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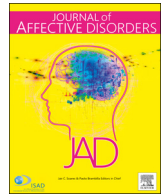
## Antenatal depression and anxiety across pregnancy in urban South Africa

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Research paper

## Antenatal depression and anxiety across pregnancy in urban South Africa

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## ABSTRACT

**Background:** Depression and anxiety in pregnancy have negative consequences for women and their offspring. High adversity places pregnant women at increased mental health risk, yet there is a dearth of longitudinal research in these settings. Little is known about the pathways by which these problems emerge or persist in pregnancy.**Methods:** Women were enrolled in a prospective pregnancy cohort in Soweto, South Africa (2014–2016) and assessed using validated measures (Edinburgh Postnatal Depression Scale EPDS  $\geq 13$ ; State Trait Anxiety Index STAI  $\geq 12$ ) in early (T1) and later pregnancy (T2). Data was available for  $n = 649$  women. Multinomial regression modelling was used to determine factors associated with transient versus persistent depression and anxiety across pregnancy. Cross-lagged panel modelling explored direction of effect between depression and anxiety, and stressors.**Results:** We found high rates of depression (T1: 27%; T2: 25%) and anxiety (T1: 15%; T2: 17%). Perceiving a partner made one's life harder increased risk of persistent depression (RR 5.92 95% CI [3.0–11.8]  $p < 0.001$ ); family stress increased risk for persistent anxiety (RR 1.71 95% CI [1.1–2.7]  $p = 0.027$ ). We find evidence of a direct effect of early depression (T1) on later family stress (T2); and early family stress (T1) on later anxiety (T2).**Limitations:** We used screening measures of depression and anxiety rather than clinical interviews.**Conclusions:** Studies which focus only on late pregnancy may underestimate risk. Early identification, in the first trimester, is critical for prevention and treatment. Partner and family stressors are a key intervention target.

## 1. Introduction

Perinatal depression and anxiety are both of public health concern given well documented negative consequences in both high income countries (HIC) (Stein et al., 2014) and low and middle income countries (LMIC) (Gelaye et al., 2016). Antenatal depression is associated with negative effects for pregnant women in terms of health behaviours, obstetric outcomes, suicide and substance use (Stein et al., 2014) and for offspring in terms of preterm birth, lower birth weight and later mental health risks (Stewart, 2011). While anxiety is still relatively under researched, there is evidence that it is associated with child emotional well-being and behaviour, and disturbances in offspring neurodevelopment (Schetter and Tanner, 2012; Stein et al.,

2014). Systematic reviews in both HIC and LMIC have identified common stressors that are associated with both depression and/or anxiety during pregnancy including a previous history of mental illness, marital conflict, an absence of support, and pregnancy complications (Biaggi et al., 2016; Fisher et al., 2012). In LMIC settings however, given the higher level of contextual adversities (Saxena et al., 2007), some additional factors have been shown to play a role including high rates of exposure to violence, extreme poverty, and epidemic levels of diseases such as HIV Rotheram-Fuller et al. (2018) (Herba et al., 2016).

Despite mounting evidence of the high triple burden of mental illness, HIV and violence on perinatal mental health in Africa (Mitchell et al., 2016) there is still a dearth of evidence from the region (Tsai et al., 2013). In South Africa, research has shown high rates of

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both antenatal depression (30–40%) (Brittain et al., 2015; Redinger et al., 2018; Rochat et al., 2011; Rotheram-Borus et al., 2011; Tomlinson et al., 2014) and antenatal anxiety (14–18%) (Redinger et al., 2018; van Heyningen et al., 2017). Current evidence in the region is limited by methodological shortcomings, including that there is substantial heterogeneity in the measurement of depression and anxiety making comparisons difficult; that most studies are cross-sectional and tend to only report on psychological problems late in pregnancy; and that almost no studies have examined anxiety on its own, or in the context of depression, despite these being known to be highly comorbid in HIC.

The Soweto First 1000 days (S1000) cohort is unique because it is one of only a handful of cohorts on the continent (and the only one in Southern Africa) to measure risk of both depression and anxiety in early and later pregnancy. Previously in this cohort, we demonstrated that risk for both depression (27%) and anxiety (15%) was already high in the first trimester of pregnancy, and that partner and family stressors played an important role in their early onset (Redinger et al., 2018).

In this manuscript we investigate the incidence and persistence of both depression and anxiety across pregnancy; we identify risk factors associated with both transient and persistent symptoms of both; and we explore potentially modifiable mechanisms in the development of depression and anxiety in pregnancy.

## 2. Methods

The Soweto First 1000 days (S1000) cohort is based in the SAMRC/Wits Developmental Pathways for Health Research Unit (DPHRU), at the Chris Hani Baragwanath Academic Hospital (CHBAH) in Soweto, South Africa. The cohort is comprised of pregnant women aged 18–44 years (median 29 years) living in Soweto and accessing antenatal services at CHBAH.

The overall aim of S1000 was to understand associations between maternal health, foetal growth and infant outcomes using repeated measures collected at 6 time points during pregnancy, with a smaller sub-sample followed up biannually to the child's second birthday. Postnatal data collection was restricted to a selected subsample of women with complete pregnancy foetal growth (ultrasound) data for all six timepoints, and given potential selection bias this data is excluded from the current analysis.

### 2.1. Research context

Soweto is a large urban area of Johannesburg, with a population of 1.6 million people, who are predominantly Black African. Although Soweto is historically poor, it is undergoing rapid urbanisation, and is evidenced to have high rates of non-communicable disease including diabetes, high blood pressure and high blood cholesterol (Lopes Ibanez-Gonzalez and Norris, 2013).

### 2.2. Recruitment

Women were consecutively recruited at the foetal medicine unit at CHBAH between 2014 and 2016. Inclusion criteria for S1000 were as follows: resident of Soweto, or the greater Soweto area, <20 weeks pregnant, no known diagnosis of epilepsy or diabetes at the time of recruitment, 18 years or older, and a naturally conceived singleton pregnancy. Psychological data was collected at two timepoints during pregnancy: at 14–18 weeks, and at 24–28 weeks - here after labelled time one (T1) and time two (T2), respectively. Of the 1055 women who completed baseline assessments, 938 had psychological data at T1; 704 had psychological data at T2. A total of 649 had psychological data at both timepoints and are included in this analysis (see Fig. 1).

