.

- The UK Cystic Fibrosis Trust – the "Insight" survey, distributed by the CF Trust, asked about all aspects of living with CF and received over 1000 responses in the last year.
- The US CF Foundation, whose similarly named "Insight" programme seeks to identify research questions which can be answered through the US CF Registry. https://www.cff.org/Get-Involved/Community/Contribute-to-Our-Research/
- The Journal of Cystic Fibrosis, who produce "CF Research News" – lay summaries of research papers.

## 5. The methods we will use

The majority of the project will be carried out using online methods to avoid the risk of cross-infection from face to face work and to maximise the reach of the surveys. We will work through the following steps.

### Step 1: Identification and invitation of potential partners

Potential partner organisations will be identified through a process of peer knowledge and consultation, through the Steering Group members' networks. Potential partners will be contacted and informed of the establishment and aims of the @questionCF.

### Step 2: Initial steering group meeting / awareness raising

The initial steering group meeting / awareness raising will have several key objectives:

- to welcome and introduce potential members of the @questionCF2 steering group & advisory panel
- to present the proposed plan for the @questionCF2 project
- to initiate discussion, answer questions and address concerns
- to identify those potential partner organisations which will commit to the @questionCF advisory panel and identify individuals who will be those organisations' representatives and the @questionCF advisory panel's principal contacts
- to establish principles upon which an open, inclusive and transparent mechanism can be based for contributing to, reporting and recording the work and progress of the @questionCF advisory panel.
- We will hold three further steering group meetings over the course of the project to guide the process.

### Step 3: Launching the project and dissemination of surveys

We will approach participants who gave us their contact details as part of the JLA PSP in CF and we will invite them to join the @question CF advisory panel. We will also publicise this engagement work via Twitter, other social media and via our website in order to open up participation to the whole CF community. Participants will be asked to complete an intial online survey (priority one) and asked if they would like to continue supporting our research by joining our advisory panel..

## Step 4: Exploring and clarifying the research question

Two initial questionnaires, for each of the four priorities, will be launched sequentially over a period of twelve months in total – one targeted at people with CF and parents of people with CF and the other at CF health care professionals, to explore thoughts, wants and needs around each of the four research priorities mentioned above.

- The survey content will be guided by the original questions submitted during the PSP that fed into the final priorities.
- We will use the online survey tool SurveyMonkey® to distribute the questionnaires and responses will be anonymous.
- We will analyse the data from the surveys in MS Excel to look for themes emerging which can be taken forward into focus groups for more detailed discussion. The process of deciding what to take forward will be agreed by the steering group.
- At this stage participants will be invited to express their interest in taking part in a focus group to further refine the questions after the surveys close.
- Surveys will be designed and managed by Nicola Rowbotham and Sherie Smith with input from the Steering group.

## Step 5: Refining priorities into 'PICO' research questions

Step 4 will produce clinical trial ideas. These raw ideas will be assembled, categorised and refined by **Sherie Smith and Nicola Rowbotham** and taken to the advisory panel. Together, the research team and the advisory panel will generate a focus group agenda from the themes that emerge.

A focus group for each of the four priorities will be attended by both lay and professional members of the CF community to discuss the ideas generated in greater depth. Where the hypothesis could be tested in a clinical trial, we will develop a PICO for each hypothesis (Population, Intervention, Comparator & Outcome).

Focus groups

- We will aim to recruit eight to ten members of the advisory panel to participate in a given focus group
- We will run one focus group for each of the research priorities we are investigating (n = 5)
- We will ensure that the group is representative of lay and professional members
- The discussion guide will be generated from the results of the surveys.
- At least one of the research team will facilitate the focus groups which will be run using online meeting software (BlueJeans®).

- The discussion will be recorded via the online meeting software.

### Step 6: Finalisation of PICO questions by @questionCF advisory panel

The aim of the final stage is to prioritise through consensus the identified PICO questions relating to the CF research priority. This will be occur through a final online prioritisation survey open to all members of the @questionCF advisory panel. A modified dephi process will be used, utilising Likert scales to enable participants to rank the trial questions in order of priority.

## 6. Dissemination of findings and research

### Findings and research

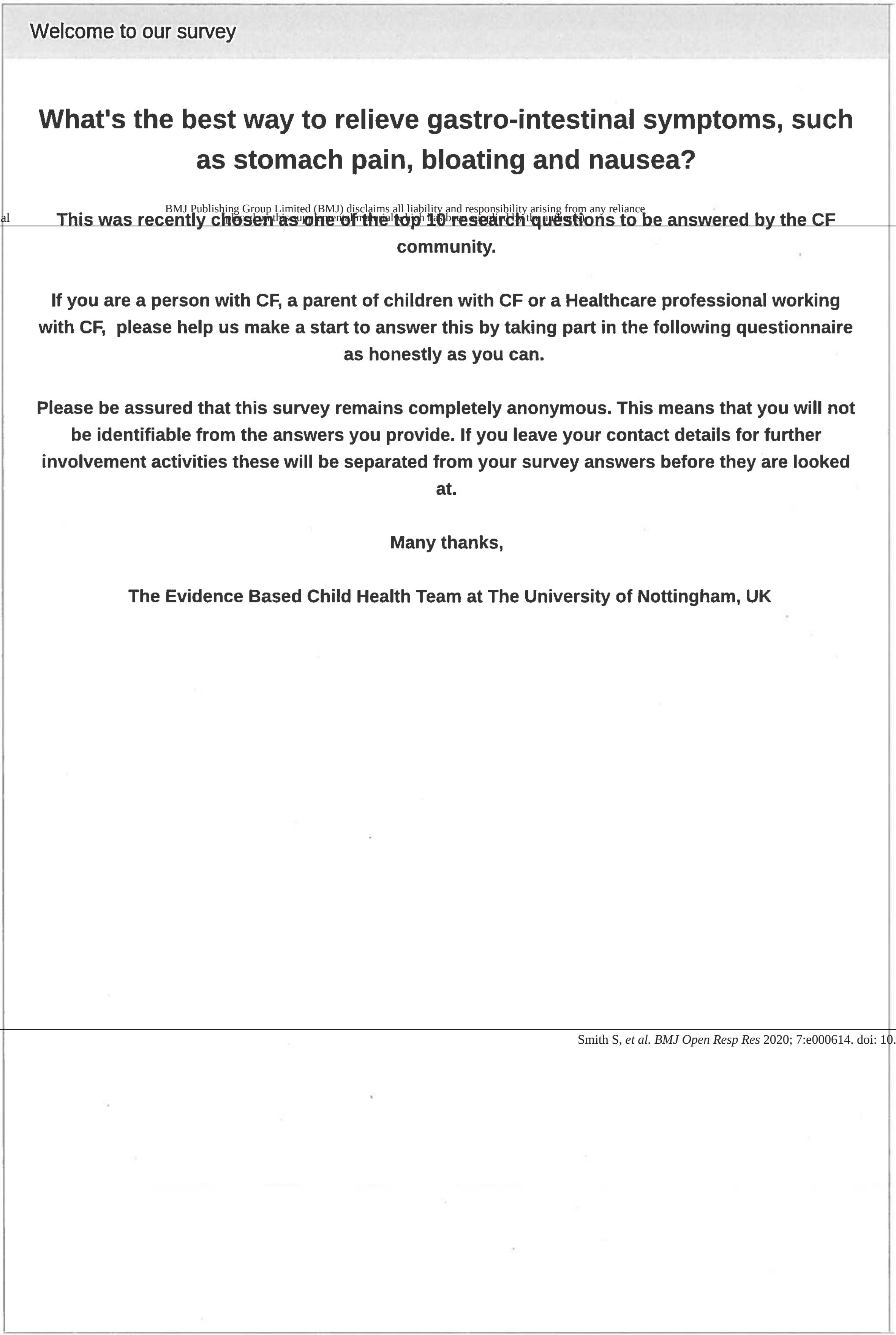
It is anticipated that the findings of the @questionCF advisory panel will be reported to funding and research agenda setting organisations such as the NIHR and the major research funding charities. Steering Group members and partners are expected to develop the findings into clinical research plans to use when approaching potential funders, or when allocating funding for research themselves, if applicable.

