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Complete List of Authors:	Dawes, Lisa; The University of Auckland; Auckland City Hospital Waugh, Jason J.S.; Auckland City Hospital; The University of Auckland, Department of Obstetrics and Gynaecology Lee, Arier; University of Auckland, Section of Epidemiology and Biostatistics Groom, KM; The University of Auckland, Liggins Institute
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TITLE PAGE

Full title

The psychological wellbeing of women at high risk of spontaneous preterm birth cared for in a specialised preterm birth clinic: a prospective longitudinal cohort study

Authors

Lisa K. Dawes (MBChB, MD)[1,2]

Jason J.S. Waugh (MBBS)[2,3]

Arier C. Lee (PhD)[4]

Katie M. Groom (MBBS, PhD)[1,2]

Affiliations

[1] Liggins Institute, The University of Auckland, Auckland, New Zealand

[2] National Women's Health, Auckland City Hospital, Auckland, New Zealand

[3] Department of Obstetrics and Gynaecology, The University of Auckland, Auckland, New Zealand

[4] Section of Epidemiology and Biostatistics, The University of Auckland, Auckland, New Zealand

Contact information for corresponding author

Lisa K. Dawes

Address: Liggins Institute, The University of Auckland, Private Bag 92019, Auckland 1142, New Zealand

Phone: +64 21 158 2076

Email: l.dawes@auckland.ac.nz

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ABSTRACT

Objectives: To assess the psychological wellbeing of pregnant women at increased risk of spontaneous preterm birth, and the impact of care from a preterm birth clinic.

Design: Single-centre longitudinal cohort study over one year, 2018-2019.

Setting: Tertiary maternity hospital in Auckland, New Zealand.

Participants: Pregnant women at increased risk of spontaneous preterm birth receiving care in a preterm birth clinic.

Intervention: Participants completed three sets of questionnaires (State-Trait Anxiety Inventory, Edinburgh Postnatal Depression Scale, 36-Item Short Form Survey) – prior to their first, after their second, and after their last clinic appointments. Study-specific questionnaires explored pregnancy-related anxiety and perceptions of care.

Primary and secondary outcome measures: The primary outcome was the mean state-anxiety score. Secondary outcomes included depression and quality of life measures.

Results: 73/97 (75.3%) eligible women participated; 41.1% had a previous preterm birth, 31.5% a second trimester loss and 28.8% cervical surgery; 20.6% had a prior mental health condition. 63/73 (86.3%) women completed all questionnaires. The adjusted mean state-anxiety score was 39.0 at baseline, which decreased to 36.5 after the second visit (difference -2.5, 95% CI -5.5 to 0.5, *P=0.1*) and to 32.6 after the last visit (difference -3.9 from second visit, 95% CI -6.4 to -1.5, *P=0.002*). Rates of anxiety (state-anxiety score >40) and depression (Edinburgh Postnatal Depression Scale score >12) were 38.4%, 34.8%, 19.0%, and 13.7%, 8.7%, 9.5% respectively, at the same time periods. Perceptions of care were favourable; 88.9% stated the preterm birth clinic made them significantly or somewhat less anxious and 87.3% wanted to be seen again in a future pregnancy.

Conclusions: Women at increased risk of spontaneous preterm birth have high rates of anxiety. Psychological wellbeing improved during the second trimester; women perceived that preterm

birth clinic care reduced pregnancy-related anxiety. These findings support the ongoing use and development of preterm birth clinics.

Strengths and limitations of this study

- This is the first study to assess the psychological wellbeing of women at high risk of spontaneous preterm birth who are cared for in a specialised preterm birth clinic.
- Strengths of the study include the prospective study design, and high rates of recruitment and participant retention in an ethnically diverse group of women.
- Limitations of the study are the modest sample size, lack of a comparison group and the use of screening tools rather than diagnostic criteria for anxiety and depression,.
- Although this study demonstrates improved psychological wellbeing of women at high risk of spontaneous preterm birth, further research is required to more directly quantify the impact of a preterm birth clinic on this.

Main Text

INTRODUCTION

Psychological disorders are common in pregnancy.[1,2] Women with high risk pregnancies are more likely to suffer psychological distress with higher rates of anxiety and depression than the general pregnant population.[3-5] Few studies have assessed the psychological wellbeing of women who are at high risk of spontaneous preterm birth, and in particular, the potential impact of care from a specialised preterm birth clinic. Preterm birth clinics provide a package of care to asymptomatic women identified to be at increased risk based on their obstetric and gynaecological history. This care includes regular visits through the second trimester for ultrasound surveillance of cervical length and provision of treatments to prevent preterm birth such as cervical cerclage and vaginal progesterone therapy when indicated.[6,7,8] Close monitoring and reassurance provided through a preterm birth clinic may reduce pregnancy-related anxiety, however, it is also possible that being labelled 'high risk' may increase psychological distress and anxiety.[9-11] Further research in this area has been recommended.[12]

There is increasing recognition of the importance of psychological wellbeing in pregnancy. Meta-analyses show that antenatal depression is associated with a modestly increased risk of preterm birth and fetal growth restriction, and decreased rates of breastfeeding initiation.[13,14] The effect of anxiety is less well evaluated, but is associated with increased pregnancy-related hypertension and caesarean section, decreased rates of exclusive breastfeeding and increased anxiety in the offspring.[15] Antenatal anxiety and depression are also strong predictors of postnatal depression.[16] Strategies for prevention, along with improvements in the recognition and treatment of psychological disorders in pregnancy, are likely to improve outcomes for women and children.[17]

This study aims to assess rates of anxiety, depression and health-related quality of life in pregnant women at high risk of spontaneous preterm birth who are cared for in a preterm birth clinic. The primary hypothesis is that women will have less anxiety after their second consultation in a preterm birth clinic compared to before their first (baseline), and this improvement will be sustained at the end of the second trimester. Secondary hypotheses are that women will have fewer symptoms of depression, improved quality of life, and less pregnancy-related anxiety over the same period.

MATERIAL AND METHODS

This longitudinal cohort study was carried out in a large tertiary maternity hospital in Auckland, New Zealand. All eligible women attending the preterm birth clinic over a 12 month period from August 2018 to August 2019 were invited to participate prior to their first appointment. This preterm birth clinic provides care to pregnant women perceived to be at high risk of spontaneous preterm birth and accepts local and regional referrals. Eligibility criteria for the preterm birth clinic include women with a previous spontaneous preterm birth, previous second trimester loss, history of extensive cervical surgery, or congenital uterine anomaly. Care through the preterm birth clinic includes initial assessment, risk factor modification, serial surveillance of cervical length until 24 weeks, and interventions such as vaginal progesterone and cervical cerclage when indicated (Supplementary Table 1). Care in the preterm birth clinic is provided by a specialist obstetric and midwifery team on a weekly basis, and is in addition to routine antenatal care.

Inclusion criteria for the study were gestational age $<24^{+0}$ weeks at first visit; live fetus; eligible for preterm birth clinic review due to $\geq$1 risk factor for spontaneous preterm birth (Supplementary Table 1); written consent obtained; and sufficient English to independently complete questionnaires. Participants completed three sets of questionnaires: prior to their first clinic appointment (baseline, Set 1), after their second appointment (usually 2-3 weeks later, Set 2), and after their last appointment (usually at 23-24 weeks of gestation, Set 3). Three women were seen for only two appointments and returned the Set 3 questionnaires by post two weeks after their last visit. Each set of questionnaires contained three validated measures: the State-Trait Anxiety Inventory (STAI), used under licence from Mind Garden Incorporated[17] which contains two subscales to allow differentiation between temporary 'state-anxiety' and the relatively stable and long-standing aspects of anxiety proneness in 'trait-anxiety';[18] the Edinburgh Postnatal Depression Scale (EPDS) which is validated for antenatal depression;[19] and the RAND 36-Item Short Form Survey (SF-36) to assess health-related quality of life.[20,21] Set 1 and 3 also included a study-specific questionnaire to assess mental health history, social support, pregnancy-related anxiety and perceptions of care. This included free text responses on pregnancy-related anxiety triggers and what helped to relieve it (Supplementary Tables 2 and 3). The study-specific questionnaires were developed by the research team and piloted for the first five women and minor changes made based on feedback.