All women provided written informed consent prior to their inclusion in the pregnancy component of the study (Soweto fetal Growth Study; SFGS). Ethical approval was obtained from the University of the

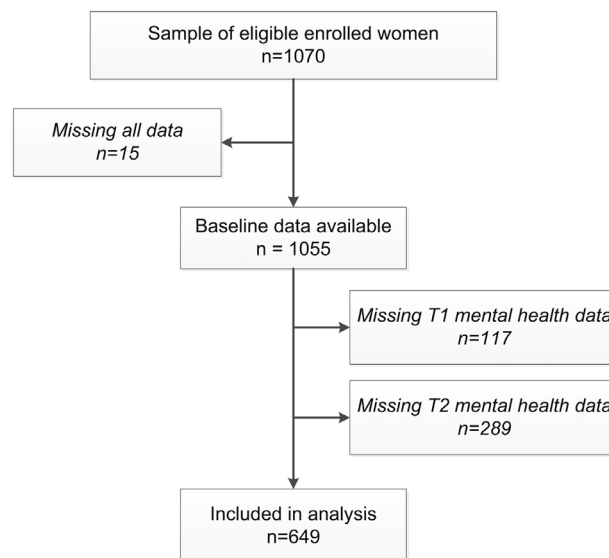


Fig. 1. Consort diagram of women included in analytic data set.

Witwatersrand's Research Ethics Committee (Medical) for data collection [M120524] and data analysis [M180949].

### 2.3. Measures

We included a wide range of potential confounding variables, chosen a priori, based on both a theoretically-driven model (Biaggi et al., 2016) and previous analysis in this population (Redinger et al., 2018).

#### 2.3.1. Maternal health and socio-demographics

Study specific questionnaires collected self-report data on covariates including maternal age, education, relationship status, number of people living in the household, parity, reproductive intention, alcohol use, cigarette use, and previous mental illnesses. HIV status was self-reported and verified against clinical records.

#### 2.3.2. Socio-economic status (SES)

SES was assessed using an 11-item self-report asset index derived from the Demographic and Health Surveys (DHS) (Booyesen et al., 2008). Scores range from 0 to 11, with a higher score representing higher SES.

#### 2.3.3. Depression

The Edinburgh Postnatal Depression Scale (EPDS) is a widely used 10-item measure of perinatal depression which has been validated for use during pregnancy in South Africa (Tsai et al., 2013) and has previously shown good psychometric properties in this population (Cronbach's  $\alpha$  0.80) (Redinger et al., 2018). Items are scored on a severity scale (0 to 3) and summed for a total possible score of 30. We used the standard cut-off score of  $\geq 13/30$  to indicate probable depression in this analysis (Gaynes et al., 2005; Shrestha et al., 2016). While recognising that the  $\geq 13/30$  cut-off is used to establish clinical risk and does not provide a clinical diagnosis, we refer to probable depression as 'depression' in this manuscript for ease of reading.

Because anxiety symptoms are a common feature of depressive episodes in pregnant women, the EPDS is constructed to measure both depressive (7 items) and anxious (3 items) symptoms (Matthey et al., 2013). Other research in South Africa using the EPDS and clinical interviews has not demonstrated adequate reliability of the 3-item anxiety subscale as a stand-alone measure of anxiety (Rochat et al., 2013; van Heyningen et al., 2018). In this research depression (as measured by the EPDS) represents a single construct, including where present,

anxious features.

#### 2.3.4. Anxiety

The State Anxiety Inventory Short Form (STAI-6) is a 6-item version of the 20-item Spielberger State-Trait Anxiety Inventory Index, which has shown good internal consistency reliability and validity when correlated with the original scale (Marteau and Bekker, 1992; Tluczek et al., 2009). This scale has been validated for use in perinatal populations (Meades and Ayers, 2011), and was previously found to have an acceptable level of reliability in this population (Cronbach's  $\alpha$  0.64) (Redinger et al., 2018). Items are scored on a severity scale (1–4) and summed for a total score of 24. We used a cut-off score of  $\geq 12/24$ , which is the same cut-off ratio as the original STAI ( $> 40/80$ ) to indicate probable anxiety. As the STAI does not provide a clinical diagnosis of anxiety, we refer to probable anxiety as assessed using with measure as ‘anxiety’ in this manuscript for ease of reading.

#### 2.3.5. Social support

A 9-item self-report questionnaire (Ramchandani et al., 2009) previously used in this population, was used to identify the absence or presence of different aspects of social support including: people available to help, a confidante, being able to speak to her partner, belonging to a community organisation/ church and having a friend with a baby. Items were used as individual variables in the analysis.

Antenatal stress: A self-report stress questionnaire previously validated in this population (Ramchandani et al., 2010, 2009) collected data on the presence or absence of 16 different stressors in the 6 months prior to the interview (prenatal and antenatal). In line with previous research, we grouped the 10 items into four categories of stressors including: relationship stress (partner violence, relationship break-up); family stress (having a fight with/being alienated from family, family member with substance abuse problem, disabled family member); economic stress (being in debt, having too little money for basics, having to support family members in financial need); and societal stress (being in danger of being killed, witnessing a violent crime). Scores for each category were used as continuous variables.

All self-report questionnaires and scales were administered through an interview in English or in the participant's home language where required, by trained research assistants with at least 3 to 5 years data collection experience. Interviews were done in a private room within the DPHRU building at CHBAH.

#### 2.3.6. Statistical analysis

Analysis was performed in StataSE version 15 (StataCorp, 2013) and MPlus version 8.3 (Muthén and Muthén, 2016). Descriptive statistics and prevalences are reported using all available data at T1 and T2, however statistical models were restricted to those women with mental health data at both timepoints ( $n = 649$ ).

#### 2.4. Data transformation

Using a standard approach missing items on psychological scales were imputed if  $\leq 20\%$  of the scale items were missing, using the median score of available scale items. Participants with  $> 20\%$  of their psychological scales items missing were excluded.

Total scores on the EPDS and STAI were dichotomised to classify participants as meeting thresholds for depression and/ or anxiety using recognised cut-offs for probable cases on screening tools ( $\geq 13$  EPDS,  $\geq 12$  STAI). Point prevalence of depression, anxiety and comorbidity were calculated using these variables. Comorbidity was calculated as the presence of both disorders at each timepoint.

Participants were then categorised into three mutually exclusive groups for both depression and anxiety caseness. Groups were defined by the presence or absence of probable cases across the two timepoints in pregnancy: 0: Absence during pregnancy (None); 1: Present at T1 but not at T2 (Early-recover); 2: not present at T1 but present at T2 (Late-

onset); and 3: present at both T1 and T2 (Persistent).