### Publicity

As well as alerting funders, partners and Steering Group members are encouraged to publish the findings of the @questionCF advisory panel using both internal and external communication mechanisms. The findings will be written up in at least one journal paper (potential publishers including Thorax and Journal of Cystic Fibrosis). We will also present findings at the European and North American Cystic Fibrosis conferences. As with all our work we will keep the CF Community informed of our findings through online lay accessible infographics, blogs and vlogs (video media).

### References

1. Rowbotham NJ, Smith S, Leighton PA, et al. The top 10 research priorities in cystic fibrosis developed by a partnership between people with CF and healthcare providers. Thorax 2017 4th August 2017; e-pub ahead of print.
2. James Lind Alliance. Cystic Fibrosis Top Ten Research Priorities 2017 [Available from: http://www.jla.nihr.ac.uk/priority-setting-partnerships/cystic-fibrosis/top-10-priorities.htm.
3. Rowbotham NJ, Smyth AR. The patient voice in research - Supporting actor or starring role? J Cyst Fibros 2017;**16**(3):313-14.



Welcome to our survey

## What's the best way to relieve gastro-intestinal symptoms, such as stomach pain, bloating and nausea?

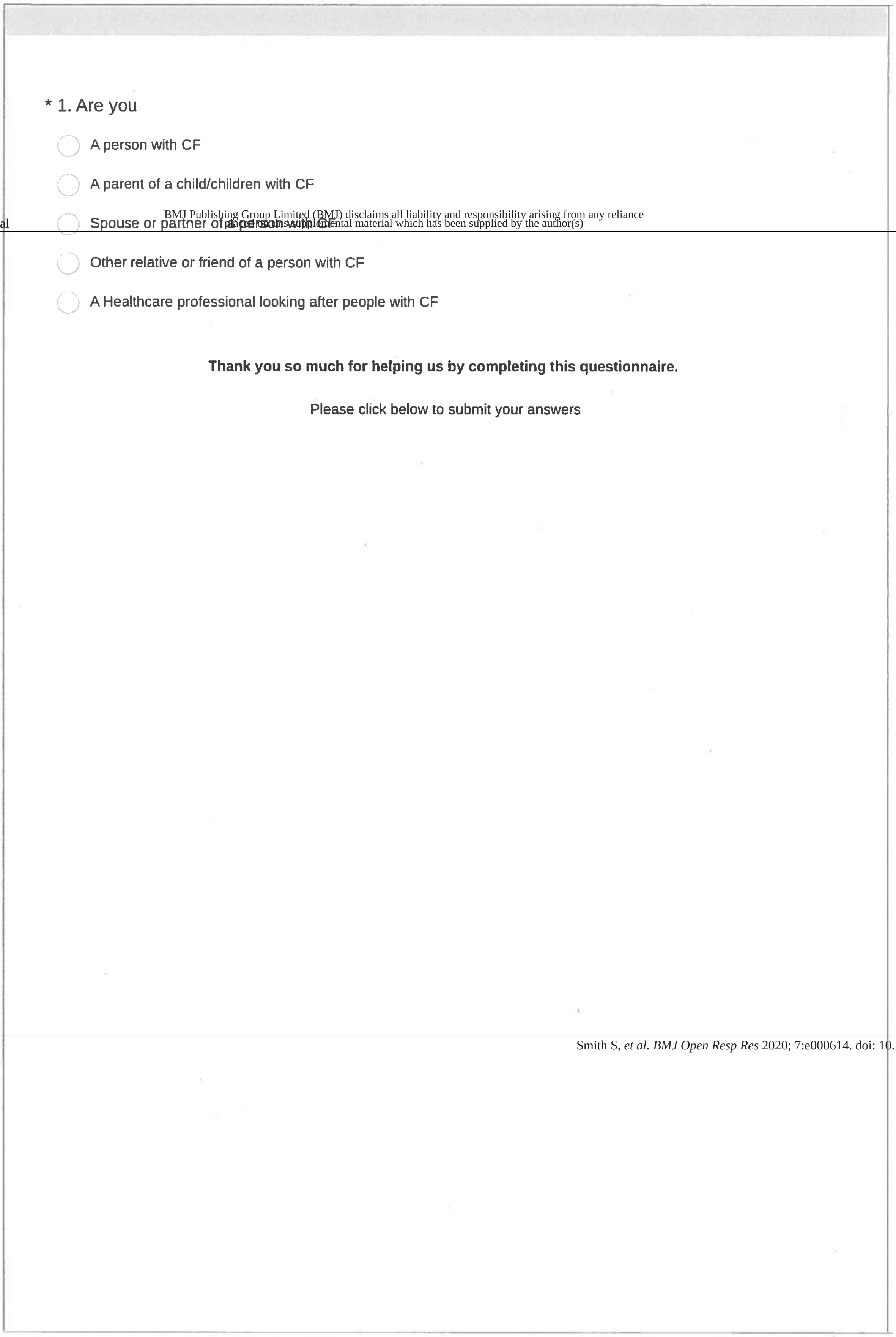
**This was recently chosen as one of the top 10 research questions to be answered by the CF community.**

**If you are a person with CF, a parent of children with CF or a Healthcare professional working with CF,  please help us make a start to answer this by taking part in the following questionnaire as honestly as you can.**

**Please be assured that this survey remains completely anonymous. This means that you will not be identifiable from the answers you provide. If you leave your contact details for further involvement activities these will be separated from your survey answers before they are looked at.**

