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Data Availability Statement: Given the confidentiality of this clinical research, our ethics committee (Comité de Protection des Personnes) is preventing us from making our data set publicly available. However, we are willing to make our data available upon request as we consider that it is important for open and reproducible science, and thus we will ensure that all interested and qualified researchers will be able to be granted access. Furthermore, Anne Omnès (anne.omnes@chunantes.fr) is the contact for data requests and she will able to approve and distribute our data upon request. **RESEARCH ARTICLE**

Desire for a child and eating disorders in women seeking infertility treatment

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Abstract

Objectives

The purpose of this study was to evaluate the prevalence of EDs in women seeking treatment for infertility, and to better characterize their clinical profile.

Study design

Sixty participants completed self-report measures that assessed EDs, desire for a child, body preoccupations, quality of life, anxiety and depression.

Results

Ten patients (17%) met criteria for a past or current ED. We showed a significant association between greater body dissatisfaction and a more ambivalent desire for a child. Furthermore, an ED was associated with (i) a lower quality of life, and (ii) more anxiety disorders.

Conclusion

Screening for a history of ED in infertile women is recommended to plan for adapted care regarding infertility but also regarding ED and psychiatric comorbidities. Therefore, the assessment has to take into account the desire for a child and the body satisfaction, that are essential parts of the ED process on the one hand and infertility process on the other. This could help with the infertility treatment and the prevention of negative maternal and fetal outcomes.

Introduction

Eating disorders (EDs) are severe illnesses affecting particularly adolescent females and young women of childbearing age. Many negative consequences, such as infertility, can result. Infertility also seems to be a symptom through which we could identify these women suffering **Funding:** The authors received no specific funding for this work.

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from undiagnosed EDs. Indeed, the eating behavior of infertile women appears to be more disturbed than in general population [1]. Little scientific studies have been done on EDs in women seeking infertility treatment. The prevalence of current or past ED was estimated between 7.6% and 16% regarding clinical EDs (Anorexia nervosa: AN; Bulimia nervosa: BN). If subclinical ED was included, the prevalence reached 16.7% to 44% [2–4]. A recent research determined the prevalence of EDs in samples of infertile women. Authors found that 20.7% of the participants met criteria for a current or past ED, which is five times higher than the US lifetime prevalence [4]. At the opposite, a recent study did not confirm a greater lifetime prevalence of EDs in women seeking infertility treatment compared to the Australian community rate [5], and another one concluded that the EDs prevalence was lower among Danish women with assisted reproductive technology treatment compared to the background population [6]. However, due to methodological differences, we cannot compare these studies.

Some pathophysiological mechanisms explaining infertility in women with EDs are well known. They have endocrine dysfunctions, affecting sex hormones levels and fertility. The functional amenorrhea is frequently secondary and reversible [7,8]. Amenorrhea could occur before the onset of significant weight loss (20–25%), during the course of dieting (50–75%), more rarely after more marked weight loss [7–9], and can persist after the weight gain. Women with BN receive infertility treatment more often than those without EDs [2,10]. Furthermore, EDs could be a consequence of infertility, due to hormonal medication, to low selfesteem or to problems in the couple. A clear association between reduced body weight and amenorrhea exists but the notion of a required critical percentage of body fat for normal menses has not been supported by empirical evidence. Thus, other factors also contribute to the development of amenorrhea [11]. Indeed, the literature on leptin provides an explanation regarding the links between the human reproduction axis and the nutrient status [10,11]. Some other neurotransmitters are involved such as beta-endorphins and ghrelin [12] or those from the corticotropic axis [13]. Furthermore, it is important to remind that patients with AN may ovulate and become pregnant despite their amenorrhea [8]. Thus, if some pathophysiological mechanisms may partially explain the link between EDs and infertility, some others remain not well understood.

A study of 151 patients with a former diagnosis of AN and with a desire for a child carried out during their follow-up, 12.5 years after hospital contact, highlighted that the difference of infertility rates could be explained by a desire for a child less present or more ambivalent [14]. Very few studies exist on the desire for a child, and more particularly in infertile women. However, we know the importance of conflict issues that may be reactivated by motherhood, in a context of EDs psychopathology. The desire for a child should be taken into account upstream of motherhood in order to prevent pregnancy as well as neonatal complications [15], to give adapted care, and also to prevent a relapse or an aggravation of an ED. Other dimensions, at the interface between infertility and EDs, should be taken into account, such as body/weight preoccupations, anxiety and depression.