#### 2.5. Descriptive statistics

Descriptive statistics summarised sample characteristics. Sensitivity analysis comparing baseline characteristics of participants included in the final analysis versus those excluded were completed using non-parametric tests (Chi-Square, Wilcoxon rank-sum). Internal consistency of EPDS and STAI-6 was examined by calculating the average inter-item correlation using Cronbach's alpha.

#### 2.6. Multinomial logistic regressions

Multinomial logistic regression models were used to determine factors associated with belonging to each of the 3 groups (early-recover, late-onset, persistent) for both depression and anxiety, with the “never present” group as the reference group.

Only T1 variables were used as exposures in the multinomial logistic regression models as our outcome variables (groups by timing of onset and recovery) were created using outcome variables at T1 and T2. To determine whether stress and support variables differed significantly from T1 to T2 we used z-tests and t-tests respectively (Supplementary Table S1). We also did cross-sectional logistic regression analyses of T2 depression and anxiety cases using T2 support and stress variables to determine associations at later pregnancy independent of timing of onset or duration (Supplementary Table S2).

#### 2.7. Cross-lagged panel analysis

Cross-lagged panel analysis was used to explore the direction of effect between depression and anxiety and the 4 categories of stress, both collected at the two timepoints. These analyses were performed as path analyses within a structural equation modelling framework using MPlus version 8.3 (Muthén and Muthén, 2016), where T2 variables were regressed onto T1 variables while accounting for T1 and T2 within variable correlations.

To increase power, we used continuous total scores for the depression and anxiety scales. While family and economic stress factors were already continuous and remained unchanged from previous analyses, for this analysis we transformed the remaining two stress variables (marital and societal stress) to be used as stress factors. The partner stress factor was created by combining the marital stress variable (partner violence, relationship break-up) and the “my partner makes my life harder” questionnaire item. Similarly, a continuous societal stress factor was created by combining the societal stress variable (being in danger of being killed, witnessing a violent crime) with an absence of practical support (created by reverse scoring the presence of practical support variable).

### 3. Results

#### 3.1. Sample

Baseline sample characteristics are shown in Table 1. The median age of women in the cohort was 29 (IQR 25–34) years, with the majority being single and having completed secondary school. Half of the cohort lived in smaller households of 3 or fewer people. Only a small percentage (2.6%,  $n = 17$ ) of women reported having been diagnosed with a mental illness previously. Sensitivity analysis found that women included in this analysis ( $n = 649$ ) had a slightly higher mean asset score (5.5, SD 1.5) than those excluded (5.2, SD 1.8) representing a score difference of 0.3 (or approximately one third of an asset).

#### 3.2. Descriptive analysis

We determined cases of probable depression, anxiety and co-

**Table 1**  
Comparison of women in S1000 study by inclusion/ exclusion in the analytic dataset.

	Total n = 1055			Excluded n = 406			Included n = 649			p-value
	Mean (SD)	n	%	Mean (SD)	n	%	Mean (SD)	n	%	
<i>Maternal demographics</i>										
Maternal age	29.8 [5.9]			30.0 [5.9]			29.6 [5.9]			0.326
Mother's education										
None or attended up to secondary		773	73.3		309	76.1		464	71.5	0.086
Tertiary & Professional training		270	25.6		92	22.7		178	27.4	
Missing		12	1.1		5	1.2		7	1.1	
Relationship status										
Single		656	62.2		249	61.3		407	62.7	0.666
Married/cohabiting		397	37.6		156	38.4		241	37.1	
Missing		2	0.2		1	0.2		1	0.2	
Household: total people										
≤ 3		493	46.7		186	45.8		307	47.3	0.665
≥ 4		527	50.0		206	50.7		321	49.5	
Missing		35	3.3		14	3.4		21	3.2	
Household: people < 5 years										
No children under 5 years		632	59.9		211	52.0		421	64.9	0.198
Children under 5 years		344	32.6		129	31.8		215	33.1	
Missing		79	7.5		66	16.3		13	2.0	
Asset score*	5.4 [1.6]			5.2 [1.8]			5.5 [1.5]			0.005
<i>Pregnancy and health characteristics</i>										
Parity										
1 (first pregnancy)		293	27.8		119	29.3		174	26.8	0.355
2 (second pregnancy)		749	71.0		281	69.2		468	72.1	
Missing		13	1.2		6	1.5		7	1.1	
Reproductive intention										
Unplanned pregnancy		514	48.7		181	44.6		333	51.3	0.811
Planned pregnancy		464	44.0		160	39.4		304	46.8	
Missing		77	7.3		65	16.0		12	1.8	
Smoked (last 3 months)										
No		962	91.2		370	91.1		592	91.2	0.837
Yes		91	8.6		34	8.4		57	8.8	
Missing		2	0.2		2	0.5		0	0.0	
Alcohol use (this pregnancy)										
No alcohol use		898	85.1		352	86.7		546	84.1	0.071
Weekly alcohol use		106	10.1		32	7.9		74	11.4	
Missing		51	4.8		22	5.4		29	4.5	
Mental illness (previous)										
No		1022	96.9		390	96.1		632	97.4	0.318
Yes		32	3.0		15	3.7		17	2.6	
Missing		1	0.1		1	0.2		0	0.0	
HIV status										
HIV-negative		704	66.7		260	64.0		444	68.4	0.137
HIV-positive		323	30.6		135	33.3		188	29.0	
Missing		28	2.7		11	2.7		17	2.6	

**Table 2**  
Participants grouped by timing of onset and duration of depression and anxiety across pregnancy (n = 649).

	Depression n (%)	Anxiety n (%)
Never met threshold	385 (59.3)	472 (72.7)
Early-recover	104 (16.0)	62 (9.6)
Late-onset	78 (12.0)	81 (12.5)
Persistent	82 (12.6)	34 (5.2)

morbidity as follows:

### 3.2.1. Depression

The EPDS showed good internal consistency at both timepoints (Cronbach's  $\alpha$  T1: 0.80 and T2: 0.81). At T1: 253/938 (27.0%) scored above the cut-off of  $\geq 13$  for depression, and at T2: 179/704 (25.4%). When restricted to women who had data at both timepoints prevalences were similar: T1: 186/649, 28.7% (95%CI 25.2–32.3); T2: 160/649, 24.7% (95%CI 21.4–28.2)

### 3.2.2. Anxiety

The STAI showed fair internal consistency at both timepoints

(Cronbach's  $\alpha$  T1: 0.65 and T2: 0.71). At T1: 137/938 (14.6%) scored above the  $\geq 12$  cut-off and at T2: 129/704 (18.3%). When restricted to women who had data at both timepoints prevalences were again similar: T1: 96/649, 14.6% (95%CI 12.1–17.8); T2: 115/649, 17.7% (95%CI 14.9–20.9)

### 3.2.3. Comorbidity

At T1: 68/938 (7.2%) and at T2: 70/704 (9.9%) of women met criteria for both depression and anxiety. When restricted to women who had data at both timepoints, prevalences were similar: T1: 49/649, 7.6% (95%CI 5.6–9.9); T2: 63/649, 9.7% (95%CI 7.5–12.2).

