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RESEARCH ARTICLE



## Impact of the trait anxiety during pregnancy on birth weight: an observational cohort study

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### ABSTRACT

To explore the effects of antenatal anxiety on fetal growth an observational cohort study was performed, including a cohort of 204 women with singleton pregnancies during the strict lockdown of the COVID-19 pandemic in 2020. Psychosocial factors, maternal demographics, obstetric outcomes, social support (Medical Outcomes Study Social Support Survey, MOS-SSS), and symptoms of anxiety (State-Trait Anxiety Inventory, STAI) and depression (Edinburgh Postpartum Depression Scale, EPDS) were studied as potential predictors of low birth weight. Main outcome measures were birth weight, head circumference and length. Results showed a negative correlation between STAI score (trait anxiety) and birth weight percentile ( $r = -0.228$ ,  $p = .047$ ). In the univariate linear regression analysis, a lower maternal weight and BMI before pregnancy, parity, increased STAI score and preterm birth below 37 weeks of gestation ( $p = .008$ ,  $p = .015$ ,  $p = .028$ ,  $p = .047$  and  $p = .022$ , respectively) were identified as predictive risk factors for low birth weight, whereas in the multivariate linear regression analysis only a lower maternal weight before pregnancy and an increased STAI score were independent predictors for low birth weight ( $p = .020$ ,  $p = .049$ , respectively). To conclude, anxiety during pregnancy impacts birth weight, and specifically the trait anxiety, is a predictor for low birth weight.

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### KEYWORDS

Anxiety; birthweight; fetal growth restriction and perinatal mental health

## Introduction

Low birth weight is a common pregnancy complication, and is considered a leading cause of stillbirth, neonatal mortality, and short- and long-term neonatal morbidity [1], including preterm birth, delayed child development, poor speech, and adolescence mental health disorders [2], affecting around 10% of births in Spain and up to 26%–28% of births in underdeveloped regions [3]. Identifying [2] predictive factors and promoting early screening for low birth weight could help to develop strategies to reduce the morbidity and mortality associated.

There are several maternal risk factors for low birth weight, such as advanced maternal age, ethnic origin, consanguinity, low body mass index, nulliparity, use of recreational drugs, and alcohol [4]. Another factor

### Contribution

- **What are the novel findings of this work?** This research highlights the relevance of the trait anxiety during pregnancy on fetal growth. In pregnant women, exposed to stressful circumstances in real life, the trait anxiety was found to be an independent predictor of low birth weight.
- **What are the clinical implications of this work?** To develop adequate strategies for early screening and treatment of anxiety symptoms and other mental health disorders during pregnancy, in order to improve the consequences of fetal growth disorders and other perinatal outcomes.

associated with low birth weight is maternal anxiety during pregnancy [5].

Anxiety is an emotion characterized by apprehension and somatic symptoms of tension in which an individual anticipates impending danger, catastrophe, or misfortune [6]. The prevalence of anxiety disorder in the general population is 13.6% [7], but increases to 15.2% during pregnancy [8,9].

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Researchers discriminate between state anxiety and trait anxiety. While state anxiety refers to a transient reaction to a stressful situation, trait anxiety is defined as a more persistent personality trait [10]. Comparatively, less research has been conducted on the role of personality predisposition to anxiety.

On 11 March 2020, the World Health Organization declared COVID-19 a global pandemic, which has resulted in a global crisis. During the SARS-CoV-2 pandemic, fear, uncertainty regarding the prognosis, and possible maternal and fetal complications associated with the virus increased the symptoms of anxiety and depression during pregnancy and the postpartum period [11,12]. There is conflicting data regarding the effect of maternal psychological distress on fetal growth. The fetoplacental-maternal unit may regulate fetal growth according to the type of psychological distress following a stressful event and even increase fetal growth in response to maternal stress in major areas of life [13]. In addition, the effect of anxiety timing on birth weight is not well understood, and data shows opposing outcomes [14–16].

Briefly, while it is clear that anxiety during pregnancy is associated with a lower birth weight [17], it is not clear whether there are any differences on the effects of anxiety based on whether it is trait or state anxiety, or whether the impact of anxiety is different depending on the gestational age at which anxiety symptoms arise.