For the purposes of this study, state-anxiety was considered the most relevant assessment for current levels of anxiety. A screen positive result was defined as a score of >40 on the STAI state-anxiety score. Pregnancy-related anxiety was also assessed using a ten-point visual analogue scale and reported separately. In the assessment of depression, a screen positive result was defined as a score of >12 on the EPDS.

Participants were contacted by telephone prior to their first appointment and invited to participate, and participant information and consent forms were provided in advance to interested women. After consenting, participants completed hard copy questionnaires independently using a private room, just prior to their first clinic consultation. The EPDS self-harm question was reviewed at completion and for any women answering 'yes, quite often' or 'sometimes', further assessment of safety was made and referral to maternal mental health services offered. No other changes were made to clinical care. All other responses were seen only by a single investigator not responsible for decisions about referral for psychological support, until completion of the study. Standard clinic practice is described in Supplementary Table 1. At the last visit, the discharging obstetrician used pre-defined criteria developed for the purposes of this study to classify ongoing preterm birth risk. Women were considered low risk if cervical length was >25 mm with fetal fibronectin <50 ng/ml (if performed), and no intervention with vaginal progesterone or cerclage required; intermediate risk if cervical length was 11-25 mm, and/or fetal fibronectin 50-199 ng/ml, and/or there was need for progesterone or cerclage; or high risk if cervical length was <10 mm, and/or fetal fibronectin ≥200 ng/ml (Supplementary Table 4).

Demographic details, pregnancy characteristics, medical history, and pregnancy outcomes were obtained from electronic medical records. These data, along with questionnaire responses were entered into a password-protected Excel spreadsheet by a single investigator.

The primary outcome was the STAI state-anxiety score. Secondary outcomes were the EPDS score, SF-36 summary quality of life scores, and pregnancy-related anxiety (as continuous measures).

Statistical analyses

A pragmatic sample size was used. We aimed to invite all eligible women over a one year period to participate. Using data from medically high risk women,[23] we estimated a sample size of 60

would provide 80% power, with alpha of 0.05, two-sided test and an estimated within subject correlation of 0.75 to detect a decrease in the mean state-anxiety score from 40.0 (SD 12.0) to 36.9.

Descriptive statistics were calculated using SPSS (version 25.0) and R software (version 3.5.3).[24,25] Thematic analysis was carried out on free-text responses using Braun and Clarke methodology by a single investigator.[26] The mixed model for repeated measures analyses (MMRM) was used to analyse repeatedly measured continuous outcomes and conducted using SAS software (version 9.4).[27] This analyses was used to test for time effect adjusting for prior diagnosis of a mental health condition, gestational age at first visit and obstetric history (categorised by no previous pregnancy beyond 12 weeks; loss/preterm birth at 12-28 weeks; loss/preterm birth at 28-37 weeks; or term birth only), and subject was included as a random effect. Kenward-Roger method was used to estimate the denominator degrees of freedom for fixed effects. Two-sided P-value <0.05 determined statistical significance. All confidence intervals (CI) are given at a two-sided 95% level.

Ethical approval

Ethical approval was granted by the New Zealand Health and Disability Ethics Committees (18/NTA/103) and institutional approval by the Auckland District Health Board Research Review Committee (A+8127) in July 2018.

Patient and public involvement

The study-specific questionnaire was piloted amongst the first five participants, who were asked for feedback on the clarity and importance of the questions. There was no other patient involvement in the study development.

RESULTS

The recruitment rate was 75.3% (73/97), participation is described in Figure 1. Demographics, obstetric characteristics and risk factors for preterm birth are detailed in Table 1. Some women had been seen in the clinic in a previous pregnancy (17/73, 23.3%) and/or for pre-pregnancy review (12/73, 16.4%).

Table 1. Demographic details, obstetric characteristics and risk factors for preterm birth

Characteristic	Number (%) or mean (SD), n=73
Ethnicity	
European	36 (49.3)
Māori	7 (9.6)
Pacific	5 (6.8)
Asian	11 (15.1)
Indian	9 (12.3)
Other	5 (6.8)
Age (years)	
Mean	34.0 (5.1)
Range	22-45
Body mass index (kg/m^2) [a]	
Mean	26.3 (6.4)
Range	19-57
Current smoker	5 (6.8)
Has a current partner	72 (98.6)
Previous diagnosis of a mental health condition (non-exclusive) [b]	
Depression	10 (13.7)
Postnatal depression	4 (5.5)
Generalised anxiety disorder	2 (2.7)
Panic disorder	1 (1.4)
Social anxiety disorder	1 (1.4)
Post-traumatic spectrum disorder	3 (4.1)
None	58 (79.4)
Currently taking medication for a mental health condition?	4 (5.5)
Currently under the care of a psychiatrist/psychologist	1 (1.4)
Nulliparous	16 (21.9)
Previous stillbirth or neonatal death ≥20^{+0} weeks	22 (30.1)
Current twin pregnancy	1 (1.4)
Reasons for preterm birth clinic referral (non-exclusive)	
Previous spontaneous preterm birth/PPROM (24^{+0} to 36^{+0} weeks) [c]	30 (41.1)
Previous second trimester loss (16^{+0} to 23^{+6} weeks)	23 (31.5)

Previous extensive cervical surgery [d]	21 (28.8)
Congenital uterine anomaly	1 (1.4)
Short cervix in current pregnancy <25 mm	5 (6.8)
≥2 surgical terminations and/or other uterine instrumentations	14 (19.2)
Other risk factors for spontaneous preterm birth	4 (5.5)
Multiple reasons for referral to the preterm birth clinic	23 (31.5)

SD, standard deviation; mm, millimetres; PPROM, pre-labour premature rupture of membranes; LLETZ, large loop excision of the transformation zone.

[a] Missing data n=2.

[b] Self-reported.

[c] Includes survivors born at 23 weeks of gestation.

[d] LLETZ with depth of excision ≥10 mm or >1 procedure, or knife cone biopsy.

The mean gestational ages at questionnaire completion were 13^{+4} weeks (SD 3^{+3}), 16^{+2} weeks (SD 3^{+2}) and 23^{+6} weeks (SD 1^{+2}). Anxiety, depression and quality of life scores and proportion of screen positive results (defined as >40 on the STAI state-anxiety scale and >12 on the EPDS) are shown in Table 2. MMRM analyses, adjusting for gestation at first visit, prior mental health condition and obstetric history (fixed effects), are described in Table 3. The primary outcome of the adjusted mean state-anxiety score was 39.0 at baseline and decreased to 36.5 after the second visit (least square means difference -2.5, 95% CI -5.5 to 0.5, *P=0.1*), with a further reduction to 32.6 after the last visit (least squares means difference -3.9 from the second visit, 95% CI -6.4 to -1.5, *P=0.002*). Adjusted secondary outcomes are reported in Table 3.