### 3.2.4. Onset and persistence

Women meeting criteria for both depression and anxiety were categorised into three groups based on timing of symptoms (See Table 2) in order to examine variations across pregnancy in terms of timing of onset, and persistence of the disorders.

### 3.2.5. Covariates

For most women rates of marital and social support (including having a confidante, your partner being a confidante and friendly health care staff) were consistently high across pregnancy, while only half of women regularly accessed community support and about a third

**Table 3**  
Factors associated with depression and anxiety by pattern of onset and recovery across pregnancy, an adjusted multinomial regression model (n = 524).

	Depression Early Recover	Late Onset	Persistent	Anxiety Early Recover	Late Onset	Persistent
<b>Age*</b>	aRR [CI] p 0.95 [0.9–1.0] 0.073	aRR [CI] p <b>0.93 [0.9–1.0]</b> <b>0.016</b>	aRR [CI] p 0.99 [0.9–1.1] 0.832	aRR [CI] p 0.95 [0.9–1.0] 0.131	aRR [CI] p 1.00 [0.9–1.1] 0.958	aRR [CI] p 0.96 [0.9–1.0] 0.300
<b>Education</b>						
Primary/ secondary	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]
Tertiary/ professional	1.10 [0.6–2.1] 0.757	0.86 [0.4–1.7] 0.660	0.49 [0.2–1.1] 0.092	1.12 [0.5–2.4] 0.761	1.27 [0.7–2.4] 0.468	<b>2.58 [1.0–6.7] 0.050</b>
<b>Relationship status</b>						
Single	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]
Married/ cohabiting	<b>1.87 [1.0–3.4]</b> <b>0.038</b>	1.17 [0.6–2.2] 0.619	1.19 [0.6–2.4] 0.626	0.71 [0.3–1.5] 0.354	1.10 [0.6–2.0] 0.765	0.79 [0.3–2.1] 0.630
<b>People in household</b>						
≤ 3	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]
≥ 4	0.95 [0.5–1.7] 0.878	1.23 [0.7–2.3] 0.509	1.05 [0.5–2.1] 0.894	1.04 [0.5–2.1] 0.921	1.36 [0.8–2.4] 0.303	1.07 [0.4–2.6] 0.884
<b>Children &lt; 5 years</b>						
No children < 5 years	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]
Children < 5 years	1.39 [0.8–2.5] 0.280	1.23 [0.7–2.3] 0.504	1.28 [0.6–2.6] 0.480	1.68 [0.9–3.3] 0.132	0.55 [0.3–1.0] 0.069	1.59 [0.6–4.0] 0.322
<b>Asset score*</b>	0.86 [0.7–1.1] 0.157	0.91 [0.7–1.1] 0.410	0.83 [0.7–1.1] 0.133	1.25 [0.9–1.6] 0.113	1.00 [0.8–1.3] 0.967	0.76 [0.6–1.0] 0.059
<b>Parity</b>						
1st pregnancy	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]
2nd+ pregnancy	0.70 [0.4–1.4] 0.301	1.56 [0.7–3.4] 0.257	<b>0.47 [0.2–1.0] 0.047</b>	1.04 [0.5–2.3] 0.915	1.16 [0.6–2.4] 0.682	0.47 [0.2–1.2] 0.102
<b>Reproductive intention</b>						
Unplanned pregnancy	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]
Planned pregnancy	0.72 [0.4–1.3] 0.253	0.75 [0.4–1.3] 0.334	0.73 [0.4–1.4] 0.351	0.72 [0.4–1.4] 0.334	0.89 [0.5–1.6] 0.696	1.39 [0.6–3.3] 0.445
<b>Smoked (last 3 months)</b>						
No	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]
Yes	0.61 [0.2–1.9] 0.384	0.62 [0.2–2.6] 0.514	0.85 [0.3–2.5] 0.774	1.55 [0.5–4.9] 0.459	0.41 [0.1–1.6] 0.199	0.71 [0.2–2.9] 0.637
<b>Alcohol use</b>						
No alcohol use	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]
Weekly alcohol use	0.95 [0.4–2.3] 0.903	1.40 [0.6–3.4] 0.461	0.79 [0.3–2.3] 0.672	0.73 [0.2–2.2] 0.580	1.77 [0.8–4.1] 0.179	2.27 [0.7–7.3] 0.170
<b>Mental illness (previous)</b>						
No	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]
Yes	1.88 [0.5–7.6] 0.374	1.92 [0.3–10.8] 0.460	2.62 [0.5–12.7] 0.231	–	<b>4.82 [1.5–16.0] 0.010</b>	1.53 [0.2–15.6] 0.718
<b>HIV status</b>						
HIV Negative	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]
HIV positive	1.42 [0.8–2.6] 0.252	1.15 [0.6–2.3] 0.675	1.22 [0.6–2.4] 0.566	1.10 [0.5–2.2] 0.788	0.65 [0.3–1.3] 0.216	1.49 [0.6–3.8] 0.401
<b>Antenatal stressors**</b>						
Marital stress	1.26 [0.7–2.3] 0.444	0.53 [0.2–1.3] 0.173	1.70 [0.9–3.1] 0.079	0.77 [0.4–1.6] 0.466	0.96 [0.5–1.9] 0.907	1.32 [0.6–3.1] 0.520
Family stress	<b>1.42 [1.0–2.0]</b> <b>0.040</b>	0.74 [0.5–1.2] 0.182	1.38 [0.9–2.0] 0.100	1.25 [0.8–1.9] 0.257	1.40 [1.0–2.0] 0.065	<b>1.71 [1.1–2.7] 0.027</b>
Economic stress	1.20 [0.9–1.6] 0.234	1.16 [0.8–1.6] 0.354	1.26 [0.9–1.8] 0.203	1.16 [0.8–1.6] 0.404	0.93 [0.7–1.3] 0.646	0.76 [0.5–1.2] 0.280
Societal stress	1.26 [0.6–2.5] 0.507	0.82 [0.3–2.0] 0.656	1.78 [0.9–3.6] 0.109	0.64 [0.3–1.6] 0.329	0.99 [0.5–2.0] 0.985	1.31 [0.5–3.5] 0.591
<b>Has practical support</b>						
No	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]
Yes	<b>0.32 [0.1–0.9]</b> <b>0.024</b>	<b>0.28 [0.1–0.9]</b> <b>0.027</b>	<b>0.26 [0.1–0.8] 0.013</b>	0.64 [0.2–2.0] 0.444	0.82 [0.3–2.4] 0.719	<b>0.18 [0.1–0.6] 0.004</b>
<b>Has confidante</b>						
No	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]
Yes	0.49 [0.2–1.4] 0.189	3.04 [0.3–27.1] 0.319	1.11 [0.3–4.1] 0.873	0.49 [0.1–1.7] 0.269	0.59 [0.2–1.9] 0.369	5.50 [0.4–69.4] 0.188
<b>Partner is confidante</b>						
No	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]
Yes	1.06 [0.3–3.8] 0.935	2.04 [0.2–16.8] 0.507	<b>0.30 [0.1–0.9] 0.028</b>	1.42 [0.3–5.8] 0.626	0.92 [0.3–3.3] 0.898	0.44 [0.1–1.8] 0.249
<b>Clinic staff are friendly</b>						
No	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]
Yes	0.55 [0.2–1.3] 0.180	2.30 [0.5–10.5] 0.281	0.63 [0.2–1.8] 0.402	1.08 [0.3–3.5] 0.891	1.49 [0.5–4.7] 0.500	0.36 [0.1–1.2] 0.108
<b>Partner makes life harder</b>						
No	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]
Yes	<b>2.48 [1.4–4.4]</b> <b>0.002</b>	1.07 [0.6–2.0] 0.827	<b>5.92 [3.0–11.8] 0.000</b>	1.13 [0.6–2.3] 0.722	1.14 [0.6–2.1] 0.667	0.96 [0.4–2.4] 0.927