Therefore, the aim of this study was to study the effects of maternal anxiety on fetal growth. Secondary objectives were to investigate the effect of anxiety timing and the potentially different effects of trait anxiety and state anxiety on fetal growth.

## Methods

### Study design

This was a prospective secondary analysis of a cohort with pregnant women recruited for the research study “Psychological impact and social support in pregnant women during the lockdown due to the SARS-CoV2 pandemic” [11]. In the present analysis, we included pregnant women that attended Hospital de la Dona Vall d’Hebron during the COVID-19 lockdown in Barcelona, Spain, which lasted from 14th March 2020 to 28th April 2020. Data collection lasted from 27th March 2020 to 31st December 2020. As expected during a strict pandemic lockdown, these women were exposed to an increased number of anxiety-triggering circumstances. Psychosocial factors, maternal demographics, and obstetric outcomes were analyzed as potential predictors of low birth weight.

### Participants

A total of 217 pregnant women attending Hospital de la Dona Vall d’Hebron during the lockdown period were offered to participate in the study. Of those, 204 (94%) accepted to participate and were included in the study. Of those, 164 (80.4%) completed the depression questionnaire (Edinburgh Postpartum Depression Scale, EPDS) [18,19] and 109 (53.4%) completed the anxiety questionnaire (State-Trait Anxiety Inventory, STAI) [20,21]. Two participants were excluded due to twin pregnancies, which have different growth patterns as compared to singleton pregnancies. Finally, 107 women were included in the analysis.

### Variables

#### Outcome variables

Neonatal birth weight (BW), head circumference (HC) and length (Lt) were the main outcome variables. Gestational age at delivery and the need for admission to the special care baby unit were also recorded.

#### Demographics and pregnancy variables

In order to describe the study population, we focused on psychosocial and demographic factors impacting birth weight [22]: maternal age, infant gender, ethnic origin, maternal height, maternal weight before pregnancy, maternal weight gain during pregnancy, parity, pregnancy-induced hypertensive disorder, gestational diabetes, preterm birth <37 weeks of gestation, smoking status, and high-risk pregnancy. Gestational age and trimester based on gestational age at the beginning of the COVID-19 lockdown in Spain (14 March 2020) were calculated for each participant so as to identify the time when anxiety symptoms due to the COVID-19 lockdown may have appeared. Maternal body mass index (BMI) at the beginning of the pregnancy was calculated based on weight before pregnancy (kg)/height ( $m^2$ ). The local protocol of the antenatal clinic [23] was used to identify participants with high-risk pregnancies.

#### Psychosocial questionnaires

During visits to the antenatal clinic, several questionnaires were prospectively administered to detect anxiety and depression symptoms, as well as the absence of social support.

The EPDS is a 10-item self-reported scale designed to specifically detect postpartum depression. Each item is rated on a 4-point scale ranging from 0 to 3, with higher scores indicating a greater severity of the depression [18]. The Spanish validation of the EPDS gave an optimal cutoff value of 10/11 for combined major and minor depression, sensitivity was 79%, and

specificity was 95.5%, with a positive predictive value of 63.2% and a negative predictive value of 97.7%. In addition, a cutoff value of 13 has a sensitivity of 62%, and a specificity of 98.1%, with a positive predictive value of 76.5% and a negative predictive value of 96.4% [19,24]. The gold standard for the diagnosis of postpartum depression is an assessment during a clinical interview with a mental health professional.

The STAI is a 40-item self-reported scale designed to detect state anxiety (STAI) and trait anxiety (STAI<sub>t</sub>). The STAI is the most used rating scale for measuring anxiety symptoms and it has been validated to Spanish population [21]. Its validity and reliability have been carefully evaluated [20]. Each item is rated on a 4-point scale ranging from 0 to 3, with higher scores indicating a greater severity of the anxiety. For comparison to international studies, the 0–3 range in the 4-point scale has been changed to 1–4, as in those studies. The STAI scale has also been validated to use it in pregnant women [8]. Range of scores for each subtest is 20–80, with higher scores indicating a greater severity of the anxiety. A cutoff value of 39–40 has been suggested as a value able to detect clinically significant symptoms of anxiety scale.

Finally, the Medical Outcomes Study Social Support Survey (MOS-SSS) is a 20-item self-reported questionnaire developed by the Rand and Medical Outcomes Study teams to measure the level of social support. This scale measures positive social interactions, as well as tangible, affectionate and emotional/informational support. The MOS-SSS has shown good reliability and validity [25]. The Spanish version of the MOS-SSS has also been validated, showing satisfactory psychometric properties [26].