**Many thanks,**

**The Evidence Based Child Health Team at The University of Nottingham, UK**



* 1. Are you

○ A person with CF

○ A parent of a child/children with CF

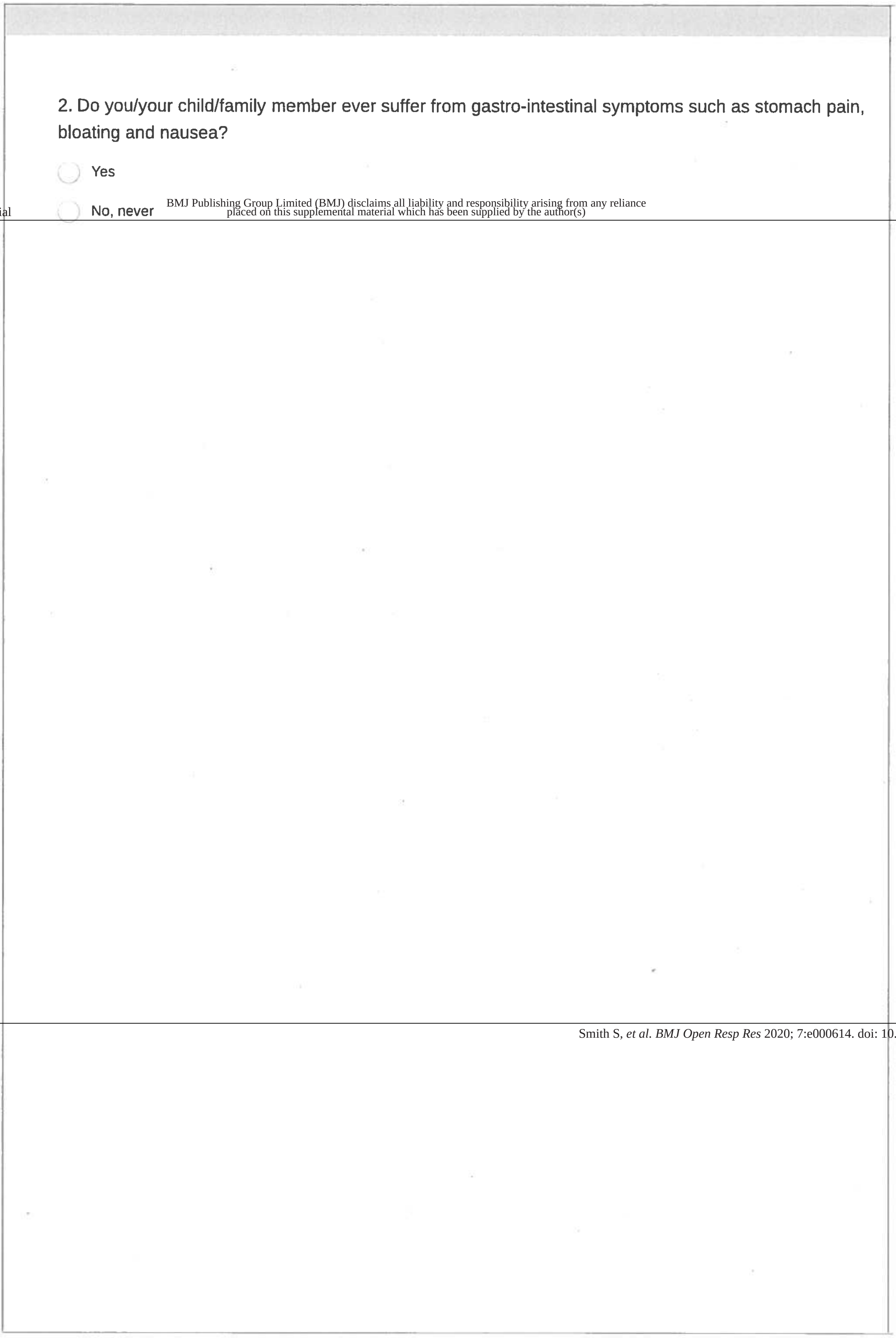
○ Spouse or partner of a person with CF

○ Other relative or friend of a person with CF

○ A Healthcare professional looking after people with CF

**Thank you so much for helping us by completing this questionnaire.**

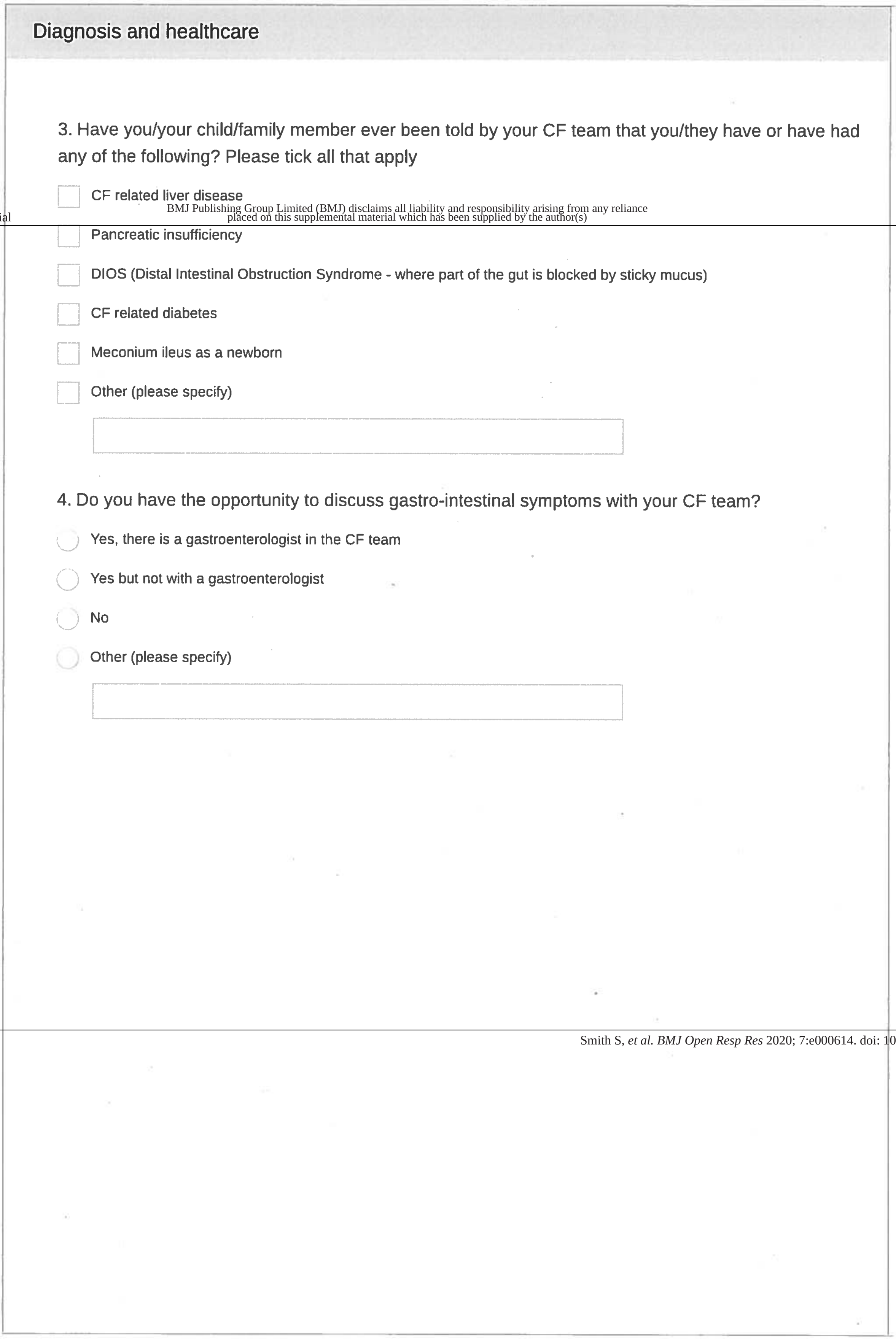
Please click below to submit your answers



2. Do you/your child/family member ever suffer from gastro-intestinal symptoms such as stomach pain, bloating and nausea?