Thus, the primary objective of the present study was to evaluate the prevalence of EDs in women seeking treatment for infertility. Secondly, it aimed at studying the clinical differences between infertile women with or without ED, in order to better characterize their profile regarding the desire for a child, body preoccupations, quality of life (QoL), anxiety and depression.

Materials and methods

Recruitment and procedures

Data were collected in the Reproductive Medicine Department at the Nantes University Hospital (France). All French-speaking women seeking treatment for infertility from the first January to the 31th of December 2014 were eligible. Exclusion criteria consisted in exclusive male infertility, pregnancy during the assessment, mental retardation, severe psychiatric conditions and protected adult. The local Research Ethics Committee (Comité de Protection des Personnes) approved this cross-sectional study, and all participants provided written informed consent.

Each participant was given a self-report questionnaire by the reproductive health care provider. The questionnaire was presented as a study regarding the desire for a child (common feature for all those patients) and EDs. Patients were also told that the research might involve a short one-time telephone interview if a current or past ED was screened—based on the SCOFF test, the lowest Body Mass Index (BMI) below or equal to 18.5 kg/m², or a disclosure of a history of ED to confirmed or not the diagnosis. This type of interview was preferred to a face-toface interview in order to decrease constraints for patients and study's cost and to favor its feasibility. If the diagnosis was confirmed, the investigator suggested the woman to disclose it to her reproductive health care provider or her general practitioner.

First step of the assessment: Pen-and-paper questionnaire

Socio demographics characteristics. We collected information about age, marital status, level of education, professional status.

Eating patterns: Screening for ED. Patients were asked about the history of BMI, of a treatment for ED and of amenorrhea or spaniomenorrhea.

The SCOFF (Sick-Control-One-Fat-Food) was used to screen for EDs [16–19]. This questionnaire with dichotomous answers assessed the main characteristics of EDs: intentional vomiting, loss of control over food, unhealthy weight loss, body image disturbance, and intrusive food thoughts. If two or more answers were positive, then an ED was suspected. This cutoff resulted in a sensibility of 94.6% and a specificity of 94.8% for SCOFF-F (French version). In addition, an area under the ROC curve of 96% confirmed an elevated level of accuracy. SCOFF-F was accurate and reliable for the quick and easy detection of patients with EDs in a French-speaking female student population [19].

Desire for a child

The FKW (Fragebogen zum kinderwunsch) questionnaire was designed to identify expectations and apprehensions related to pregnancy, birth and parenthood, using 20 rating questions (1 = not at all, 5 = very true) [20]. A global score was calculated and three dimensions were evaluated: (a) enhancement of self-esteem, (b) emotional stabilization, (c) ambivalence. This questionnaire has already been used in infertile women [21].

Body image concerns

The BSQ (Body Shape Questionnaire) is a self-questionnaire evaluating weight and shape preoccupations. The score ranges from 34 to 204 and a score higher than 140 indicates a major concern for weight and/or shape [22, 23]. A factor analysis generated four factors: "social avoidance and shame of the exposure of the body", "body dissatisfaction compared to the lower parts of the body", "using laxatives and vomiting in order to reduce body dissatisfaction", "unsuited cognitions and behaviors in order to control the weight".

Anxiety and depression

The Hospital Anxiety and Depression Scale (HAD) consists of two sub-scales which evaluate anxiety (HAD-A) and depression (HAD-D), based on fourteen items, firstly in a dimensional approach to get a global score. Secondly, in a categorical approach, we obtained three

categories of severity score for each sub-scale: a score below or equal to 7 indicating "normal level", a score between 8 and 10 meaning "borderline abnormal level", and a score above or equal to 11 suggesting "abnormal level" [24].

Quality of life

The FertiQol aims to measure QoL in people experiencing fertility problems. We used the 24 items assessing the core of QoL (which consists of the four dimensions: "emotional", "mind/ body", "relational", "social"), as well as overall life and physical health (2 items) [25].