(continued on next page)

Table 3 (continued)

	Depression			Anxiety		
	Early Recover	Late Onset	Persistent	Early Recover	Late Onset	Persistent
<b>Community organisation</b>						
Does not attend/ irregularly	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]
Attends regularly	1.00 [0.6–1.7] 0.998	0.90 [0.5–1.6] 0.734	0.69 [0.4–1.3] 0.248	0.76 [0.4–1.4] 0.404	0.62 [0.4–1.1] 0.093	1.08 [0.5–2.6] 0.864
<b>Has friend with baby</b>						
No or sees irregularly	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]	1.00 [1.0–1.0]
Yes, sees regularly	1.24 [0.7–2.2] 0.458	1.14 [0.6–2.1] 0.665	0.86 [0.4–1.7] 0.654	1.07 [0.6–2.1] 0.838	1.35 [0.8–2.4] 0.303	1.59 [0.7–3.8] 0.298

\* Age and asset score are continuous variables; \*\*Antenatal stressors are continuous scores.

had a friend with a baby who they saw regularly. There were decreases in almost all categories of stressors from T1 to T2, most notably in family stress (T1: 0.65, T2: 0.53,  $p < 0.001$ ), economic stress (T1: 1.3, T2: 1.11,  $p < 0.001$ ) and marital stress (T1: 0.20, T2: 0.16,  $p = 0.010$ ) (Supplementary Table 1). The number of women reporting that their partner “makes their life harder” increased over the pregnancy from 39% (T1) to 44% (T2) ( $p = 0.042$ ).

### 3.3. Factors associated with transient, late onset or persistent depression

The adjusted multinomial regression models for depression are presented in Table 3.

#### 3.3.1. Early-recover depression

The factors associated with belonging to this group were largely partner and family related. We found that being married/ cohabiting with partner (RR 1.87 95% CI [1.0–3.4]  $p = 0.038$ ), feeling their partner made their life harder (RR 2.48 95% CI [1.4–4.4]  $p = 0.002$ ), and family stress (RR 1.42 95% CI [1.0–2.0]  $p = 0.040$ ) were associated with increased risk, while having practical support (RR 0.32 95% CI [0.1–0.9]  $p = 0.024$ ) were associated with decreased risk.

#### 3.3.2. Late onset depression

No factors were associated with increased risk in the adjusted model, however, having practical support (RR 0.28 95% CI [0.1–0.9]  $p = 0.027$ ) was associated with decreased risk for late onset depression.

#### 3.3.3. Persistent depression

Having a partner perceived to make one's life harder (RR 5.92 95% CI [3.0–11.8]  $p < 0.001$ ) was associated with an increased risk of persistent depression. Similarly being able to confide in one's partner (RR 0.30 95% CI [0.1–0.9]  $p = 0.028$ ) was associated with decreased risk along with reporting practical support (RR 0.26 95% CI [0.1–0.8]  $p = 0.013$ ), and it not being the first pregnancy (RR 0.47 95% CI [0.2–1.0]  $p = 0.047$ ).

The unadjusted multinomial regression models are presented in Supplementary Table 3 showing that higher level of education, economic stressors and smoking did not remain significant in adjusted models. Having a confidante, a friendly clinic and links to a community organisation were attenuated support variables in the adjusted models.

### 3.4. Factors associated with transient, late onset or persistent anxiety

The adjusted multinomial regression models for anxiety are presented in Table 3.

#### 3.4.1. Early-recover anxiety

No factors were associated with belonging to this group in the adjusted models.

#### 3.4.2. Late-onset anxiety

History of mental illness (RR 4.82 95% CI [1.5–16.0]  $p = 0.010$ )

was the only factor associated with increased risk of late-onset anxiety.

#### 3.4.3. Persistent anxiety

Family stress (RR 1.71 95% CI [1.1–2.7]  $p = 0.027$ ) and tertiary level of education (RR 2.58 95% CI [1.0–6.7]  $p = 0.050$ ) were associated with increased risk of persistent anxiety (although confidence intervals for the latter are close to 1). Practical support was the only factor associated with a decreased risk of persistent anxiety (RR 0.18 95% CI [0.1–0.6]  $p = 0.004$ ).