### Data sources and measurements

Study data were prospectively collected from electronic medical records (SAP® software) and managed using REDCap™ electronic data capture tools hosted at [VHIR- VALL DE HEBRON HOSPITAL] [27].

Regarding biometric variables, birth weight was measured in kg, and HC and Lt were measured in cm. For birth weight percentiles, the curves were adapted to Spanish populations [28] by adjusting for sex and gestational age. For HC and Lt percentiles, the Spanish curves were used [29].

Tobacco use was considered if the patient had smoked during the first trimester of pregnancy according to the patient medical records. EPDS variables were transformed to categorical, setting a cutoff value of 10.

### Statistical analysis

Regarding descriptive statistics, continuous variables were reported as the mean and standard deviation, while categorical variables were reported as frequency and percentage. A univariate regression analysis was performed to identify the psychosocial and demographic factors impacting birth weight. A Pearson's coefficient correlation was performed for quantitative variables and birth weight. A multivariable analysis clustered all significant variables from the previous univariate test and measured their combined effect on birth weight. Statistical significance was set at an  $\alpha$  error  $<0.05$ . All reported probability values were two-tailed. The SPSS software, IBM SPSS Statistics for Windows, version 23 (IBM Corp.) was used for statistical purposes.

### Results

#### Demographics, obstetric outcomes, neonatal outcomes, and scores in psychosocial questionnaires

The STAI questionnaire was completed during the lockdown period by 107 women who had agreed to participate in the study and had available data. Figure 1 shows the flow diagram of participants. Table 1 shows descriptive demographics, obstetric outcomes and neonatal outcomes, and scores of the psychosocial questionnaires completed by the participants included in the study.

#### Analysis of a potential correlation between anxiety and birth weight percentile

There was a negative correlation between STAI<sub>t</sub> score and birth weight percentile ( $r = -0.228$ ,  $p = .047$ ) (Figure 2). There was also a negative correlation between STAI<sub>s</sub> score and birth weight percentile, but it

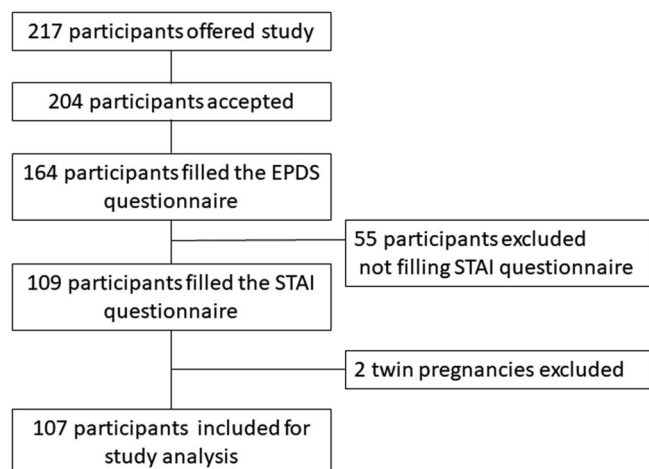


Figure 1. Flow diagram.

**Table 1.** Maternal demographics, obstetric outcomes, neonatal outcomes, and data from psychosocial questionnaires ( $n = 107$ ).

Variables	M $\pm$ SD
Maternal age (years)	32 $\pm$ 6
Maternal weight before pregnancy	70.5 $\pm$ 15.1
BMI before pregnancy	26.3 $\pm$ 4.9
Maternal weight gain during pregnancy	13.4 $\pm$ 5.7
STAI	41.7 $\pm$ 10.6
STAI	40.5 $\pm$ 7.9
MOS-SSS	87.4 $\pm$ 10.9
Gestational age at study inclusion (weeks)	17.1 $\pm$ 8.8
Gestational age at delivery (days)	276 $\pm$ 8
Birth weight (g)	3259 $\pm$ 438
Centile of birth weight	46.83 $\pm$ 2.9
Birth length (cm)	50.1 $\pm$ 2.2
Centile of birth length	56.3 $\pm$ 29.4
Birth head circumference (cm)	34.6 $\pm$ 1.64
Centile of birth head circumference	50.5 $\pm$ 27
	N (%)
Ethnic origin	
Caucasian	76 (7)
Latin American	27 (25.2)
Smokers	8 (7.5)
Nulliparous	65 (60.7)
Hypertension induced pregnancy	3 (2.8)
Gestational diabetes	8 (7.5)
High risk pregnancy	40 (37.4)
Preterm birth < 37 w	3 (2.8)
EPDS > 10	28 (26.2)
Trimester of study inclusion	
First trimester	37 (34.6)
Second trimester	44 (41.1)
Third trimester	26 (24.3)
New-born gender (female)	
Female	59 (55.1)
Male	48 (44.8)
Birth weight below 10th centile	16 (10.3)
SCBU admission	3 (2.8)