○ Yes

○ No, never



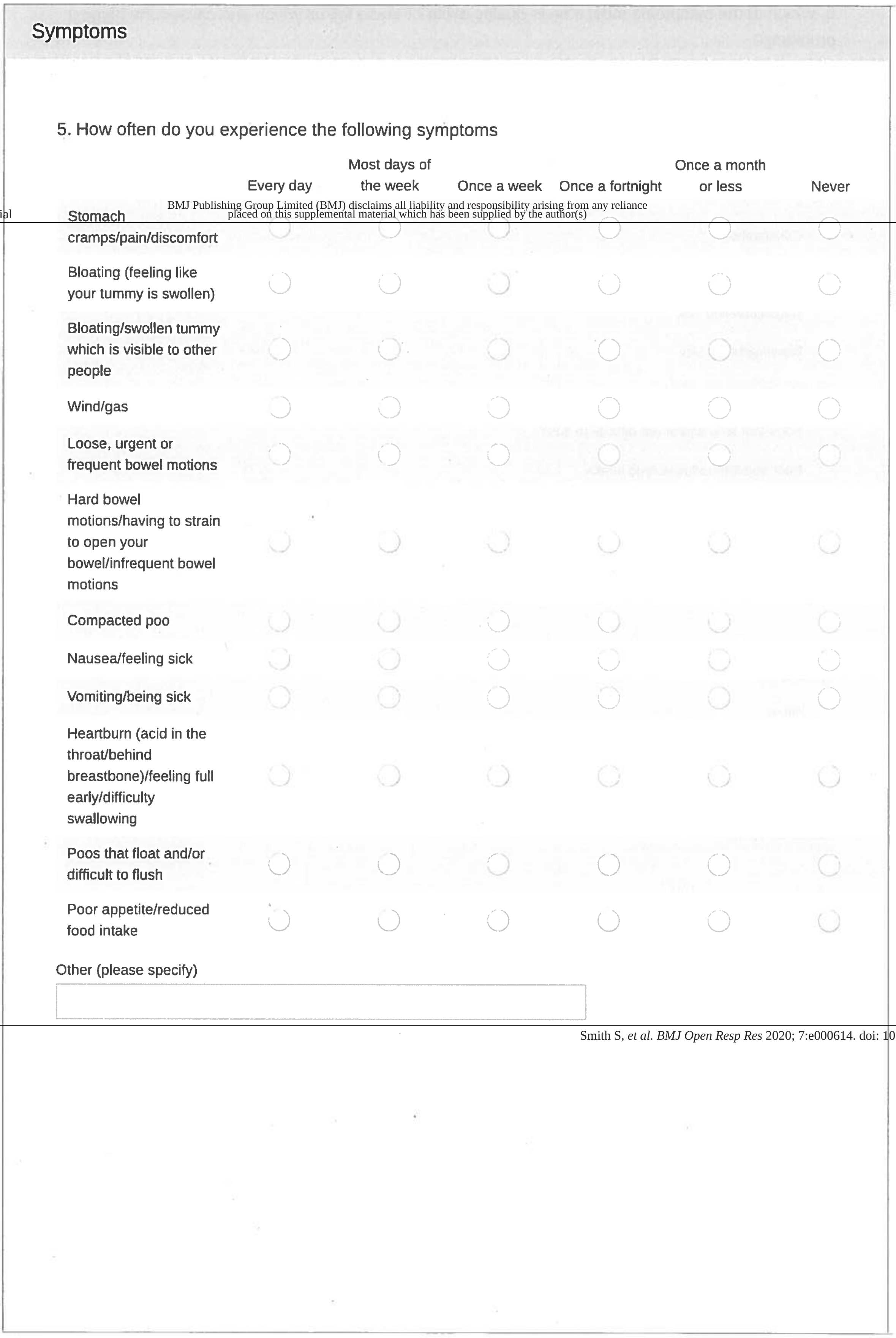
## Diagnosis and healthcare

3. Have you/your child/family member ever been told by your CF team that you/they have or have had any of the following? Please tick all that apply

☐ CF related liver disease
☐ Pancreatic insufficiency
☐ DIOS (Distal Intestinal Obstruction Syndrome - where part of the gut is blocked by sticky mucus)
☐ CF related diabetes
☐ Meconium ileus as a newborn
☐ Other (please specify)

4. Do you have the opportunity to discuss gastro-intestinal symptoms with your CF team?

○ Yes, there is a gastroenterologist in the CF team
○ Yes but not with a gastroenterologist
○ No
○ Other (please specify)



## Symptoms

5. How often do you experience the following symptoms

| | Every day | Most days of the week | Once a week | Once a fortnight | Once a month or less | Never |
|---|---|---|---|---|---|---|
| Stomach cramps/pain/discomfort | ○ | ○ | ○ | ○ | ○ | ○ |
| Bloating (feeling like your tummy is swollen) | ○ | ○ | ○ | ○ | ○ | ○ |
| Bloating/swollen tummy which is visible to other people | ○ | ○ | ○ | ○ | ○ | ○ |
| Wind/gas | ○ | ○ | ○ | ○ | ○ | ○ |
| Loose, urgent or frequent bowel motions | ○ | ○ | ○ | ○ | ○ | ○ |
| Hard bowel motions/having to strain to open your bowel/infrequent bowel motions | ○ | ○ | ○ | ○ | ○ | ○ |
| Compacted poo | ○ | ○ | ○ | ○ | ○ | ○ |
| Nausea/feeling sick | ○ | ○ | ○ | ○ | ○ | ○ |
| Vomiting/being sick | ○ | ○ | ○ | ○ | ○ | ○ |
| Heartburn (acid in the throat/behind breastbone)/feeling full early/difficulty swallowing | ○ | ○ | ○ | ○ | ○ | ○ |
| Poos that float and/or difficult to flush | ○ | ○ | ○ | ○ | ○ | ○ |
| Poor appetite/reduced food intake | ○ | ○ | ○ | ○ | ○ | ○ |

Other (please specify)

6. Which of the symptoms most affects quality of life? Please tell us which one causes the biggest problems?

○ Stomach cramps/pain
○ Bloating
○ Wind/gas
○ Diarrhoea
○ Constipation
○ Compacted poo
○ Nausea/feeling sick
○ Vomiting/being sick
○ Heartburn/indigestion
○ Poos that float and/or are difficult to flush
○ Poor appetite/reduced food intake
○ A combination of symptoms (please tell us more in the box below)

In what way(s) does this symptom affect your or your child's/family member's life?