Second step of the assessment: Diagnosis of ED with a structured telephone interview

We performed a clinical interview using the DSM-IV diagnostic criteria for AN, BN and BED, and partly based on the MINI (Mini International Neuropsychiatric Interview), which is a structured interview aiming to assess axis 1 psychiatric disorders.

Statistical analysis

EDs prevalence was determined using the participants' diagnoses from the MINI Module H. The entire sample was divided in two groups: "ED" (current or past) and "no-ED" group. We decided to pool patients with current and past ED into a single group as ED are long-standing disorders and relapses are prevalent, as well as underlying ongoing vulnerability. Furthermore, pooling those patients enabled us to have larger groups to facilitate statistical analyses.

Descriptive statistics were applied to describe and summarize the entire sample then the two groups, for each variable regarding socio demographic, infertility and eating characteristics.

We performed comparison tests based on ED groups for those variables. Chi-square comparisons were run for each qualitative variable (or Fisher's exact test if expected frequencies were lesser than 5 in one of the modalities). Mann-Whitney test was used for each quantitative variable. The type I error was set at 5%.

Then, we run a model for each following variables: desire for a child, QoL, anxiety and depression, body preoccupations. To do so, we performed univariate analyses with linear regressions for quantitative variables and logistic regressions for qualitative variables in order to select variables to include in multiple regressions, with a threshold set at 25%. Afterwards, we performed multiple regressions using a backward selection with selected variables. Linear regressions for quantitative variables and logistic regressions for qualitative variables. Linear regressions for quantitative variables and logistic regressions for qualitative variables. Linear regressions for quantitative variables and logistic regressions for qualitative variables were conducted. The type I error was set at 5%.

Data were analyzed using Stata v13 (Stata Corp, College Station, Texas, 2014).

Results

Out of the 71 participants included in the study, 60 (85%) returned their self-report questionnaire.

Prevalence of EDs in infertile women

Out of the 60 participants, 19 (32%) had a telephone interview, among which 10 women (17%) met the criteria for a current or past ED. Five patients (8%) met criteria for a past AN, one patient for a current AN, two patients for a past BN, one patient for a current BN, and one patient for a past BED.

Comparisons between "ED" and "No-ED" groups

Socio-demographic characteristics. We have not found any significant differences between the two groups regarding sociodemographic characteristics, current and ideal BMI, and history of amenorrhoea or spaniomenorrhea (Table 1).

Desire for a child. The desire for a child was not significantly associated to whether the patient suffered from an ED or not, either with the univariate analysis (Table 2) or after adjustment with the multiple regressions presented in Table 3. However, according to the multiple regression for the global score, the higher the BMI, the higher the desire for a child global score was. Furthermore, the dimension "ambivalence" was significantly associated to the BSQ score: the higher the BSQ score, the more the woman's desire for a child was ambivalent. Similarly, the lower the BMI, the more the woman's desire for a child was ambivalent. In addition, a higher BSQ score was significantly associated to a higher FKW score regarding the two other dimensions: "enhancement of self-esteem" and "emotional stabilization".

| Table 1. Comparaison of "ED" and "No ED" groups, accord | ing to the sociodemographic | , infertility and eating characteristics. |
|---|-----------------------------|---|
|---|-----------------------------|---|