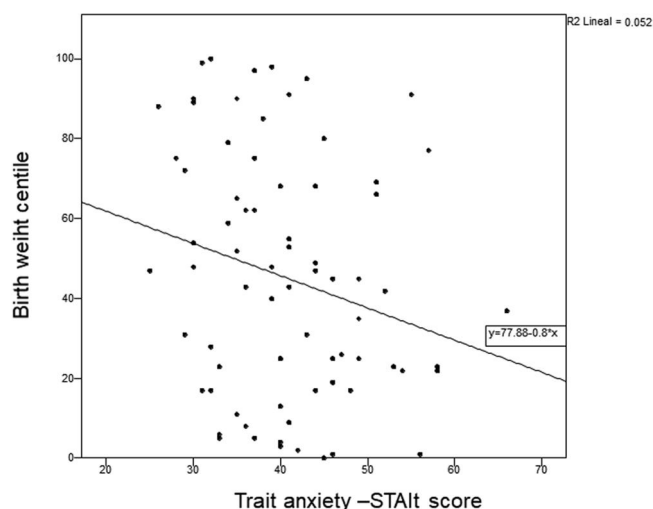
M: Mean; SD: Standard deviation; SCBU = Special care baby unit.

was not statistically significant ( $r = -0.183$ ,  $p = .060$ ). Other neonatal biometric parameters (HC and Lt) did not show a correlation with STAI or STAI.

There was a negative correlation between STAI score and gestational age at the beginning of the lockdown period ( $r = -0.223$ ,  $p = .022$ ), which means that the lower the gestational age when lockdown started, the higher the state anxiety during pregnancy. However, gestational age at the beginning of the lockdown did not show any correlation with birth weight ( $r = 0.115$ ,  $p = .242$ ). On the other hand, there was a certain correlation between gestational age at the beginning of the lockdown period and birth weight percentile ( $r = 0.170$ ,  $p = .082$ ).

### Regression analysis of birth weight predictors

A univariate linear regression analysis was performed to identify demographic, obstetric, and psychosocial variables as potential risk factors of low birth weight. A lower maternal weight and BMI before pregnancy, higher parity, an increased STAI score and preterm

**Figure 2.** Graphical representation of the correlation between STAI score and birth weight percentile.

birth below 37 weeks of gestation ( $p = .008$ ,  $p = .015$ ,  $p = .028$ ,  $p = .047$ , and  $p = .022$ , respectively), were identified as predictive risk factors for low birth weight percentiles.

In addition, an increased STAI score, tobacco use, and a lower gestational age at the beginning of the lockdown period showed a trend for prediction of lower birth weight percentiles, as shown in Table 2.

A multivariate linear regression analysis (Table 3) was performed with those variables identified as risk factors for low birth weight percentiles in the univariate linear regression analysis. When combining maternal weight before pregnancy, parity, STAI score and smoking status, only a lower maternal weight before pregnancy and an increased STAI score were independent predictors for low birth weight percentile ( $p = .020$ ,  $p = .049$ , respectively).

### Discussion

The present study shows, firstly, that anxiety symptoms during pregnancy are associated with lower birth weight percentiles. Secondly, trait anxiety (STAI) shows a higher association with lower birth weight percentiles than state anxiety (STAI). Thirdly, regarding the effect of anxiety timing on fetal growth, although there was a certain trend, it is not clear whether the appearance of anxiety symptoms at an earlier gestational age is associated with lower birth weight percentiles. In addition, there was a negative correlation between state anxiety and gestational age at the time when anxiety symptoms first appear, suggesting that women experienced higher state anxiety



**Table 2.** Univariate linear regression analysis to explore a potential correlation between birth weight percentile (adjusted for gestational age at delivery and neonate gender) and risk factors.