7. Have you/your child/family member had to miss out on work, school or other activity because of this symptom?

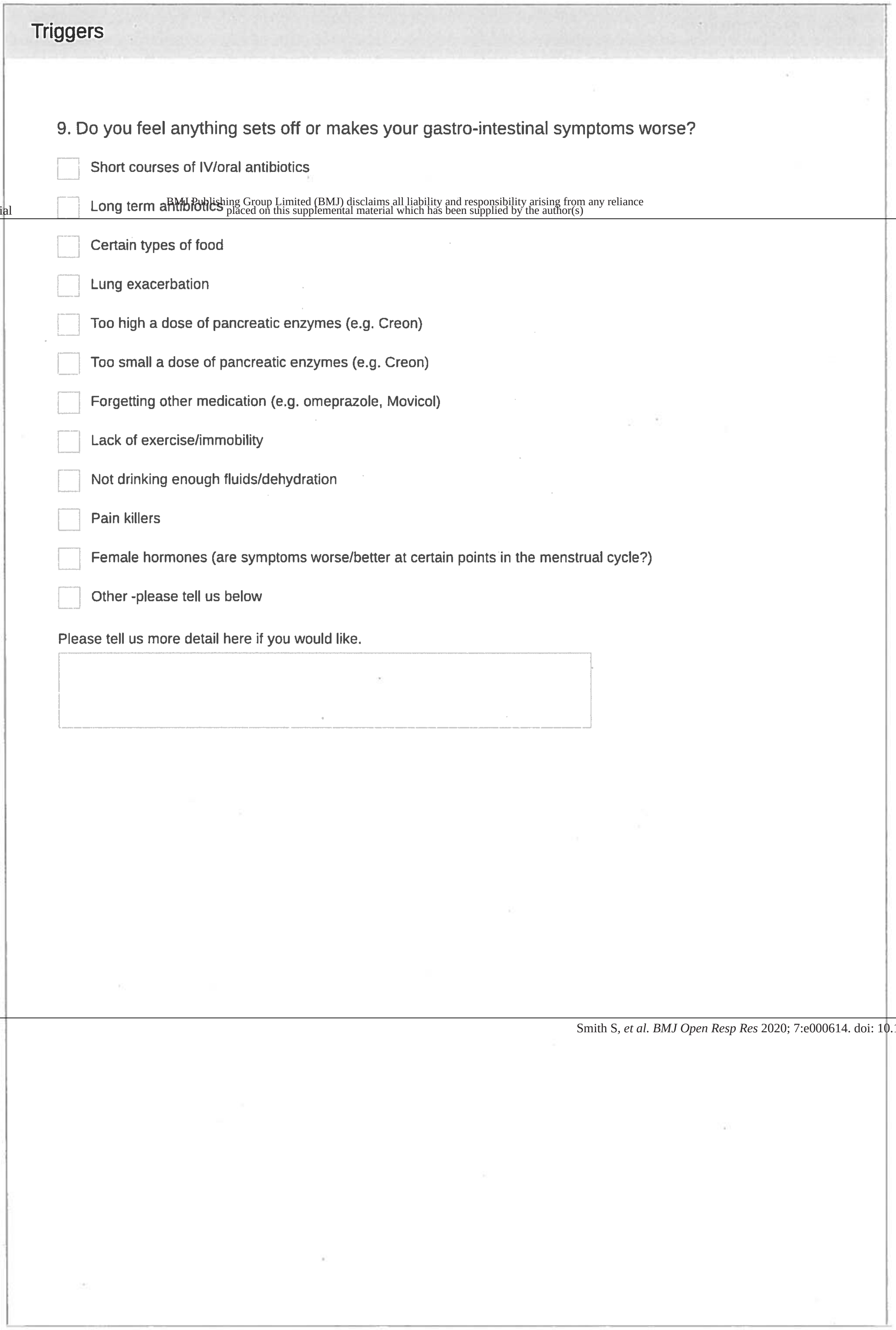
○ Often
○ Sometimes
○ Never

Please tell us more

8. Have any of these symptoms ever affected confidence or self-image?

○ Yes
○ No

*If yes, please help us understand by briefly explaining how.*



## Triggers

9. Do you feel anything sets off or makes your gastro-intestinal symptoms worse?

- ☐ Short courses of IV/oral antibiotics
- ☐ Long term antibiotics
- ☐ Certain types of food
- ☐ Lung exacerbation
- ☐ Too high a dose of pancreatic enzymes (e.g. Creon)
- ☐ Too small a dose of pancreatic enzymes (e.g. Creon)
- ☐ Forgetting other medication (e.g. omeprazole, Movicol)
- ☐ Lack of exercise/immobility
- ☐ Not drinking enough fluids/dehydration
- ☐ Pain killers
- ☐ Female hormones (are symptoms worse/better at certain points in the menstrual cycle?)
- ☐ Other -please tell us below

Please tell us more detail here if you would like.

## Relief of symptoms

10. Are symptoms relieved by any medication?

○ Yes

○ No

11. If so what do you find helps?

☐ Antacid medication (such as calcium carbonate tablets, Gaviscon, Maalox)

☐ Acid suppression medication (such as omeprazole, ranitidine)

☐ Anti-sickness (such as cyclizine, ondansetron, metaclopramide)

☐ Pancreatic enzymes (eg Creon)

☐ Laxatives (such as Movicol, sodium picosulphate)

☐ Other (please specify)