Table 2. Anxiety, depression and quality of life scores (unadjusted)

	Set 1 (baseline), n=73		Set 2, n=69		Set 3, n=63	
	Mean (SD) or proportion (%)	95% CI	Mean (SD) or proportion (%)	95% CI	Mean (SD) or proportion (%)	95% CI
STAI state-anxiety score	38.6 (11.9)	36.8 – 41.3	36.2 (11.6)	33.5 – 38.9	32.0 (9.8)	29.6 – 34.4
STAI state-anxiety positive screen [a]	28/73 (38.4)	27.2 – 49.5	24/69 (34.8)	23.5 – 46.0	12/63 (19.0)	9.4 – 28.7
STAI trait-anxiety score	37.3 (10.1)	35.0 – 39.6	36.5 (9.6) [b]	34.2 – 38.8	34.9 (10.8)	32.2 – 37.6
STAI trait-anxiety positive screen [a]	28/73 (38.4)	27.2 – 49.5	23/68 (33.8) [b]	22.6 – 45.1	15/63 (23.8)	13.3 – 34.3
EPDS score	7.3 (4.6)	6.2 – 8.4	6.0 (4.5)	4.9 – 7.1	5.4 (5.1)	4.1 – 6.6
EPDS positive screen [c]	10/73 (13.7)	5.8 – 21.6	6/69 (8.7)	2.0 – 15.3	6/63 (9.5)	2.3 – 16.8
Summary mental health score [d]	63.8 (15.9) [d]	60.0 – 67.8	65.7 (17.0) [f]	61.5 – 69.9	72.4 (17.9) [e]	67.8 – 77.0
Summary physical health score [d]	69.3 (21.5) [c]	64.3 – 74.3	66.0 (24.1) [h]	60.2 – 71.8	71.3 (22.7) [c]	65.6 – 77.0
Pregnancy-related anxiety [i]	4.9 (2.5) [c]	4.3 – 5.5	-	-	2.7 (2.5)	2.1 – 3.3

STAI, State Trait Anxiety Inventory; SD, standard deviation; CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale.

[a] Positive screen defined as STAI score >40.

[b] Missing score for one woman as one incomplete question.

[c] Positive screen defined as EPDS >12.

[d] Using the RAND 36-Item Short Form Survey. Higher scores associated with better quality of life.

[e] Missing scores for nine women as one or more incomplete questions.

[f] Missing scores for five women as one or more incomplete questions.

[g] Missing scores for four women as one or more incomplete questions.

[h] Missing scores for three women as one or more incomplete questions.

[i] Visual analogue scale, 0 = not at all anxious, 10 = extremely anxious.

Table 3. Mixed model for repeated measures analyses for anxiety, depression and quality of life scores

	STAI state-anxiety score			EPDS score			Summary physical health score [a]			Summary mental health score [a]		
Fixed effect	**P value** [b]			**P value** [b]			**P value** [b]			**P value** [b]		
Questionnaire set number	<0.0001			0.0001			0.3			<0.0001		
Gestation at first visit [c]	0.7			0.4			0.2			0.2		
Prior mental health condition [c]	0.7			0.09			0.6			0.006		
Obstetric history [c, d]	0.4			0.04			0.8			0.3		
Least squares means	**Estimate**	**95% CI**		**Estimate**	**95% CI**		**Estimate**	**95% CI**		**Estimate**	**95% CI**	
Set 1	39.0	35.6 – 42.4		7.5	6.1 – 8.9		70.9	63.9 – 77.8		60.7	55.8 – 65.6	
Set 2	36.5	33.0 – 40.0		6.3	4.9 – 7.7		67.2	60.1 – 74.4		62.5	57.5 – 67.4	
Set 3	32.6	29.1 – 36.1		5.7	4.3 – 7.1		71.5	64.3 – 78.6		69.5	64.6 – 74.5	
Least squares means difference	**Estimate**	**95% CI**	**P value** [e]	**Estimate**	**95% CI**	**P value** [e]	**Estimate**	**95% CI**	**p value** [e]	**Estimate**	**95% CI**	**P value** [e]
Set 2 - 1	-2.5	-5.5 – 0.5	0.1	-1.2	-2.3 – -0.2	0.02	-3.7	-10.1 – 2.8	0.3	1.8	-3.1 – 6.6	0.5
Set 3 - 1	-6.4	-8.8 – -4.0	<0.0001	-1.8	-2.6 – -1.0	<0.0001	0.6	-4.6 – 5.8	0.8	8.9	4.7 – 13.0	<0.0001
Set 3 - 2	-3.9	-6.4 – -1.5	0.002	-0.6	-1.4 – 0.2	0.2	4.2	-1.1 – 9.6	0.1	7.1	-3.0 – -11.2	0.001

STAI, State Trait Anxiety Inventory; EPDS, Edinburgh Postnatal Depression Scale; CI, confidence interval.

[a] RAND 36-Item Short Form Survey. Higher scores associated with better quality of life.

[b] Pr > F. Type 3 tests of fixed effects.

[c] Analysis adjusted for these factors.

[d] Categorised by no previous pregnancy beyond 12 weeks; loss/preterm birth at 12-28 weeks; loss/preterm birth at 28-37 weeks; or term birth only.

[e] Pr > |t|

One woman was referred to maternal mental health services following review of the EPDS self-harm question. Preterm birth clinic clinicians referred six women to the women's health social work for psychological support and two to maternal mental health services as part of routine practice. None of the women who completed the Set 3 questionnaires reported having a new diagnosis of a mental health condition during the study period made by a health practitioner. One woman declined to complete the last set of questionnaires after a diagnosis of severe depression.

Women had mixed feelings about referral to the clinic prior to review, but following their last visit 56/63 (88.9%) reported care in the preterm birth clinic made them significantly or somewhat less anxious. The majority (55/63, 87.3%) would want to be cared for in a preterm birth clinic again in another pregnancy. The seven women who did not, had already had a term birth since their prior early birth, or were referred for cervical surgery or multiple uterine instrumentations only (and only one required an intervention greater than surveillance in their current pregnancy) (Supplementary Table 5).

The predominant themes causing pregnancy-related anxiety at baseline were preterm birth, pregnancy loss, and concern for the baby's health. Many women were anxious about extremely early birth – *"being born too early to do anything about it,"* and were worried about reaching milestones – *"getting to 24 weeks to be deemed to have a 'viable' pregnancy."* Women were worried about history repeating itself – *"I am scared that it might happen again,"* and how they would cope if it did – *"my ability to manage emotions associated with NICU [neonatal intensive care unit] if this baby is early."* Fewer women were anxious about the risks of chromosomal or fetal anomalies.

When asked at clinic discharge what they found most helpful to relieve pregnancy-related anxiety, the main theme was medical support, including close monitoring, the preterm birth clinic, regular ultrasound scans, and support and communication from doctors – *"the fortnightly visits have really helped me! Lots of reassurance," "follow up from the preterm birth clinic," "the weekly check-ups and reassurance from the doctors and how quickly they acted when there was an issue,"* and *"the support of specialists who are willing to listen."* Other themes included support from family and friends, distraction, relaxation techniques and prayer.

The mean number of clinic visits was 5.4 (SD 2.1), range 1-11. Clinic interventions and pregnancy outcomes are reported in Table 4. Elective cervical cerclage is reserved for the highest risk women, and was performed in 17/72 cases (23.6%, excludes one women with local follow up after the first visit as no further data collected), usually at 12-14 weeks gestation. The remaining women had ultrasound surveillance of cervical length as their primary management. The overall rate of birth <37 weeks was 17/72 (23.6%), including two spontaneous second trimester losses. One extremely early preterm birth followed pre-labour fetal demise, all other preterm births occurred following spontaneous labour or preterm pre-labour rupture of membranes. Of pregnancies that reached ≥20^{+0} weeks 67/69 (97.1%) babies were alive at hospital discharge.