In the unadjusted multinomial regression models for anxiety (see supplementary Table 4) increasing age, asset score, parity and links to a community support organisation were associated with decreased risk in the persistent and late-onset anxiety group. Having children under 5 in the home was associated with increased risk for early pregnancy anxiety (early-recover) only.

### 3.5. Cross-lagged path analysis

Using repeated measures of depression and anxiety at early (T1) and late (T2) pregnancy we examined the direction of effect between these constructs, and stressors at T1 and T2.

The regression and correlation coefficients of the cross-lagged models are shown in Tables 4 and 5. Figures illustrating the cross-lagged models can be found in Supplementary Figures S1 (Depression) and S2 (Anxiety).

#### 3.5.1. Depression

All correlation coefficients between measures taken at the same time point are positive, suggesting that perceived stress and depressive scores are positively associated. This was strongest for depressive scores and partner stress at T1 [B (SE) = 0.368 (0.034)  $p < 0.001$ ].

Autoregressive path coefficients provide evidence of a large component of stability across the two timepoints of depression across pregnancy.

Cross-lagged paths suggest depression in early pregnancy is associated with later stressors over and above the baseline correlation and stability of depression. There is strong evidence of a direct effect of early depression on later family stress [B (SE) = 0.170 (0.036)  $p < 0.001$ ]. The cross-lagged paths between early depression to later partner, economic and societal stress suggest that there is evidence for paths in both directions.

#### 3.5.2. Anxiety

The correlation coefficients between measures of anxiety and stress taken at the same timepoint suggest that anxiety is correlated at both timepoints with partner stress T1: [0.109 (0.039)  $p = 0.005$ ] T2: [0.170 (0.038)  $p < 0.001$ ] and family stress T1: [0.088 (0.039)  $p = 0.024$ ] T2: [0.207 (0.038)  $p < 0.001$ ]. Anxiety is not correlated with economic stress in early pregnancy, but shows a weak correlation in late pregnancy [0.119 (0.039)  $p = 0.002$ ]. Anxiety is also not correlated with societal stress in early pregnancy, and only weakly correlated in later pregnancy [0.090 (0.040)  $p = 0.024$ ].

**Table 4**  
Standardised estimates for Cross-lagged panel models of depression and stress.

		Estimate	SE	CI	CI	P-value
<b>PARTNER STRESS</b>						
<b>Correlations</b>	EPDS_T1 on PARTNER_T1	0.368	0.034	0.30	0.44	<0.001
	EPDS_T2 on PARTNER_T2	0.253	0.037	0.18	0.33	<0.001
<b>Autoregressive paths</b>	EPDS_T2 on EPDS_T1	0.393	0.036	0.32	0.46	<0.001
	PARTNER_T2 on PARTNER_T1	0.438	0.034	0.37	0.51	<0.001
<b>Crosslagged paths</b>	PARTNER_T1 on EPDS_T2	0.065	0.038	-0.01	0.14	0.091
	EPDS_T1 on PARTNER_T2	0.096	0.037	0.02	0.17	0.010
<b>FAMILY STRESS</b>						
<b>Correlations</b>	EPDS_T1 on FAMILY_T1	0.273	0.036	0.20	0.34	<0.001
	EPDS_T2 on FAMILY_T2	0.200	0.038	0.13	0.27	<0.001
<b>Autoregressive paths</b>	EPDS_T2 on EPDS_T1	0.398	0.034	0.33	0.47	<0.001
	FAMILY_T2 on FAMILY_T1	0.400	0.034	0.33	0.47	<0.001
<b>Crosslagged paths</b>	FAMILY_T1 on EPDS_T2	0.069	0.037	-0.00	0.14	0.063
	EPDS_T1 on FAMILY_T2	0.170	0.036	0.10	0.24	<0.001
<b>ECONOMIC STRESS</b>						
<b>Correlations</b>	EPDS_T1 on ECONOMIC_T1	0.261	0.037	0.19	0.33	<0.001
	EPDS_T2 on ECONOMIC_T2	0.156	0.039	0.08	0.23	<0.001
<b>Autoregressive paths</b>	EPDS_T2 on EPDS_T1	0.403	0.034	0.34	0.47	<0.001
	ECONOMIC_T2 on ECONOMIC_T1	0.424	0.033	0.36	0.49	<0.001
<b>Crosslagged paths</b>	ECONOMIC_T1 on EPDS_T2	0.054	0.037	-0.02	0.13	0.144
	EPDS_T1 on ECONOMIC_T2	0.085	0.036	0.01	0.16	0.020
<b>SOCIETAL STRESS</b>						
<b>Correlations</b>	EPDS_T1 on SOCIETAL_T1	0.199	0.038	0.13	0.27	<0.001
	EPDS_T2 on SOCIETAL_T2	0.075	0.040	-0.00	0.15	0.058
<b>Autoregressive paths</b>	EPDS_T2 on EPDS_T1	0.403	0.033	0.34	0.47	<0.001
	SOCIETAL_T2 on SOCIETAL_T1	0.157	0.039	0.08	0.23	<0.001
<b>Crosslagged paths</b>	SOCIETAL_T1 on EPDS_T2	0.069	0.037	-0.00	0.14	0.061
	EPDS_T1 on SOCIETAL_T2	0.084	0.039	0.01	0.16	0.032

Autoregressive path coefficients provide evidence of a large component of stability across the two timepoints of anxiety across pregnancy.

Cross-lagged paths suggest a direct effect of early family stress on later anxious symptoms [B (SE) = 0.086 (0.038)  $p < 0.025$ ].