12. Are symptoms relieved by any non-medical interventions?

○ No

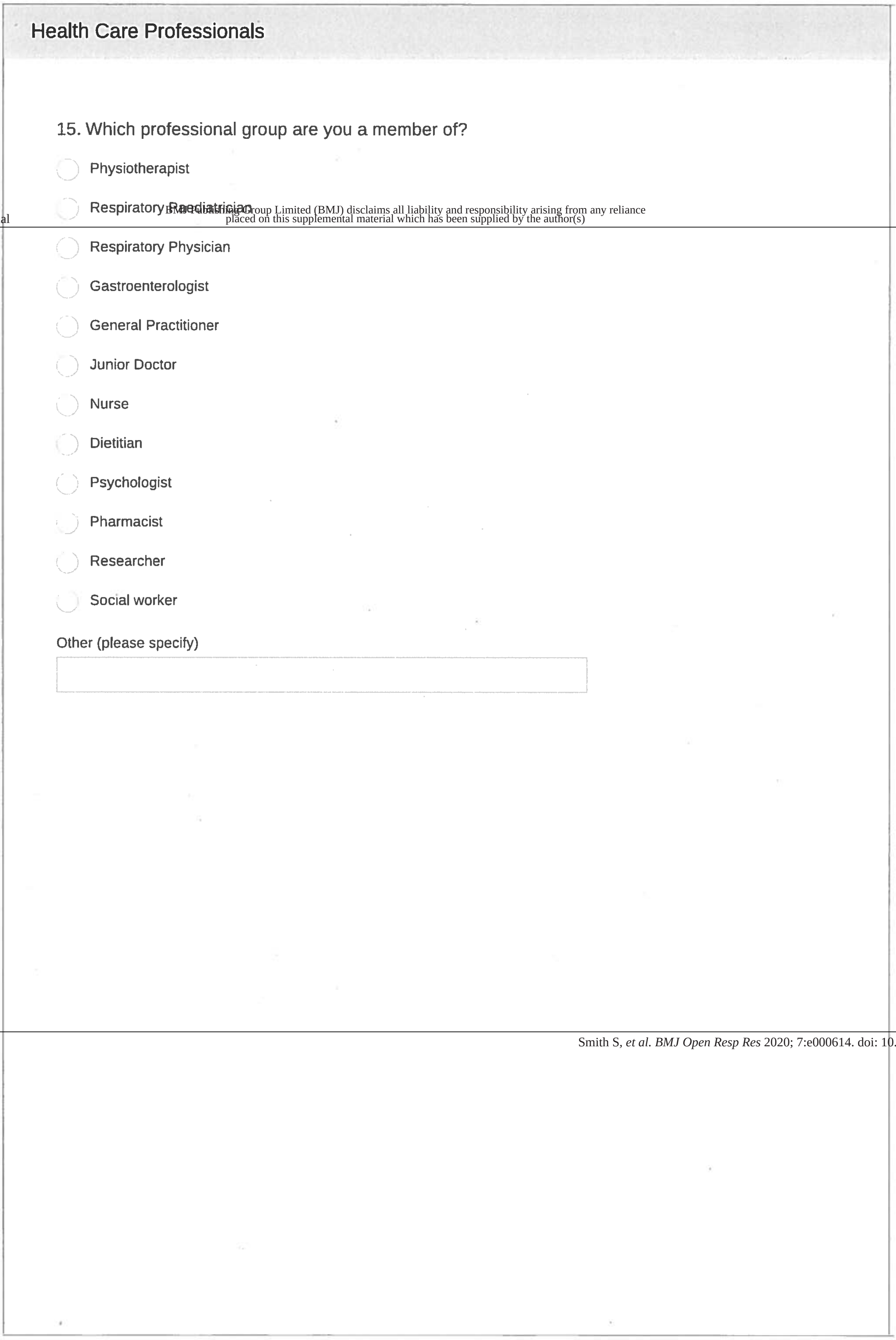
○ Diet

○ Exercise

Please tell us about anything else that helps

13. Are symptoms relieved by anything else e.g. live yoghurt, relaxation, mindfulness, drinking plenty water)?

14. Is there anything you/your child/family member do to help prevent symptoms?



## Health Care Professionals

15. Which professional group are you a member of?

○ Physiotherapist

○ Respiratory Paediatrician

○ Respiratory Physician

○ Gastroenterologist

○ General Practitioner

○ Junior Doctor

○ Nurse

○ Dietitian

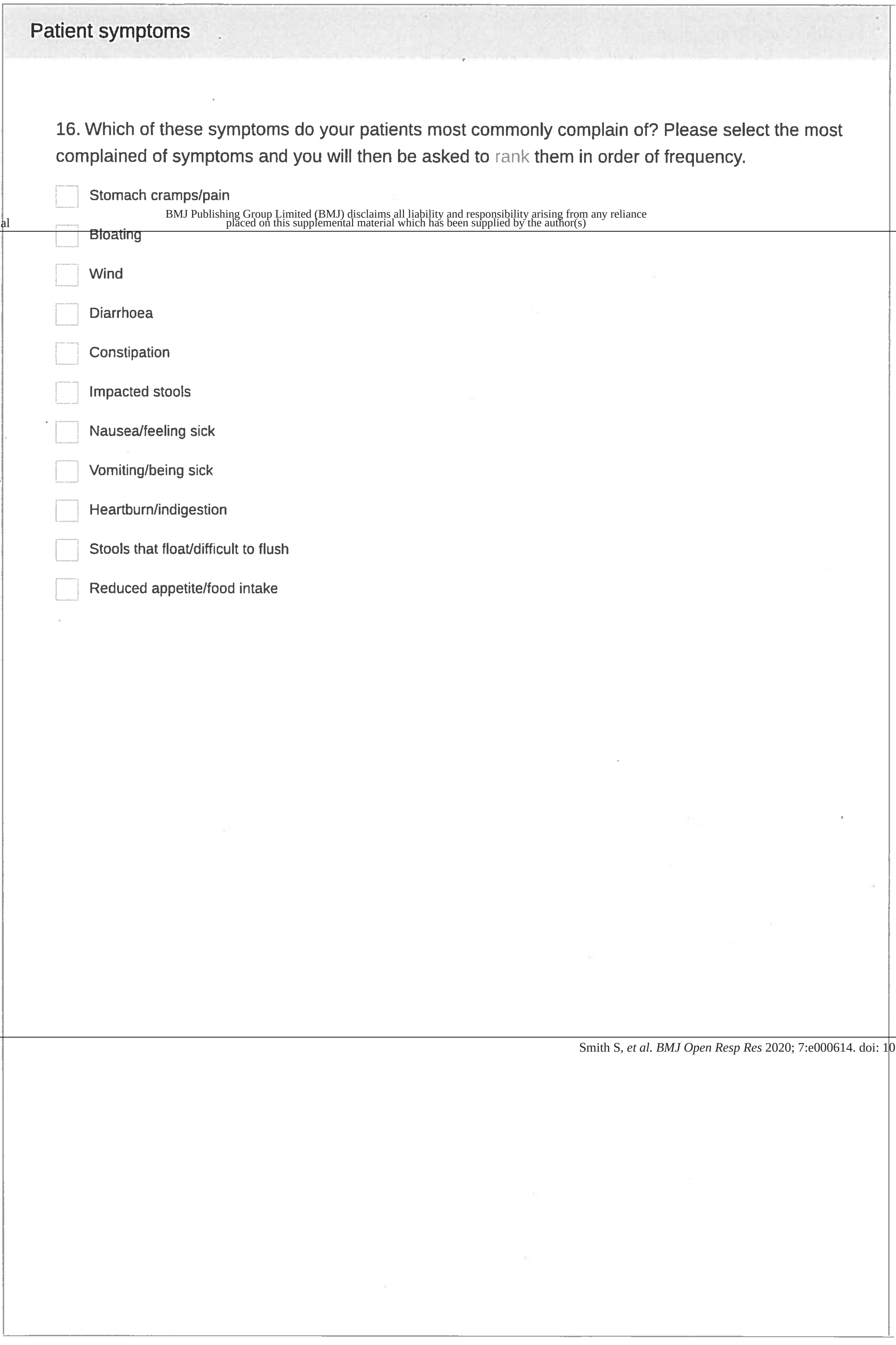
○ Psychologist

○ Pharmacist

○ Researcher

○ Social worker

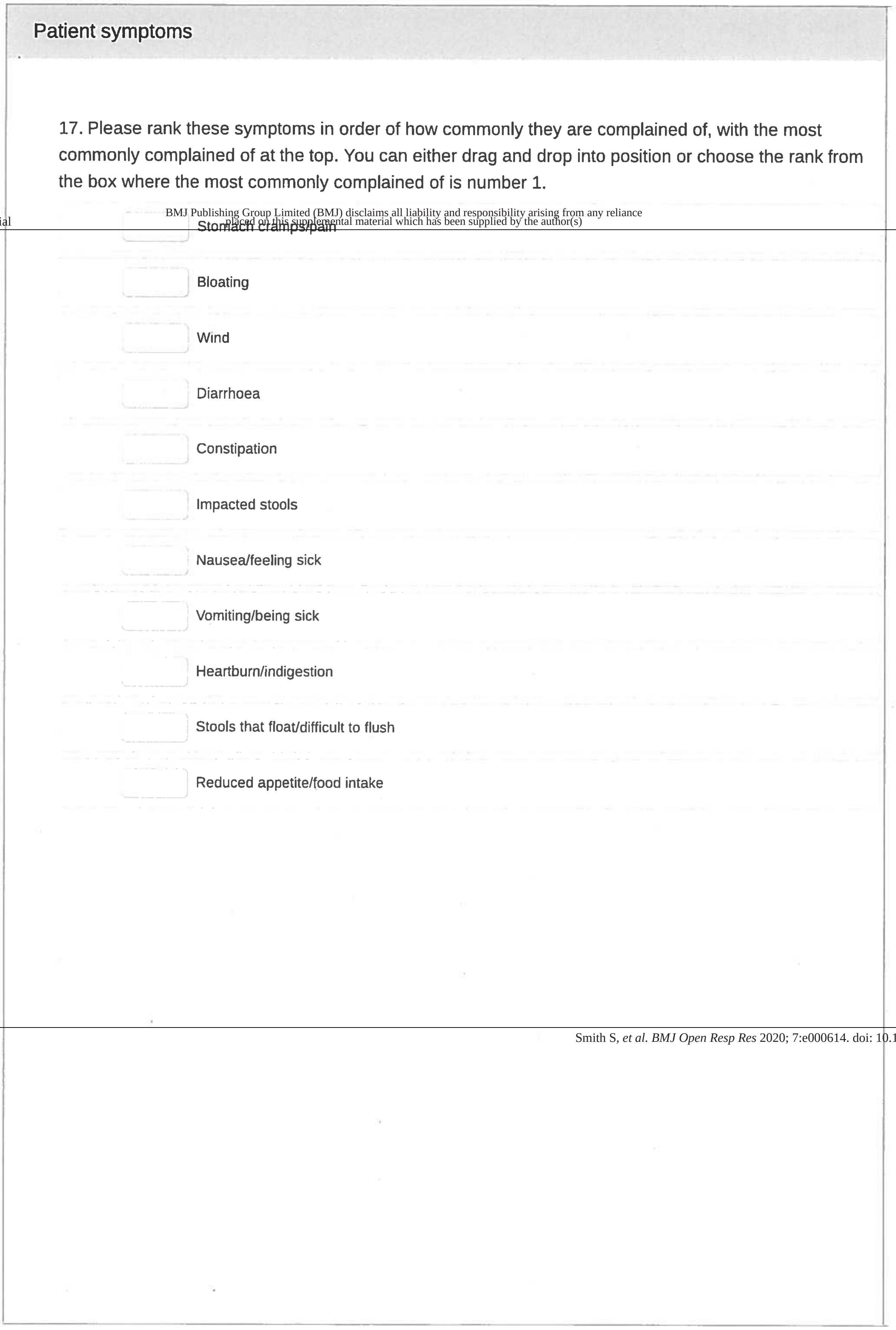
Other (please specify)



## Patient symptoms

16. Which of these symptoms do your patients most commonly complain of? Please select the most complained of symptoms and you will then be asked to rank them in order of frequency.

☐ Stomach cramps/pain
☐ Bloating
☐ Wind
☐ Diarrhoea
☐ Constipation
☐ Impacted stools
☐ Nausea/feeling sick
☐ Vomiting/being sick
☐ Heartburn/indigestion