Table 4. Preterm birth clinic interventions and pregnancy outcomes [a]

Characteristics	**Proportion (%) or mean (SD)**
Shortest transvaginal cervical length measurement	
Mean (SD) (in mm)	27.0 (9.1)
Range (in mm)	0-39
Number <25 mm (threshold for intervention)	21/72 (29.2)
Treatments given to reduce the risk of preterm birth	
Cervical cerclage only	16/72 (22.2)
Vaginal progesterone only	4/72 (5.6)
Both cervical cerclage and vaginal progesterone	10/72 (13.9)
No treatment	40/72 (55.6)
Antenatal hospital admission from clinic due to preterm birth risk	2/72 (2.8)
Risk of preterm birth for those who had an exit visit [b]	
Low	45/66 (68.2)
Intermediate	18/66 (27.3)
High	3/66 (4.5)
Pregnancy outcome	
Termination of pregnancy for fetal anomalies	2/72 (2.8)
First trimester miscarriage (<13^{+0} weeks)	1/72 (1.4)
Second trimester loss (13^{+1} to 22^{+6} weeks)	2/72 (2.8)
Extremely early preterm birth (23^{+0} to 27^{+6} weeks) [d]	3/72 (4.2)
Very early preterm birth (28^{+0} to 31^{+6} weeks)	1/72 (1.4)

Moderate to late preterm birth (32^{+0} to 36^{+6} weeks)	11/72 (15.3)
Term birth ($\geq 37^{+0}$ weeks)	52/72 (72.2)
Mode of birth for pregnancies that reached $\geq 20^{+0}$ weeks [e]	
Normal vaginal birth	44/68 (64.7)
Instrumental birth	7/68 (10.3)
Caesarean section	17/68 (25.0)
Neonatal outcome for pregnancies that reached $\geq 20^{+0}$ weeks [e f]	
Alive at hospital discharge	67/69 (97.1)
Early neonatal death	1/69 (1.4)
Stillbirth	1/69 (1.4)

[a] Excluding one with all follow up at local hospital after first visit as no further data collected.

[b] Risk assessment defined in Supplementary Table 4. Quantitative fetal fibronectin was included in 29/66 (44%) cases. Excludes six women who did not have an exit appointment. Includes three women who did not complete Set 3 questionnaires – for two the exit visit was their second visit, both were high risk and delivered prior to planned completion of the Set 3 questionnaires by post; and one who declined.

[d] Includes one pre-labour fetal demise.

[e] Excluding one termination of pregnancy >20 weeks.

[f] Includes one set of twins.

DISCUSSION

This is the first study to assess the psychological wellbeing of women receiving care in a specialised preterm birth clinic. It identifies high rates of psychological distress, with 38.4% and 13.7% of women having significant symptoms of anxiety and depression, respectively, at the beginning of the second trimester. Whilst the change in mean state-anxiety scores after two clinic visits did not reach statistical significance, improvement may still be clinically important. Adjusted mean state-anxiety scores were significantly improved by clinic discharge, with rates of anxiety half that of baseline. Although depression was less common than anxiety, the adjusted mean EPDS score improved by the second clinic visit and this was sustained to the end of the second trimester. Quality of life improved with regard to mental health, but not physical health. Pregnancy-related anxiety scores also improved and women perceived care in the preterm birth clinic to be a significant factor in relieving anxiety.

A number of studies have reported rates of anxiety and depression in pregnancy, with a wide range of estimates.[1,2] In systematic review, the overall prevalence of a clinical diagnosis of an anxiety disorder in pregnancy was 15.2%, with rates of self-reported anxiety of 18.2%, 19.1% and 24.6% in the first, second and third trimesters respectively.[2] Women with high risk pregnancies have higher rates of anxiety than low risk women; 45.0% vs 16.7% in one study.[23] Rates of depression were 7.4%, 12.8% and 12.0% in the general pregnant population in the first, second and third trimesters,[1] and ranged from 11% to 28% in studies on high risk pregnancies.[3,4,23,28,29] The high rates of anxiety seen in our study are consistent with published literature for high risk pregnancies with rates of depression in the lower range of those previously reported.

Although we do not have data for the whole pregnancy, it seems that gestational changes in rates of anxiety in women at high risk of spontaneous preterm birth may not follow the same trends as in the general pregnant population in which rates rise throughout pregnancy.[2] In our study, anxiety was highest at the beginning of the second trimester and then decreased to levels similar to those seen in general pregnant populations by the end of the second trimester. This may be due to reduced anxiety over second trimester loss once this gestational time period is complete (31.5% of our cohort had experienced a second trimester loss previously). However, advancing gestation is unlikely to be the sole factor in anxiety levels returning to those of the general pregnant population, as the risk of early preterm birth was still ongoing at the time of last clinic visit. This, along with women's perception of care, suggests that preterm birth clinic care may have had a role in improving psychological wellbeing. The provision of an overall ongoing risk assessment at the final clinic visit is likely to be beneficial; the majority of women were considered to have a relatively low ongoing risk of preterm birth and encouraged to return to a low risk model of maternity care.

Whilst there is some evidence that simply labelling a pregnancy 'high risk' may increase anxiety and fear, other studies identified that women embrace this label in a positive way.[10,11] A qualitative study has assessed women's perceptions of care in a preterm birth clinic in the United Kingdom, with all women viewing their high risk status positively.[11] These women reported that regular reassurance from the clinic was a helpful coping strategy and that other health professionals were not always sensitive to their worries about having another preterm birth.[11] Our results are consistent with these findings.

Preterm birth clinics offer individualised, coordinated and evidence-based care with the aim of reducing spontaneous preterm birth and improving perinatal outcome. Any potential to reduce psychological distress is an additional benefit. Further research should aim to include a comparison group to more directly quantify the effect of preterm birth clinics in improving psychological wellbeing. A larger sample size would also be required to direct practice change if considering the psychological, as well as clinical, benefit of preterm birth clinics. However the new knowledge from our study should reassure clinicians and policy makers that preterm birth clinics do not seem to cause psychological harm.

Symptoms of anxiety and depression were under-recognised by clinicians in this study, with low referral rates for psychological support or maternal mental health review based on usual indications. Early recognition of anxiety and depression with provision of support or referral for other interventions may reduce maternal morbidity and improve pregnancy outcomes, and is likely to reduce the risk of postnatal depression.[30] Our findings suggest there are currently missed opportunities for care and preterm birth clinics should ensure they have referral pathways and access to psychological assessment and support, or should incorporate this into part of standard care within the clinic.

The main limitations of our study are the lack of a comparison group and modest sample size. The most appropriate comparison is with women of similar preterm birth risk who do not receive care in a preterm birth clinic; however, withholding clinic care is not possible when a clinic is well established within an area and available to all. Use of the general population or a medically high risk group as a comparator is not appropriate as background anxiety levels for these women may increase over gestation due to increasing risk of other pregnancy complications, whereas the risk of preterm birth decreases with advancing gestation. Sample size was directed by the duration of the study and the number of women referred to the preterm birth clinic over the 12 month period. We are aware that not all women eligible for the clinic (and therefore for the study) were referred during this time period, and the women seen may have a higher risk profile than those who were eligible but not referred.

A further limitation is the use of screening tests rather than diagnostic criteria for anxiety and depression. Whilst diagnostic interviews are the gold standard, they are time consuming, require special training and are expensive.[31] Screening tests are reliable and have been validated for use in pregnancy.[28,32-38] The STAI with a cut-off >40 has a sensitivity of 81% and specificity of

80% for diagnosis of an anxiety disorder in pregnancy when compared to DSM-IV criteria.[39] The EPDS is also accurate, with a cut-off of >12 used in pregnancy, giving a sensitivity of 83% and specificity of 90% for detection of major depression.[40] Participant dropout may have influenced the study outcome as the majority were due to pregnancy loss or extremely early preterm birth, and these women may have had the highest risk pregnancies and hence highest levels of psychological distress. However, unadjusted analysis of only the 63 women who completed all assessments showed similar results to those presented here.

Strengths of this study include longitudinal assessment of a high risk cohort with a high recruitment rate in an ethnically diverse group of women. Although undertaken at a single site, referrals are accepted from the wider region, improving generalisability of results. There were multiple clinicians working in the clinic over the study period (two lead obstetricians, three senior obstetric trainees, and three specialist midwives), so an individual clinician is unlikely to have had significant influence over outcomes. Variation in practice between preterm birth clinics has been recognised as an issue,[41,42] however the general principles of care identified by women as factors that reduced anxiety i.e. close surveillance and regular ultrasound scans, are similar across clinics globally.