| | N (%) or m (+/- sd) | | | | | |
|--|--------------------------|------------------|---------------------|---------|--|--|
| Variables | Total sample (n = 60) | "ED" (n = 10) | "No ED" (n = 50) | p-value | | |
| Age | 32 (+/-4) | 31 (+/-4) | 32 (+/-4) | 0.40 | | |
| Level of education | | | | | | |
| <12 years | 12 (30%) | 3 (30%) | 9 (18%) | 0.64 | | |
| >12 years | 42 (70%) | 6 (60%) | 36 (72%) | | | |
| Current professional status | | | | | | |
| Active | 53 (88%) | 9 (90%) | 44 (88%) | 1 | | |
| Inactive | 7 (12%) | 1 (10%) | 6 (12%) | | | |
| Children | | | | | | |
| no | 43 (72%) | 8 (80%) | 35 (70%) | 0.71 | | |
| yes | 17 (28%) | 2 (20%) | 15 (30%) | | | |
| Period of infertility treatment | | | | | | |
| First referring | 4 (6%) | 0 (0%) | 4 (8%) | 0.51 | | |
| < 1 year | 16 (27%) | 1 (10%) | 15 (30%) | | | |
| 1< <2 years | 16 (27%) | 4 (40%) | 12 (24%) | | | |
| > 2 years | 24 (40%) | 5 (50%) | 19 (38%) | | | |
| History of amenorrhea or spaniomenorrhea | | | | | | |
| yes | 25 (42%) | 6 (60%) | 19 (38%) | 0.30 | | |
| no | 35 (58%) | 4 (40%) | 31 (62%) | | | |
| Current BMI | 24.4 (+/-5.38) | 23.3 (+/-6.9) | 24.6 (+/-5.1) | 0.11 | | |
| Ideal BMI | 21.8 (+/-2.9) | 21.5 (+/-4.6) | 21.8 (+/- 2.4) | 0.13 | | |
| History of BMI < or = 18.5 | | | | | | |
| yes | 19 (32%) | 7 (70%) | 12 (24%) | <0.01 | | |
| no | 41 (68%) | 3 (30%) | 38 (76%) | | | |
| Screening test SCOFF | | | | | | |
| Positive | 7 (12%) | 6 (60%) | 1 (2%) | <0.001 | | |
| Negative | 53 (88%) | 4 (40%) | 49 (98%) | | | |
| | | | | | | |

n: number; m: mean; sd: standard deviation;ED: eating disorder; BMI: body mass index (kg/m²); p-value(Mann-Whitney test for quantitative variables, Fischer test for qualitative variables) bold p-value: significant with a threshold at 0.05

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| | N (%) or m (+/-sd) | | | | |
|------------------------------------|--------------------------|------------------|---------------------|---------|--|
| Variables | Total sample (n = 60) | "ED" (n = 10) | "No ED" (n = 50) | p-value | |
| Global score | 34.7 (+/-6.9) | 36.0 (+/-5.9) | 34.4 (+/-7.1) | 0.53 | |
| "Enhancement of self-esteem" score | 27.7(+/-5.4) | 28.1(+/-5.3) | 27.6 (+/-5.4) | 0.73 | |
| "Emotional stabilization" score | 20.9 (+/-3.2) | 22.1(+/-3.3) | 20.7(+/-3.2) | 0.20 | |
| "Ambivalence" score | 13.9 (+/-4.3) | 14.2 (+/-6.0) | 13.9 (+/-4.0) | 0.99 | |

Table 2. Comparison of "ED" and "no ED" groups, according to the desire for a child assessed with the FKW questionnaire (global score and three dimensional scores).

n: number; m: mean; sd: standard deviation; ED: eating disorder; p-value(Mann-Whitney test for quantitative variables)

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Anxiety and depression. The anxiety global score was significantly higher in the ED group than in the no-ED group, contrary to the depression global score that was not significantly different depending on the groups. However, the percentage of depression "borderline abnormal level" was more important in the ED group than in the no-ED group (results not shown).

Quality of life. Our univariate analysis indicated a lower QoL score in women suffering from EDs, and more particularly regarding the "emotional" and "mind/body" scores (results not shown). Multiple regressions for the 4 dimensions of the quality of life, presented in the Table 4, highlighted that the "emotional" score was lower if the anxiety, QoL depression score and the FKW "emotional stabilization" scores were higher. Furthermore, the "mind/body" scores was lower when the anxiety score or the age was higher. Moreover, the "relational" and "social" scores were associated with the depression score. Finally, patients with EDs tended to have significantly a lower QoL, more particularly in the dimensions "emotional" and "mind/body", independently of depression or anxiety, whereas there is no significant association between having an ED and the dimensions "relation" and "social" of the quality of life.