## 4. Discussion

### 4.1. Summary

Our results show concerning rates of both depression and anxiety in both early and later pregnancy. If depression is present early it tends to persist throughout pregnancy while anxiety increases during pregnancy. We provide strong evidence for a direct effect of depression in

**Table 5**  
Standardised estimates for cross-lagged panel models of anxiety and stress.

		Estimate	SE	CI	CI	p-value
<b>PARTNER STRESS</b>						
<b>Correlations</b>	ANXIETY_T1 on PARTNER_T1	0.109	0.039	0.03	0.19	0.005
	ANXIETY_T2 on PARTNER_T2	0.170	0.038	0.10	0.24	<0.001
<b>Autoregressive paths</b>	ANXIETY_T2 on ANXIETY_T1	0.228	0.037	0.16	0.30	<0.001
	PARTNER_T2 on PARTNER_T1	0.467	0.031	0.41	0.53	<0.001
<b>Crosslagged paths</b>	ANXIETY_T2 on PARTNER_T1	0.055	0.038	-0.02	0.14	0.150
	PARTNER_T2 on ANXIETY_T1	0.047	0.035	-0.02	0.12	0.176
<b>FAMILY STRESS</b>						
<b>Correlations</b>	ANXIETY_T1 on FAMILY_T1	0.088	0.039	0.01	0.16	0.024
	ANXIETY_T2 on FAMILY_T2	0.207	0.038	0.13	0.28	<0.001
<b>Autoregressive paths</b>	ANXIETY_T2 on ANXIETY_T1	0.226	0.037	0.15	0.30	<0.001
	FAMILY_T2 on FAMILY_T1	0.446	0.032	0.38	0.51	<0.001
<b>Crosslagged paths</b>	ANXIETY_T2 on FAMILY_T1	0.086	0.038	0.01	0.16	0.025
	FAMILY_T2 on ANXIETY_T1	0.026	0.035	-0.04	0.09	0.461
<b>ECONOMIC STRESS</b>						
<b>Correlations</b>	ANXIETY_T1 on ECONOMIC_T1	-0.040	0.039	-0.12	0.04	0.312
	ANXIETY_T2 on ECONOMIC_T2	0.119	0.039	0.04	0.20	0.002
<b>Autoregressive paths</b>	ANXIETY_T2 on ANXIETY_T1	0.236	0.037	0.16	0.31	<0.001
	ECONOMIC_T1 on ECONOMIC_T2	0.446	0.032	0.38	0.51	<0.001
<b>Crosslagged paths</b>	ANXIETY_T2 on ECONOMIC_T1	0.049	0.038	-0.03	0.12	0.206
	ECONOMIC_T1 on ANXIETY_T1	0.004	0.035	-0.06	0.07	0.915
<b>SOCIETAL STRESS</b>						
<b>Correlations</b>	ANXIETY_T1 on SOCIETAL_T1	0.068	0.039	-0.01	0.14	0.084
	ANXIETY_T2 on SOCIETAL_T2	0.090	0.040	0.01	0.17	0.024
<b>Autoregressive paths</b>	ANXIETY_T2 on ANXIETY_T1	0.233	0.037	0.16	0.31	<0.001
	SOCIETAL_T1 on SOCIETAL_T2	0.174	0.039	0.10	0.25	<0.001
<b>Crosslagged paths</b>	ANXIETY_T2 on SOCIETAL_T1	0.012	0.038	-0.06	0.09	0.746
	SOCIETAL_T1 on ANXIETY_T1	0.016	0.039	-0.06	0.09	0.685

early pregnancy on later family stressors, while family stressors in early pregnancy are related to increases in anxiety later in pregnancy.

#### 4.2. Prevalence, incidence and timing of onset of depression and anxiety

Our finding that depression (24–28%) and anxiety (14–18%) are high in pregnancy (almost double those seen in HIC) is similar to other research in South Africa and other LMIC (Fisher et al., 2012; Sowa et al., 2015). A unique contribution of this longitudinal research is that we illustrate for the first time in Africa that risks for both depression and anxiety emerge earlier in the pregnancy than have been previously reported, and that they change over the course of pregnancy. Unlike previous studies, we do not find an association between previous mental illness and depression during pregnancy. We do however find an association between previous mental illness and late onset anxiety (RR 4.82 95% CI [1.5–16.0]  $p = 0.010$ ) although numbers are a small ( $n = 7$ ) and confidence intervals are wide.

Most studies of perinatal mental health in Africa to date have been cross-sectional (Sawyer et al., 2010) or, if longitudinal, they have tended to measure mental health only once, usually in later pregnancy, with follow up during the postnatal period. For example, one study in South Africa reported on depression rates at more than one time-point in pregnancy, but their published analysis focused only on trajectories from the later time point in pregnancy into the postnatal period without interrogating changes in antenatal depression cases over the course of pregnancy (Garman et al., 2019). Another study in South Africa has identified the potential risk of early-onset chronic depression during pregnancy (Rochat et al., 2011) however that research was limited by only measuring depression in later pregnancy with retrospective self-report of the timing of onset. This precludes an understanding of the timing of the first emergence of risk, which could inform prevention and treatment opportunities given that early pregnancy onset versus late-onset depression have different etiologies across pregnancy (Woody et al., 2017).

That depression and anxiety risk is present as early as the first trimester, with approximately 1 in 10 women having comorbid depression and anxiety across pregnancy warrants attention for two reasons. First, the chronicity of mental health problems has a negative influence on prognosis, so identifying these at the earliest opportunity is beneficial. Second, there are known effects of depression on health-related behaviours such as lower attendance at antenatal care (Evans et al., 2001), negative perceptions of health care services (Rochat et al., 2006) lower hygiene behaviours (Grigoriadis et al., 2013) and increased risk of substance and alcohol use (Arch, 2013; Marcus, 2009) - all of which can affect the health and wellbeing of both mother and foetus (Stein et al., 2014).

These effects are not to be underestimated. For example, in HIC studies have shown that depression is associated with obstetric complications (Accortt et al., 2015), preterm delivery and low birth weight (Grote et al., 2010), while both depression and anxiety are associated with self-harm or suicide (Gavin et al., 2011; Sareen et al., 2005). Evidence suggests that offspring born to antenatally depressed or anxious mothers are at increased risk of childhood emotional problems and risk of depression in later adolescence, independent of the mother's postnatal mental health (Pearson et al., 2013). Leaving these conditions either undetected or untreated could have substantial long-term consequences.

Our finding that depression and anxiety remain stable or increase during pregnancy highlights the importance of early pregnancy screening and intervention in public health settings. Other studies have shown that antenatal depression and anxiety are both risk factors for postnatal mental health problems (Milgrom et al., 2008). We know from the literature that perinatal depression is associated with decreased treatment adherence (including ART), decreased breastfeeding duration and also the negative affect it has on infant bonding (Stein et al., 2014). In settings such as South Africa, this is particularly

concerning given the already high rates of maternal and child morbidity and mortality (Houle et al., 2013). While screening and interventions for mental health problems may be considered resource-intensive, public health services cannot afford to ignore mental health problems which could potentially worsen health outcomes (even if only indirectly) by lowering maternal health care engagement and adherence (Sowa et al., 2015).