CONCLUSION

Women at increased risk of spontaneous preterm birth have high rates of anxiety in early pregnancy. Improvements in psychological wellbeing were seen during the time these women were cared for in a specialised preterm birth clinic through the second trimester. Women's perceptions of a preterm birth clinic were favourable and they attributed the care received as being a significant factor in reducing pregnancy-related anxiety. Findings of this study support the ongoing use and development of these specialised clinics.

FIGURE LEGEND

Figure 1. Participant recruitment and study flow diagram

TOP, termination of pregnancy.

[a] Reasons not eligible: 19 were pre-pregnancy consultations, 2 had previously participated in study (both with pregnancy losses), 9 had insufficient English (including one who provided consent but was then identified to have insufficient written English when attempted first set of questionnaires and was withdrawn from the study), 3 were >24 weeks at first visit, and 12 had a single visit planned only.

[b] Distressed with new diagnosis of severe hypertension and fetal growth restriction, subsequently had fetal demise before last visit.

[c] Gestational ages at delivery 16^{+1}, 22^{+3}, 23^{+4} and 24^{+4} weeks.

[d] Recent diagnosis of severe depression with acute distress.

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Competing interests statement

None of the authors have any competing interests to declare.

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Data sharing statement

Not applicable.

Contribution to authorship

All authors fulfil the authorship requirements described by the International Committee of Medical Journal Editors. LD was the lead investigator and was responsible for writing the first draft of the study protocol, obtaining ethical approval, the majority of data collection and analysis and wrote the first draft of the manuscript. KG was the supervising investigator, she conceived the idea for the study and provided substantial contribution to the study protocol, ethical approvals, analysis and interpretation of results. AL made substantial contributions to the statistical analyses and interpretation of results. JW made substantial contributions to the study design and interpretation of results. All authors critically reviewed the manuscript and approved the final version of the manuscript submitted for publication.

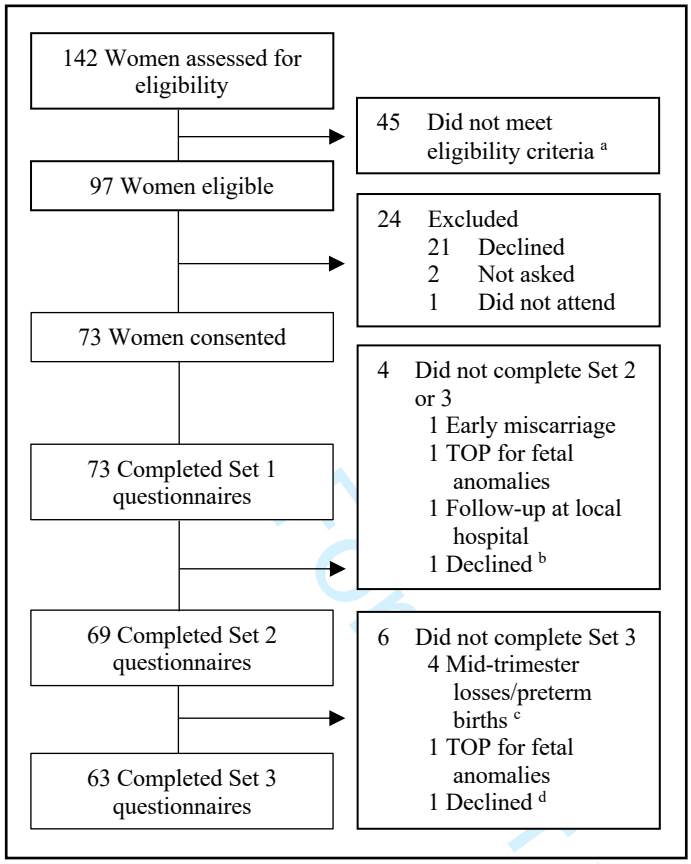
References

1. Bennett HA, Einarson A, Taddio A, et al. Prevalence of depression during pregnancy: Systematic review. *Obstet Gynecol*. 2004;103(4):698-709.
2. Dennis C-L, Falah-Hassani K, Shiri R. Prevalence of antenatal and postnatal anxiety: Systematic review and meta-analysis. *Br J Psychiatry*. 2017;210(5):315-23.
3. Dagklis T, Tsakiridis I, Chouliara F, et al. Antenatal depression among women hospitalized due to threatened preterm labor in a high-risk pregnancy unit in Greece. *J Matern Fetal Neonatal Med*. 2018;31(7):919-25.
4. Thiagayson P, Krishnaswamy G, Lim ML, et al. Depression and anxiety in Singaporean high-risk pregnancies: Prevalence and screening. *Gen Hosp Psychiatry*. 2013;35(2):112-6.
5. Fairbrother N, Young AH, Zhang A, et al. The prevalence and incidence of perinatal anxiety disorders among women experiencing a medically complicated pregnancy. *Arch Womens Ment Health*. 2017;20(2):311-9.
6. Vernet G, Watson H, Ridout A, et al. The role of PTB clinics: A review of the screening methods, interventions and evidence for preterm birth surveillance clinics for high-risk asymptomatic women. *Womens Health Bulletin*. 2017;4(4):2-9.
7. National Institute for Health and Care Excellence. Preterm Labour and Birth 2015. Available from: https://www.nice.org.uk/guidance/ng25/resources/preterm-labour-and-birth-pdf-1837333576645.
8. Jin W, Hughes K, Sim S, et al. The contemporary value of dedicated preterm birth clinics for high-risk singleton pregnancies: fifteen-year outcomes from a laeding maternal centre. *J Perinat Med.* Published online first: 20 May 2021. doi:10.1515/jpm-2021-0020.
9. Stahl K, Hundley V. Risk and risk assessment in pregnancy; do we scare because we care? *Midwifery*. 2003;19(4):298-309.
10. Simmons HA, Goldberg LS. 'High-risk' pregnancy after perinatal loss: Understanding the label. *Midwifery.* 2011;27(4):452-7.
11. O'Brien ET, Quenby S, Lavender T. Women's views of high risk pregnancy under threat of preterm birth. *Sex Reprod Healthc*. 2010;1(3):79-84.
12. Malouf R, Redshaw M. Specialist antenatal clinics for women at high risk of preterm birth: A systematic review of qualitative and quantitative research. *BMC Pregnancy Childbirth*. 2017;17(1):51.