| Variables | Coefficient ß | SE | P-value | [CI-95%] | |
|--|------------------------------|------------------------------------|---------------|--------------|--|
| Multiple regression 1: "Desire for a child" global score (R ² adjusted = 0.15) | | | | | |
| Current BMI | 0.53 | 0.216 | 0.001 | [0.22–0.85] | |
| ED | 2.32 | 2.23 | 0.302 | [-2.14–6.78] | |
| | Multiple regression 2: "Ambi | valence" score (R ² adj | usted = 0.24) | | |
| BSQ score | 0.10 | 0.02 | <0.001 | [0.05–0.14] | |
| Current BMI | -0.41 | 0.11 | <0.001 | [-0.630.18] | |
| ED | -2.72 | 1.46 | 0.068 | [-5.65–0.21] | |
| Multiple regression 3: "Emotional stabilization" score (R ² adjusted = 0.27) | | | | | |
| BSQ score | 0.05 | 0.01 | 0.001 | [0.02–0.08] | |
| QoL «emotional» score | -0.17 | 0.08 | 0.031 | [-0.330.02] | |
| ED | -0.93 | 1.13 | 0.412 | [-3.201.33] | |
| Multiple regression 4: "Enhancement of self-esteem" score (R ² adjusted = 0.15) | | | | | |
| BSQ score | 0.08 | 0.02 | <0.001 | [0.04–0.13] | |
| ED | -1.61 | 1.82 | 0.380 | [-5.27–2.04] | |

Table 3. Multiple regressions based on the desire for a child assessed with the FKW questionnaire (global score and three dimensional scores).

ED: eating disorder; BMI: body mass index (kg/m²); BSQ: body shape questionnaire; QoL: quality of life SE: standard error; [CI-95%]: 95% confidence interval; bold p-value: significant with a threshold at 0.05 R² adjusted: adjusted multiple correlation coefficient (=the percent of variance explained by covariates)

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| Variables | Coefficient ß | SE | P-value | [CI-95%] | | |
|--|---------------|-----|---------|-------------|--|--|
| Multiple regression 1: "Emotional"score (R ² adjusted = 0.60) | | | | | | |
| Anxiety score | -0.6 | 0.2 | 0.001 | [-0.80.3] | | |
| Depression score | -0.4 | 0.2 | 0.042 | [-0.800.01] | | |
| ED | -4.0 | 1.3 | 0.003 | [-6.51.5] | | |
| Desire for a child—Dimension "emotional stabilization" | -0.4 | 0.1 | 0.013 | [-0.70.1] | | |
| Multiple regression 2: "Mind/body" score (R ² adjusted = 0.55) | | | | | | |
| ED | -5.0 | 1.2 | <0.001 | [-7.52.5] | | |
| Having at least one child | 2.7 | 1.1 | 0.016 | [0.5–4.9] | | |
| Age | -0.3 | 0.1 | 0.009 | [-0.50.1] | | |
| Anxiety score | -0.8 | 0.2 | <0.001 | [-0.80.2] | | |
| Multiple regression 3: "Relational" score (R ² adjusted = 0.20) | | | | | | |
| Depression score | -0.5 | 0.2 | 0.002 | [-0.80.2] | | |
| ED | -2.3 | 1.2 | 0.072 | [-4.8–0.21] | | |
| Multiple regression 4:"Social" score (R ² adjusted = 0.37) | | | | | | |
| Depression score | -1.0 | 0.2 | <0.001 | [-1.40.7] | | |
| ED | -2.8 | 1.5 | 0.06 | [-5.70.1] | | |

Table 4. Multiple regressions based on the quality of life in infertile women assessed with the questionnaire FertiQoL (four dimensional scores).

ED: eating disorder; BMI: body mass index (kg/m²); SE: standard error; [CI-95%]: 95% confidence interval; bold p-value: significant with a threshold at 0.05; R² adjusted: adjusted multiple correlation coefficient (=the percent of variance explained by covariates)

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Discussion

The purpose of this study was to estimate the prevalence of EDs in women seeking treatment for infertility and to characterize their clinical profile. We reported 17% of participants meeting criteria for a past or current ED, corresponding to more than the prevalence in general population, which is estimated in literature from 1 to 4% [26, 27]. Our result was pretty close to those found in literature, in particular to the study of Freizinger et al. [4]. Seventy percent of the patient in the ED group reported a BMI in the normal range. However, participants' BMI may have been lower at the beginning of the infertility treatment. Indeed, two-thirds of our sample had been treated for infertility for over a year, and such treatment may contribute by itself to an increase of weight. Furthermore, reproductive health professionals could have given advice to patients on nutrition, which modified their eating behaviors. Almost one quarter of our participants were overweight and 15% obese. These results are in line with those obtained by Rodino et al. [28]. As previously reported, a high BMI does not automatically indicate a BED [4].