☐ Stools that float/difficult to flush
☐ Reduced appetite/food intake



## Patient symptoms

17. Please rank these symptoms in order of how commonly they are complained of, with the most commonly complained of at the top. You can either drag and drop into position or choose the rank from the box where the most commonly complained of is number 1.

☐ Stomach cramps/pain

☐ Bloating

☐ Wind

☐ Diarrhoea

☐ Constipation

☐ Impacted stools

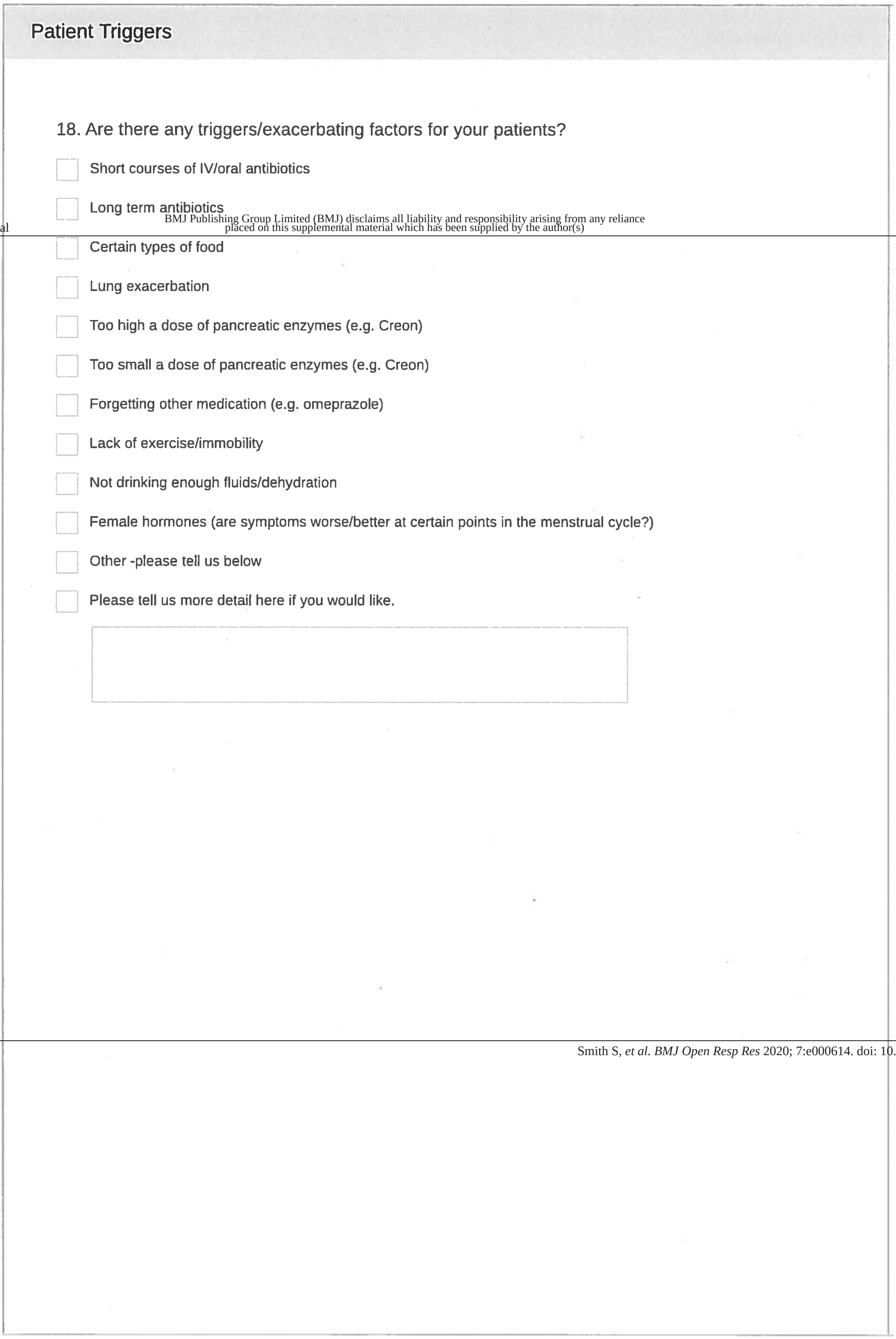
☐ Nausea/feeling sick

☐ Vomiting/being sick

☐ Heartburn/indigestion

☐ Stools that float/difficult to flush

☐ Reduced appetite/food intake



## Patient Triggers

18. Are there any triggers/exacerbating factors for your patients?

☐ Short courses of IV/oral antibiotics

☐ Long term antibiotics

☐ Certain types of food

☐ Lung exacerbation

☐ Too high a dose of pancreatic enzymes (e.g. Creon)

☐ Too small a dose of pancreatic enzymes (e.g. Creon)

☐ Forgetting other medication (e.g. omeprazole)

☐ Lack of exercise/immobility

☐ Not drinking enough fluids/dehydration

☐ Female hormones (are symptoms worse/better at certain points in the menstrual cycle?)