13. Grigoriadis S, VonderPorten EH, Mamisashvili L, et al. The impact of maternal depression during pregnancy on perinatal outcomes: A systematic review and meta-analysis. *J Clin Psychiatry*. 2013;74(4):e321-41.
14. Grote NK, Bridge JA, Gavin AR, et al. A meta-analysis of depression during pregnancy and the risk of preterm birth, low birth weight, and intrauterine growth restriction. *Arch Gen Psychiatry*. 2010;67(10):1012-24.
15. Field T. Prenatal anxiety effects: A review. *Infant Behav Dev*. 2017;49:120-8.
16. Robertson E, Grace S, Wallington T, et al. Antenatal risk factors for postpartum depression: A synthesis of recent literature. *Gen Hosp Psychiatry*. 2004;26(4):289-95.
17. Giardinelli L, Innocenti A, Benni L, et al. Depression and anxiety in perinatal period: Prevalence and risk factors in an Italian sample. *Arch Womens Ment Health*. 2012;15(1):21-30.
18. Mind Garden. State-Trait Anxiety Inventory for Adults: Mind Garden; 2018 [Available from: https://www.mindgarden.com/145-state-trait-anxiety-inventory-for-adults.
19. Spielberger C, Gorsuch R, Lushene R. STAI: Manual for the State-Trait Anxiety Inventory (STAI). California: Consulting Psychologists Press; 1970.
20. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression: Development of the 10-item edinburgh postnatal depression scale. *Br J Psychiatry*. 1987;150(6):782-6.
21. Ware JE, Sherbourne CD. The MOS 36-Item Short-Form Health Survey (SF-36): I. Conceptual framework and item selection. *Med Care.* 1992;30(6):473-83.
22. RAND Corporation. 36-Item Short Form Survey (SF-36) 2018 [Available from: https://www.rand.org/health/surveys_tools/mos/36-item-short-form.html.
23. King NMA, Chambers J, O'Donnell K, et al. Anxiety, depression and saliva cortisol in women with a medical disorder during pregnancy. *Arch Womens Ment Health*. 2010;13(4):339-45.
24. IBM Corp. IBM SPSS Statistics for Windows. 25.0 ed. New York: IBM Corp; 2017.
25. R Core Team. R: A language and environment for statistical computing. 3.5.3 ed. Vienna, Austria: R Foundation for Statistical Computing; 2019.
26. Braun V, Clarke V. Using thematic analysis in psychology. Qualitative Research in *Psychology.* 2006;3(2):77-101.
27. SAS Institute. SAS Software. 9.4 ed. Cary, NC: SAS Institute; 2017.
28. Adouard F, Glangeaud-Freudenthal NMC, Golse B. Validation of the Edinburgh Postnatal Depression Scale (EPDS) in a sample of women with high-risk pregnancies in France. *Arch Womens Ment Health*. 2005;8(2):89-95.

29. Brandon AR, Trivedi MH, Hynan LS, et al. Prenatal depression in women hospitalized for obstetric risk. *J Clin Psychiatry*. 2008;69(4):635-43.
30. Austin M. Antenatal screening and early intervention for "perinatal" distress, depression and anxiety: where to from here? *Arch Womens Ment Health*. 2004;7(1):1-6.
31. Evans K, Spiby H, Morrell CJ. A psychometric systematic review of self-report instruments to identify anxiety in pregnancy. *J Adv Nurs.* 2015;71(9):1986-2001.
32. Gunning MD, Denison FC, Stockley CJ, et al. Assessing maternal anxiety in pregnancy with the State-Trait Anxiety Inventory (STAI): Issues of validity, location and participation. *J Reprod Infant Psychol.* 2010;28(3):266-73.
33. Grant N, Raouf S. A prospective population-based study to investigate the effectiveness of interventions to prevent preterm birth. *BJOG.* 2016;123:96.
34. Murray D, Cox JL. Screening for depression during pregnancy with the Edinburgh Depression Scale (EPDS). *J Reprod Infant Psychol.* 1990;8(2):99-107.
35. Bunevicius A, Kusminskas L, Pop VJ, et al. Screening for antenatal depression with the Edinburgh Depression Scale. *J Psychosom Obstet Gynecol.* 2009;30(4):238-43.
36. Gibson J, McKenzie-McHarg K, Shakespeare J, et al. A systematic review of studies validating the Edinburgh Postnatal Depression Scale in antepartum and postpartum women. *Acta Psychiatr Scand*. 2009;119(5):350-64.
37. Adewuya AO, Ola BA, Dada AO, et al. Validation of the Edinburgh Postnatal Depression Scale as a screening tool for depression in late pregnancy among Nigerian women. *J Psychosom Obstet Gynecol*. 2006;27(4):267-72.
38. Felice E, Saliba J, Grech V, et al. Validation of the Maltese version of the Edinburgh Postnatal Depression Scale. *Arch Womens Ment Health*. 2006;9(2):75-80.
39. Grant K, McMahon C, Austin M-P. Maternal anxiety during the transition to parenthood: A prospective study. *J Affect Disord*. 2008;108(1):101-11.
40. National Institute of Health and Clinical Excellence. Antenatal and Postnatal Mental Health: Clinical Management and Service Guidance 2014. Available from: https://www.nice.org.uk/guidance/cg192.
41. Care A, Ingleby L, Alfirevic Z, et al. The influence of the introduction of national guidelines on preterm birth prevention practice: UK experience. *BJOG.* 2019;126(6):763-9.

42. Dawes L, Groom K, Jordan V, et al. The use of specialised preterm birth clinics for women at high risk of spontaneous preterm birth: a systematic review. *BMC Pregnancy Childbirth*. 2020;20(1):58.



Supplementary Information

Supplementary Table 1. Standard practice in the preterm birth clinic

Clinic referral criteria	At least one of the following risk factors for spontaneous preterm birth: ▪ Previous spontaneous preterm birth or PPROM <36 weeks of gestation ▪ Previous spontaneous second trimester loss at 16^{+0} to 24^{+0} weeks of gestation ▪ Previous LLETZ with >10 mm depth of excision or ≥2 procedures of any depth ▪ Previous knife cone biopsy or trachelectomy ▪ Congenital uterine and/or cervical anomaly ▪ Short cervix detected on transvaginal ultrasound scan in current pregnancy of <25 mm at $<24^{+0}$ weeks of gestation ▪ Other risk factors e.g. ≥2 surgical termination of pregnancy and/or evacuation of retained products of conception procedures, complicated caesarean section at full dilatation, history of diethylstilboestrol exposure (woman or her mother), known collagen or connective tissue disorders
Initial consultation at around 12 weeks	Obstetric and medical review is undertaken to identify risk factors for preterm birth, along with vaginal examination, microbiological swabs, midstream urine for culture and transvaginal ultrasound assessment of the cervix.[1] Women are provided with information regarding their individualised risk for preterm birth and counselled on potential interventions including lifestyle and behaviour change (including support for smoking cessation), serial cervical length assessment, cervical cerclage and progesterone therapy, and an individualised plan of care is made. History-indicated (elective) cervical cerclage is generally reserved for women with multiple second trimester miscarriages or spontaneous preterm births, in line with current evidence.[2] Progesterone is not offered as prophylactic treatment and use is considered only in women who develop a short cervix.
Psychological support	Clinician assessment of psychological wellbeing was performed during routine clinical assessment. Referral to women's health social work or maternal mental health services was offered to women identified as needing additional psychological support.
Subsequent reviews	In the majority of cases, subsequent visits are fortnightly from 14 to 24 weeks and include a review of pregnancy progress and transvaginal ultrasound assessment of the cervix. Ultrasound-indicated cervical cerclage or vaginal progesterone are recommended if the cervix shortens to <25 mm. Decisions regarding these interventions are made on an individual basis including further review of risk factors, other signs and symptoms and cervical length.
On-going care	Women are discharged back to their lead maternity carer at 23 to 25 weeks. An overall risk assessment for very early preterm birth is

	made at the final visit and includes the selective use of quantitative fetal fibronectin and the QUiPP App for those thought at highest risk. The QUiPP App[3] combines history, cervical length and fetal fibronectin to predict spontaneous preterm birth within certain timeframes and is used to guide decisions on hospital admission and antenatal corticosteroid use.

LLETZ, large loop excision of the transformation zone; PPROM, preterm pre-labour rupture of membranes.