To our knowledge, no study has been conducted on the desire for a child in infertile women based on the presence of ED or not. Some studies focused on the desire for a child in infertile women without taking into account EDs [21, 29]. Another study evaluated the desire for a child in students with a different questionnaire, taking into account EDs. It has been shown that the desire for a child in AN women is significantly lower than in students without ED or in BN women [30]. Our study cannot emphasize any significant difference between the ED and non-ED group regarding the desire for a child. However, we highlighted a significant association between the desire for a child and (i) weight/shape preoccupations and (ii) current BMI, which are important variables in women with EDs. Indeed, a woman greatly concerned about her weight/shape or having a low BMI tends to have a more ambivalent desire for a child.

Furthermore, anxiety in infertile women was more frequent in the ED group than in the non-ED group. The literature suggests that infertile women tend to have more often psychiatric disorders than fertile women [21, 31–33].

Finally, infertility is linked to the QoL. Several studies reported the negative impact of infertility on mental and social health [34–36]. The assessment of QoL and its evolution became important during the infertile women's care. Moreover, EDs are an important cause of physical and psychosocial morbidity in young women [37], and consequently impact the QoL, and more particularly mental health. It has been noticed in the literature that a general trend for greater levels of comorbid pathologies is linked to higher ED symptoms' severity, and women suffering from subclinical EDs appear to be more affected than women without EDs. These high levels of comorbid psychiatric symptoms negatively affect QoL, with the greatest prevalence in AN or BN [38]. Interestingly, this present study has originally attempted to link QoL, infertility, and EDs by considering anxiety and depression that were associated with a lower QoL. We highlighted the association between EDs and infertile women's QoL, independently of the presence of anxiety or depression, by insisting on the "emotional" and "mind-body" dimensions.

It is worth reporting that the assessment of the sexuality in infertile women is clearly important since the sexuality is closely linked to fertility/infertility and to EDs. Sexual dysfunction may impact fertility and the diagnosis and treatment of infertility may reinforce or lead to sexual dysfunction. Impaired sexuality in women suffering from ED, in both quantitative and qualitative terms, has been widely described in the literature, and it is a major issue. Sexual dysfunction was found to be a relevant concern in both AN and BN patients and was associated with different EDs [39]. We intended to study that variable. Unfortunately, the questionnaire we had chosen (Sexual History Form) appeared inappropriate, leading to non-analyzable results (results non reported).

These results must be viewed in the light of several limitations. Firstly, the small number of participants in the study limited the statistical power. However, we were dealing with a very specific population for which recruiting this number of patients was already quite challenging. Secondly, the tendency to give socially desirable responses cannot be ignored in this particular population of infertile women who expect a lot from the reproductive health care providers and treatment. Denial is often part of having an ED and may impact self-questionnaires and structured interviews. Furthermore, this study may include a selection bias regarding the prevalence. However, in order to limit this bias, the assessment with self-questionnaires was offered to each patient who was suitable for the study and presented as a study regarding the desire of a child (common feature for all these patients) and ED.

However, this study completes the few papers on this subject and leads to potential clinical impact. Screening a history of ED in infertile woman is strongly recommended to plan adapted care regarding infertility but also regarding ED and concurrent psychiatric disorders. Therefore, the assessment has to take into account the desire for a child and body satisfaction, which are essential parts of the EDs process on the one hand and infertility process on the other. This could help with the infertility treatment and the prevention of negative maternal and foetal outcomes. The interest of joint collaboration between the reproductive health care provider and the psychiatrist is emphasized in such cases.

Author Contributions

Conceptualization: MB TF JBH PB MGB.

Data curation: MGB.

Formal analysis: MB JBH MGB.

Investigation: MB AC SM TF PB MGB.

Methodology: MB AC SM TF JBH PB MGB.

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Supervision: MGB.

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Writing – original draft: MB JBH MGB.

Writing – review & editing: MB AC SM TF JBH PB MGB.

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