Risk factors	Standardized coefficient	95% Coefficient Interval	p Value
Ethnicity	-.087	-15.009 to 5.771	.380
Caucasian ethnicity	.007	-12.895 to 13.985	.941
Maternal weight	.256	.155 to .998	.008
Body Mass Index (BMI)	.234	.295 to 2.721	.015
Parity	.213	1.479 to 25178	.028
Maternal weight gain	.019	-1.058 to 1.269	.858
Hypertensive disorders during pregnancy	-.075	-49.659 to 21.884	.443
Gestational Diabetes	.007	-21.657 to 23.372	.940
Tobacco	-.168	-41.738 to 2.652	.084
STAI score	-.228	-1.599 to -.010	.047
STAI score	-.183	-1.042 to .022	.060
EPDS score	-.147	-2.192 to .308	.138
MOS-SSS score	-.048	-.764 to .475	.645
Depression disorder	-.008	-26.796 to 24681	.935
Preterm birth < 37w	-.221	-75.966 to -5996	.022
Trimester of pregnancy	.125	-3597 to 14.119	.241
High Risk Pregnancy	.039	-9.766 to 14695	.690
Gestational age at beginning lockdown	.170	-.070 to 1157	.082

**Table 3.** Multivariate lineal regression analysis to explore a potential correlation between birth weight percentile (adjusted for gestational age at delivery and neonate gender) and risk factors.

Risk factors	Standardized coefficient	95% Coefficient Interval	p Value
Maternal weight	.265	.088 to 0.979	.020
STAI score	-.220	-1.544 to -.004	.049
Tobacco	-.089	-33.90 to 14.279	.419
Parity	.131	-5.765 to 22.461	.242

when exposed to the stressful event at a lower gestational age [9,11].

Meta-analyses have identified an association between antenatal anxiety and low birth weight (OR = 1.80) [30]. The mechanism underlying this effect is known as “fetal programming” [31]. Several studies using animal models have proved that maternal distress negatively influences infant outcomes in childhood and adulthood [32]. Evidence suggests that this occurs *via* effects on the development of the fetal nervous system, and maternal mood disorders have also been shown to activate the maternal hypothalamic-pituitary-adrenal (HPA) axis and program the HPA axis and physiology of the fetus [33,34]. Maternal anxiety during pregnancy may increase fetal exposure to maternal glucocorticoids, leading to low birth weight and higher glucocorticoid levels in the neonate [35]. Cortisol levels in cord blood are increased in intrauterine growth retardation, implicating endogenous cortisol in fetal growth. While lipophilic steroids easily cross the placenta, fetal glucocorticoid levels are much lower than levels in maternal circulation [36,37]. Studies of 11 $\beta$ -HSD-2 null mice provide evidence for a causal association between 11 $\beta$ -HSD-2, reduced birth weight, and anxiety-like behavior in adulthood [38]. This finding is consistent with findings that antenatal maternal stress affects neurodevelopment [39].

A second area of knowledge concerns the effects of anxiety on infant birth weight. These studies can be classified according to the type of psychological stressor investigated. Some evidence suggests that major life events consistently predicted lower fetal growth or birth weight, whereas measures of perceived stress had small or negligible effects. However, chronic stressors, such as racial disparities, have been even more reliable predictors of low birth weight [40]. Recent experimental evidence suggests that the nature of stressful life events, as well as the timing of exposure to such events, are important determinants of these type of psychological stressors effects [41]. In the present study, the COVID-19 pandemic lockdown was considered as an important stressful event, where anxiety symptoms were increased in pregnant women [11]. In addition, women with higher rates of trait anxiety were more likely to give birth to babies with a lower birth weight. Our findings are consistent with those of a study that explored the potential association between trait anxiety and low birth weight [42]. However, that study did not assess state anxiety. In our study, although only trait anxiety showed a statistically significant correlation with birth weight percentile, state anxiety showed a certain trend for predicting low birth weight percentile.

The effect of trait anxiety on birth weight may be explained by the fact that trait anxiety is related to more prolonged and therefore can increase levels of glucocorticoids on maternal blood and activating the fetal HPA axis for a longer period. However, this hypothesis needs further research to be confirmed.