This research contributes to the very limited evidence on the prevalence of anxiety across pregnancy globally. The number of studies which have examined antenatal anxiety (as compared to or together with antenatal depression) is generally limited (Dennis et al., 2017), and is particularly limited in Africa. Of studies of perinatal mental health in Africa, approximately 20 have examined antenatal depression while very few have investigated anxiety (Dennis et al., 2017; Sawyer et al., 2010; Sowa et al., 2015). Only one other study in South Africa (van Heyningen et al., 2017) has specifically examined antenatal anxiety, finding similar rates to this research, but like most studies in Africa to date, uses a cross-sectional design. One longitudinal study of 778 women in Ghana and Cote d'Ivoire (Barthel et al., 2016) found distinct trajectories by examining anxiety in later pregnancy through to the postpartum. That anxiety is largely understudied is concerning because depression and anxiety are known to be highly comorbid, with Stein-Pearson et al. showing that associations attributed to one, might include causes associated with the other, suggesting that while comorbidity is common, disorders are likely distinct and screening and treatment approaches may need to differ (Stein et al., 2014). Understanding the onset and timing of anxiety is therefore as important as it is for depression, and potentially even more so given the growing evidence from HIC studies of programming effects on children (Glover et al., 2010).

#### 4.3. Stressors and support in the development of depression and anxiety across pregnancy

For all women, pregnancy brings with it many adjustments, which can be stressful for both prospective parents and their families, in particular when pregnancies are either unplanned or unwanted (Tomlinson et al., 2014). In S1000, a cohort which is largely generalisable to most urbanised and highly transitioned contexts across Africa, stressors were high in early pregnancy and became attenuated during pregnancy, with the exception of partner stress (particularly feeling that your partner makes your life harder), which increased significantly towards the end of pregnancy. While the vast majority of women reported high levels of both practical and emotional support, the impact of the absence of support, and the importance of the potentially negative perceptions of support by women with depression, were clearly demonstrated in this study.

In all the cross-lagged models examining the direction of effect between depression and stressors across the pregnancy, we see evidence of a direct effect of depression scores in early pregnancy to reporting of stress in later pregnancy. This effect from early depression to later stress is strongest for family stress in later pregnancy. This may indicate two possibilities: the depression symptoms (including low mood, irritability, low of interest) may lead to a change in behaviours (with pregnant women becoming more sensitive to criticism, irritable and potentially withdrawing from relationships), making family interactions difficult and strained; or the depression leads to a more pessimistic outlook by the pregnant women on family relationships, which she then reports as higher family stress (Rochat et al., 2006). Family stress was also associated with a twofold increase in risk for persistent anxiety, and an increased risk of early pregnancy anxiety. When examining the direction of this effect between anxiety and family stress across the pregnancy, we show that family stress in early pregnancy predicts an increase in anxiety scores in later pregnancy. This is plausible in terms of both the literature, and pragmatically, as without family support pregnancies are likely highly distressing and this may become heightened

as the birth of the child becomes more imminent.

Importantly, we find that these stressors are likely modifiable because support has a protective effect for most women, particularly depressed women, in this cohort and in the literature (Biaggi et al., 2016). Traditional African families are large and consist of many extended families members living together and taking care of one another (Makiwane et al., 2017). The support offered by these extended families serves as a buffer for high rates of stress (Casale and Wild, 2013). It is possible that in populations such as Soweto, the nature of urbanisation separates women from their extended family. We see in this cohort that about half of women were living in a household with a maximum of 3 people, including themselves. It is possible that family stress is experienced in an exaggerated way in this cohort because women are not benefitting from the support offered by larger extended families.

Like many studies, we find that a stressed or poor quality partner relationship and an absence of partner support is associated with poorer mental health (Dennis et al., 2017). We show that the perception of a difficult relationship or an unsupportive partner increases risk, which is greatest in the group of women with persistent depression. We also show that being able to speak to or confide in one's partner is associated with decreased risk of persistent depression. This suggests that supportive partners are central to a woman's mental health in pregnancy. While we also show that partner stress early in the pregnancy is associated with later depression, it is noteworthy that we also demonstrate that depression early in the pregnancy is linked to later partnership stress, highlighting the reciprocal nature of both. Since partner support is shown to be important for a variety of pregnancy and child outcomes, this research highlights the importance of attending to the partner relationship in the interests of good pregnancy care and better mental health. It suggests that mental health problems such as depression during pregnancy, could potentially be instrumental in the development of partner stress and marital conflict, which could disrupt the benefits of partner support (Pilkington et al., 2015).

Further research should consider including both pregnant women and their partners accounts of the presence or absence of partnership stress, difficulties and support during pregnancy. This is important because at least some evidence has suggested that fathers are also vulnerable to perinatal depression and that this vulnerability is heightened in the presence of maternal depression, with concerning consequences for parenting capacities (Gutierrez-Galve et al., 2015). In African settings pregnancy services are highly feminised and there are barriers to partner engagement, including cultural practices limiting the involvement of fathers when children are born out of wedlock (Van den Berg and Makusha, 2018). Increased public awareness of and greater acknowledgement of the contribution partners may make to healthier happier pregnancies is needed (Yargawa and Leonardi-Bee, 2015).

#### 4.4. Limitations

Although some women were excluded because they did not have data at both time points, sensitivity analysis found little to no differences in baseline characteristics between those included and excluded from this analysis. While the two mental health scales used (EPDS and STAI) are well validated and widely used, they are not diagnostic measures of depression or anxiety. It would be important to interrogate who provides women with practical and emotional support, as this would determine who interventions to reduce the risk for depression and anxiety.

#### Conclusion

To the best of our knowledge, this is the first study of its kind to investigate the timing of onset and duration of both probable depression and anxiety during pregnancy, their comorbidity and to examine the potentially modifiable mechanisms involved in their onset and persistence.

#### Author statement

##### Authorship contribution

SR: conceptualisation of the paper, data cleaning, analysis and interpretation, drafting of manuscript. RMP: supervision of data analysis and interpretation, critical revision of the manuscript. BH: review and interpretation of data analysis, critical revision of the manuscript. SAN: study conceptualisation, study funding, interpretation of results and critical revision of the manuscript. TJR: conceptualisation of the paper, data analysis and interpretation, drafting of manuscript.

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##### Declaration of Competing Interest

The authors declare no conflict of interest.

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##### Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2020.08.010.

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