Supplementary Table 2. Study specific questionnaires from Set 1

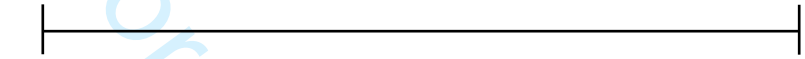
Study specific questionnaire Set 1
1. Which ethnic group do you belong to? Mark the space or spaces which apply to you. ☐ New Zealand European ☐ Māori ☐ Samoan ☐ Cook Island Māori ☐ Tongan ☐ Niuean ☐ Chinese ☐ Indian ☐ Other such as Dutch, Japanese, Tokelauan. Please state: _____
2. Were you aware that you had an increased risk of your baby being born early in this pregnancy before you got pregnant? ☐ Yes If yes, please go to question 3 ☐ No If no, please go to question 4
3. Did you contemplate not getting pregnant prior to this pregnancy because you were worried about your increased chance of having a baby born early? ☐ Yes ☐ No
4. Once you were pregnant, did your lead maternity carer (midwife, GP or obstetrician) identify that there was an increased chance of your baby being born early in this pregnancy? ☐ Yes If yes, please go to question 5 ☐ No If no, please go to question 6
5. How did you feel when your lead maternity carer (midwife, GP or obstetrician) identified that there was an increased chance of your baby being born early in this pregnancy? ☐ Very anxious ☐ Somewhat anxious ☐ No different / the same ☐ Somewhat reassured ☐ Very reassured
6. How did you feel after your maternity care provider (midwife, GP or obstetrician) suggested you come to the Preterm Birth Clinic? ☐ Significantly more anxious ☐ Somewhat more anxious ☐ No different / the same ☐ Somewhat more reassured ☐ Significantly more reassured
7. How did you feel after you read the pamphlet about what to expect in the Preterm Birth Clinic that was included with your appointment details? ☐ Significantly more anxious ☐ Somewhat more anxious ☐ No different / the same ☐ Somewhat more reassured

- ☐ Significantly more reassured

8. Do you have a partner?
   - ☐ Yes
   - ☐ No

9. How would you describe your social support network (for example your partner, whānau/family, friends)?
   - ☐ Very unsupportive
   - ☐ Somewhat unsupportive
   - ☐ Neither supportive nor unsupportive
   - ☐ Somewhat supportive
   - ☐ Very supportive

10. Note how anxious (on average) you have felt about your pregnancy over the past 7 days with a mark (|) on the line below.



11. What are you most anxious about in this pregnancy? *(space for response)*

12. What do you find most helpful to relieve any pregnancy-related anxiety? *(space for response)*

13. Have you ever been diagnosed with any of the following mental health conditions?
   - ☐ Depression
   - ☐ Postnatal depression
   - ☐ Generalised anxiety disorder
   - ☐ Post-traumatic stress disorder
   - ☐ Social anxiety disorder
   - ☐ Panic disorder
   - ☐ Obsessive-compulsive disorder
   - ☐ Bipolar disorder
   - ☐ Schizophrenia
   - ☐ Borderline personality disorder
   - ☐ Other, please name _____
   - ☐ None

14. Are you currently taking any prescribed medication for a mental health condition?
   - ☐ Yes. If so, what is the name of this medication? _____
   - ☐ No

15. Have you ever taken any prescribed medication for a mental health condition?
   - ☐ Yes. If so, what is the name of this medication? _____
   - ☐ No

16. Are you currently under the care of a psychiatrist or psychologist?
   - ☐ Yes. If so, what is this for? _____
   - ☐ No

17. Have you ever been seen by a psychiatrist?
   - ☐ Yes. If so, when was this and what was it for? _____
   - ☐ No

18. Are you taking any pregnancy supplements or probiotics, other than folic acid, Elevit or iodine?

☐ Yes. If so, what is the name of the supplement/s? _____ ☐ No

Supplementary Table 3. Study specific questionnaires from Set 3

Study specific questionnaire Set 3
1. How have you found the quality of your general pregnancy care? ☐ Very low quality ☐ Low quality ☐ Neither high or low quality ☐ High quality ☐ Very high quality
2. How have you found the quality of your care through the Preterm Birth Clinic? ☐ Very low quality ☐ Low quality ☐ Neither high or low quality ☐ High quality ☐ Very high quality
3. Do you think that being seen in a preterm birth clinic made you more or less anxious about your pregnancy? ☐ Significantly more anxious ☐ Somewhat more anxious ☐ Neither more or less anxious ☐ Somewhat less anxious ☐ Significantly less anxious
4. If you have another pregnancy, would you want to be cared for through a preterm birth clinic again? ☐ Yes ☐ No ☐ Unsure
5. Note how anxious (on average) you have felt about your pregnancy over the past 7 days with a mark (|) on the line below. Not at all anxious ——— Extremely anxious
6. What are you most anxious about in this pregnancy? *(space for response)*
7. What do you find most helpful to relieve any pregnancy-related anxiety? *(space for response)*
8. Have you been diagnosed with a mental health condition since you were first seen in the Preterm Birth Clinic this pregnancy? ☐ Yes, if so please provide details_____ ☐ No

Supplementary Table 4. Criteria for risk classification for study purposes at discharge from the preterm birth clinic

Risk classification	Criteria
Low	Cervical length >25 mm, AND Quantitative fetal fibronectin level of <50 ng/ml if performed (based on usual clinical indications), AND No intervention (progesterone or cerclage) required during the current pregnancy due to cervical change
Intermediate	Shortened cervical length to 11-25 mm, AND/OR Quantitative fetal fibronectin level of 50-199 ng/ml if performed (based on usual indications), AND/OR Need for progesterone and/or cerclage during the current pregnancy due to cervical change
High	Shortened cervical length to <10 mm, AND/OR Quantitative fetal fibronectin level of ≥200 ng/ml if performed (based on usual indications)

Supplementary Table 5. Women's knowledge of their preterm birth risk and their perceptions of preterm birth clinic care

Question and response	Number (%)
Set 1 (baseline)	
1. Were you aware that you had an increased risk of your baby being born early before you got pregnant?	
Yes	59/73 (80.8)
No	14/73 (19.2)
2. Did you contemplate not getting pregnant because you were worried about your increased chance of having a baby born early? [a]	
Yes	19/59 (32.2)
No	40/59 (67.8)
3. Once you were pregnant, did your lead maternity carer (midwife, GP or obstetrician) identify that there was an increased chance of your baby being born early?	
Yes	51/71 (71.8)
No	20/71 (28.2)
4. How did you feel when your lead maternity carer (midwife, GP or obstetrician) identified that there was an increased chance of your baby being born early? [b]	
Very anxious	11/51 (21.6)
Somewhat anxious	20/51 (39.2)
Neither anxious nor relieved	12/51 (23.5)
Somewhat relieved	5/51 (9.8)
Very relieved	3/51 (5.9)
5. How did you feel after your maternity care provider (midwife, GP or obstetrician) suggested you come to the Preterm Birth Clinic?	
Significantly more anxious	8/71 (11.3)
Somewhat more anxious	12/71 (16.9)
Neither more or less anxious	11/71 (15.5)
Somewhat less anxious	24/71 (33.8)
Significantly less anxious	16/71 (22.5)
6. How did you feel after you read the pamphlet about what to expect in the Preterm Birth Clinic that was included with your appointment details?	
Significantly more anxious	1/69 (1.4)
Somewhat more anxious	13/69 (18.8)
Neither more or less anxious	30/69 (43.5)
Somewhat less anxious	20/69 (29.0)
Significantly less anxious	5/69 (7.2)
8. How would you describe your social support network (for example your partner, whānau/family, friends)?	
Very unsupportive	7/72 (9.7)
Somewhat unsupportive	1/72 (1.4)
Neither supportive nor unsupportive	2/72 (2.8)
Somewhat supportive	6/72 (8.3)
Very supportive	56/72 (77.8)
Set 3 (after last visit)	

1. How have you found the quality of your general pregnancy care?	
Very low quality	0/63 (0.0)
Low quality	1/63 (1.6)
Neither high or low quality	4/63 (6.3)
High quality	13/63 (20.6)
Very high quality	45/63 (71.4)
2. How have you found the quality of your care through the Preterm Birth Clinic?	
Very low quality	0/63 (0.0)
Low quality	1/63 (1.6)
Neither high or low quality	1/63 (1.6)
High quality	12/63 (19.0)
Very high quality	49/63 (77.8)
3. Do you think that being seen in a preterm birth clinic made you more or less anxious about your pregnancy?	
Significantly more anxious	2/63 (3.2)
Somewhat more anxious	2/63 (3.2)
Neither more or less anxious	3/63 (4.8)
Somewhat less anxious	14/63 (22.2)
Significantly less anxious	42/63 (66.7)
4. If you have another pregnancy, would you want to be cared for through a preterm birth clinic again?	
Yes	55/63 (87.3)
No	7/63 (11.1)
Unsure	1/63 (1.6)

GP, general practitioner.