☐ Other -please tell us below

☐ Please tell us more detail here if you would like.

## Relief of symptoms for patients

19. Do you find any medication helps relieve your patients symptoms?

○ Yes

○ No

20. If so what do you find helps?

☐ Antacid medication (such as omeprazole)

☐ Anti-sickness (such as ondansetron, metoclopramide)

☐ Pancreatic enzymes (eg Creon)

☐ Laxatives

☐ Other (please specify)

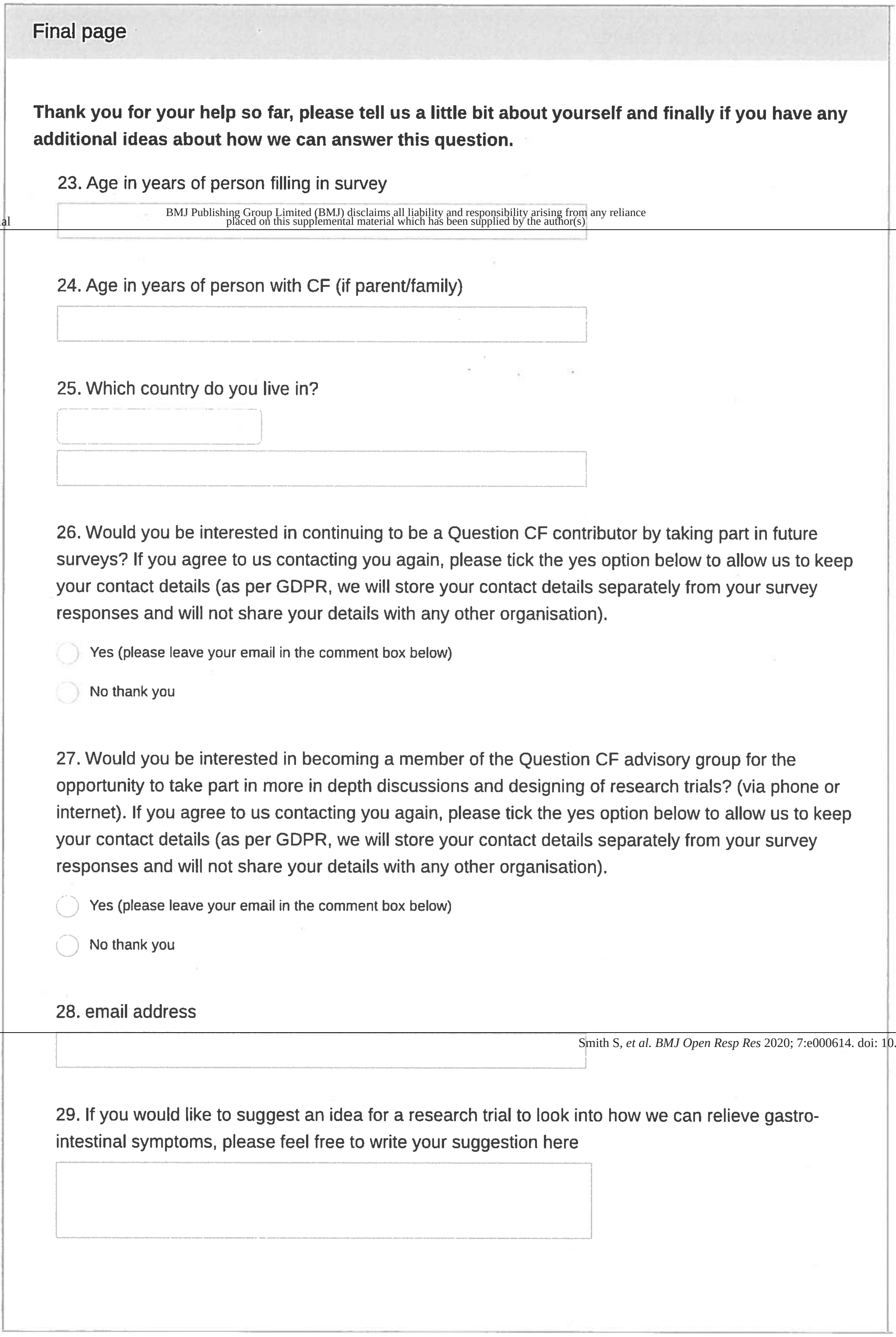
21. Do you find a certain type of diet or change in diet helps relieve symptoms?

○ Yes

○ No

Please let us know what helps

22. Please tell us if there anything else which helps to relieve symptoms.



## Final page

**Thank you for your help so far, please tell us a little bit about yourself and finally if you have any additional ideas about how we can answer this question.**

23. Age in years of person filling in survey

24. Age in years of person with CF (if parent/family)

25. Which country do you live in?

26. Would you be interested in continuing to be a Question CF contributor by taking part in future surveys? If you agree to us contacting you again, please tick the yes option below to allow us to keep your contact details (as per GDPR, we will store your contact details separately from your survey responses and will not share your details with any other organisation).

○ Yes (please leave your email in the comment box below)

○ No thank you

27. Would you be interested in becoming a member of the Question CF advisory group for the opportunity to take part in more in depth discussions and designing of research trials? (via phone or internet). If you agree to us contacting you again, please tick the yes option below to allow us to keep your contact details (as per GDPR, we will store your contact details separately from your survey responses and will not share your details with any other organisation).

○ Yes (please leave your email in the comment box below)

○ No thank you

28. email address

29. If you would like to suggest an idea for a research trial to look into how we can relieve gastro-intestinal symptoms, please feel free to write your suggestion here

## Thank you for your contribution, it is very much appreciated

please click below to submit your answers

Supplementary file 2. Number of responses to each question (see blank version of survey for questions).

| Question | Total no. responses | Applies to Lay (L) / Professional (P)/ All (A) | | Question | Total no. responses | Applies to Lay (L) / Professional (P)/ All (A) |
|---|---|---|---|---|---|---|
| 1 | 276 | A | | 25 | 233 | A |
| 2 | 168 | L | | 26 | 230 | A |
| 3 | 151 | L | | 27 | 225 | A |
| 4 | 155 | L | | 28 | 159 | A |
| 5 | 147 | L | | 29 | 27 | A |
| 6 | 146 | L | | | | |
| 7 | 147 | L | | | | |
| 8 | 147 | L | | | | |
| 9 | 139 | L | | | | |
| 10 | 141 | L | | | | |
| 11 | 106 | L | | | | |
| 12 | 136 | L | | | | |
| 13 | 70 | L | | | | |
| 14 | 74 | L | | | | |
| 15 | 104 | P | | | | |
| 16 | 99 | P | | | | |
| 17 | 94 | P | | | | |
| 18 | 93 | P | | | | |
| 19 | 90 | P | | | | |
| 20 | 87 | P | | | | |
| 21 | 88 | P | | | | |
| 22 | 29 | P | | | | |
| 23 | 225 | A | | | | |
| 24 | 93 | L | | | | |