On the other hand, exposure to psychological stressors can be a predictor of increased birth weight when controlling for gestational age [13]. There is data suggesting that the fetoplacental-maternal unit may regulate

fetal growth according to the type of stressful event and even increase fetal growth in response to maternal stress due to major stressful events [13].

Regarding the effect of anxiety timing on birth weight, our study shows a certain correlation between the timing of anxiety symptoms (gestational age at the beginning of the lockdown) and birth weight percentile, indicating that the earlier the stressful event occurs during pregnancy, the lower the birth weight percentile. However, when analyzing the effect of prenatal anxiety timing in other studies, data were inconsistent. Some studies suggest that psychosocial distress during late pregnancy (30th week of gestation) is a predictor of low birth weight [14,15,43]. On the other hand, gestation lengths and predicted birth weight was lower for participants exposed to a stressful event, such as an ice storm, at an earlier gestational age compared to the third trimester [16]. Therefore, it is likely that, in a stressful event, such as a natural disaster or a lockdown due to a pandemic, the earlier the gestational age at which the mother is exposed to such stressful event, the lower the birth weight percentile.

In this sense, we have included in the analyses birth weight percentiles adjusted for gestational age and gender, since the effect on birth weight for preterm neonates may have led to bias in many of the studies already published, and our aim was to focus exclusively on low birth weight.

Antenatal anxiety and depression symptoms may place a greater financial burden [44] on healthcare systems. Consequently, an early identification of pregnant women with anxiety or depression symptoms and access to perinatal mental health services are crucial for reducing the impact of perinatal mental disorders and potentially neonatal outcomes. There are already several screening strategies for depression and anxiety during pregnancy [45,46], and there is evidence suggesting that an appropriate and timely intervention may minimize symptoms during pregnancy and the postpartum period [47]. Some mindfulness-based interventions for stress management have shown a reduction in the percentage of neonates with a low birth weight [48].

Since the conditions in this study were very specific, as it was conducted during a lockdown due to a global pandemic, the external validity of our results may be limited. Nevertheless, the results of this study may be extrapolated to a population living with chronic stress and showing a higher prevalence of anxiety.

The main limitation of this study is the small sample size. Nevertheless, this study was designed around

specific stressful circumstances, during the COVID-19 pandemic lockdown, which represented an ideal scenario for investigating the effects of anxiety on birth weight, despite the reduced sample size [9]. Another limitation of this study may be the selection bias due to including different anxiety symptoms according to the trimester of pregnancy. However, in a previous study conducted by our group [11], no statistically significant differences were found when analyzing STAI and STAI-t scores according to trimester of pregnancy. Finally, anxiety cannot be induced in an experimental research setting for ethical reasons. Therefore, the fact that this study included patients that were exposed to stressful circumstances in real life is the major strength of the present study.

In conclusion, our results show that anxiety during pregnancy impacts birth weight. More specifically, trait anxiety, which is associated with personality traits, is a predictor for low birth weight. A deeper understanding of the mechanisms underlying a stressful event that may impact neonatal outcomes may help to promote the development of interventions that may reduce the effect of psychosocial stressors during pregnancy, thus improving maternal and neonatal outcomes.

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## Author contributions

MS: Data collection, protocol and project development, manuscript writing and editing; JT: Data collection, protocol and project development, manuscript writing and editing; AHF: Data collection, project development, manuscript writing and editing; GP: Protocol and project development, manuscript writing and editing; MED: Protocol and project development, manuscript writing and editing; JR: Protocol and project development, manuscript editing; NM: Data analysis, manuscript writing and editing; EC: Protocol and project development, manuscript writing and editing; MB: Protocol and project development, manuscript writing and editing.

## Ethics statement

This study was approved by the Institutional Review Board of Vall d'Hebron Research Institute PR(AMI)186/2020 on 27 March 2020. Informed consent was obtained from all participants.




## Disclosure statement

No potential conflict of interest was reported by the author(s).

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## Data availability statement

The data that support the findings of this study are available on request from the corresponding author, [MB]. The data are not publicly available due to [restrictions e.g. their containing information that could compromise the privacy of research participants]. The participants of this study did not give written consent for their data to be shared publicly, so this should be obtained before sharing for ethical reasons.

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