Denominator reflects numbered of respondents that answered each individual question.

[a] Only answered if responded 'Yes' to question 1.

[b] Only answered if responded 'Yes' to question 3.

References for Supplementary Material

1. Auckland District Health Board. Referral to the National Women's Health Preterm Birth Clinic Auckland: Auckland District Health Board; 2019. Available from: http://nationalwomenshealth.adhb.govt.nz/assets/Uploads/PTB-Clinic-Referral-Guidelines-ACH-May2019.pdf
2. Vernet G, Watson H, Ridout A, Shennan A. The Role of PTB Clinics: A Review of the Screening Methods, Interventions and Evidence for Preterm Birth Surveillance Clinics for High-Risk Asymptomatic Women. Women Health Bull. 2017;4(4):e12667.
3. Kuhrt K, Smout E, Hezelgrave N, Seed PT, Carter J, Shennan AH. Development and validation of a tool incorporating cervical length and quantitative fetal fibronectin to predict spontaneous preterm birth in asymptomatic high-risk women. Ultrasound in Obstetrics & Gynecology. 2016;47(1):104-9.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6-7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5,8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	7-8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	N/A
		(*c*) Explain how missing data were addressed	19
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed	19
		(*e*) Describe any sensitivity analyses	N/A

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Fig 1
		(b) Give reasons for non-participation at each stage	Fig 1
		(c) Consider use of a flow diagram	Fig 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9-10
		(b) Indicate number of participants with missing data for each variable of interest	9-10
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	10
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	11-12
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11-12
		(*b*) Report category boundaries when continuous variables were categorized	11
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	16-17
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18-19
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	18-19
Generalisability	21	Discuss the generalisability (external validity) of the study results	19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	20

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The psychological wellbeing of women at high risk of spontaneous preterm birth cared for in a specialised preterm birth clinic: a prospective longitudinal cohort study

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TITLE PAGE

Full title

The psychological wellbeing of women at high risk of spontaneous preterm birth cared for in a specialised preterm birth clinic: a prospective longitudinal cohort study

Authors

Lisa K. Dawes (MBChB, MD)[1,2]

Jason J.S. Waugh (MBBS)[2,3]

Arier C. Lee (PhD)[4]

Katie M. Groom (MBBS, PhD)[1,2]

Affiliations

[1] Liggins Institute, The University of Auckland, Auckland, New Zealand

[2] National Women's Health, Auckland City Hospital, Auckland, New Zealand

[3] Department of Obstetrics and Gynaecology, The University of Auckland, Auckland, New Zealand

[4] Section of Epidemiology and Biostatistics, The University of Auckland, Auckland, New Zealand

Contact information for corresponding author

Lisa K. Dawes

Address: Liggins Institute, The University of Auckland, Private Bag 92019, Auckland 1142, New Zealand

Phone: +64 21 158 2076

Email: l.dawes@auckland.ac.nz

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ABSTRACT

Objectives: To assess the psychological wellbeing of pregnant women at increased risk of spontaneous preterm birth, and the impact of care from a preterm birth clinic.

Design: Single-centre longitudinal cohort study over one year, 2018-2019.

Setting: Tertiary maternity hospital in Auckland, New Zealand.

Participants: Pregnant women at increased risk of spontaneous preterm birth receiving care in a preterm birth clinic.

Intervention: Participants completed three sets of questionnaires (State-Trait Anxiety Inventory, Edinburgh Postnatal Depression Scale, 36-Item Short Form Survey) – prior to their first, after their second, and after their last clinic appointments. Study-specific questionnaires explored pregnancy-related anxiety and perceptions of care.

Primary and secondary outcome measures: The primary outcome was the mean state-anxiety score. Secondary outcomes included depression and quality of life measures.

Results: 73/97 (75.3%) eligible women participated; 41.1% had a previous preterm birth, 31.5% a second trimester loss and 28.8% cervical surgery; 20.6% had a prior mental health condition. 63/73 (86.3%) women completed all questionnaires. The adjusted mean state-anxiety score was 39.0 at baseline, which decreased to 36.5 after the second visit (difference -2.5, 95% CI -5.5 to 0.5, *P=0.1*) and to 32.6 after the last visit (difference -3.9 from second visit, 95% CI -6.4 to -1.5, *P=0.002*). Rates of anxiety (state-anxiety score >40) and depression (Edinburgh Postnatal Depression Scale score >12) were 38.4%, 34.8%, 19.0%, and 13.7%, 8.7%, 9.5% respectively, at the same time periods. Perceptions of care were favourable; 88.9% stated the preterm birth clinic made them significantly or somewhat less anxious and 87.3% wanted to be seen again in a future pregnancy.

Conclusions: Women at increased risk of spontaneous preterm birth have high levels of anxiety. Psychological wellbeing improved during the second trimester; women perceived that

preterm birth clinic care reduced pregnancy-related anxiety. These findings support the ongoing use and development of preterm birth clinics.

Strengths and limitations of this study

- This is the first study to assess the psychological wellbeing of women at high risk of spontaneous preterm birth who are cared for in a specialised preterm birth clinic.
- Strengths of the study include the prospective study design, and high rates of recruitment and participant retention in an ethnically diverse group of women.
- Limitations of the study are the modest sample size, lack of a comparison group and the use of screening tools rather than diagnostic criteria for anxiety and depression,.
- Although this study demonstrates improved psychological wellbeing of women at high risk of spontaneous preterm birth, further research is required to more directly quantify the impact of a preterm birth clinic on this.

Main Text

INTRODUCTION

Psychological disorders are common in pregnancy.[1,2] Women with high risk pregnancies are more likely to suffer psychological distress with higher rates of anxiety and depression than the general pregnant population.[3-5] Few studies have assessed the psychological wellbeing of women who are at high risk of spontaneous preterm birth, and in particular, the potential impact of care from a specialised preterm birth clinic. Preterm birth clinics provide a package of care to asymptomatic women identified to be at increased risk based on their obstetric and gynaecological history. This care includes regular visits through the second trimester for ultrasound surveillance of cervical length and provision of treatments to prevent preterm birth such as cervical cerclage and vaginal progesterone therapy when indicated.[6,7,8] Close monitoring and reassurance provided through a preterm birth clinic may reduce pregnancy-related anxiety, however, it is also possible that being labelled 'high risk' may increase psychological distress and anxiety.[9-11] Further research in this area has been recommended.[12]

There is increasing recognition of the importance of psychological wellbeing in pregnancy. Meta-analyses show that antenatal depression is associated with a modestly increased risk of preterm birth and fetal growth restriction, and decreased rates of breastfeeding initiation.[13,14] The effect of anxiety is less well evaluated, but is associated with increased pregnancy-related hypertension and caesarean section, decreased rates of exclusive breastfeeding and increased anxiety in the offspring.[15] Antenatal anxiety and depression are also strong predictors of postnatal depression.[16] Strategies for prevention, along with improvements in the recognition and treatment of psychological disorders in pregnancy, are likely to improve outcomes for women and children.[17]

This study aims to assess rates of anxiety, depression and health-related quality of life in pregnant women at high risk of spontaneous preterm birth who are cared for in a preterm birth clinic. The primary hypothesis is that women will have less anxiety after their second consultation in a preterm birth clinic compared to before their first (baseline), and this improvement will be sustained at the end of the second trimester. Secondary hypotheses are that women will have fewer symptoms of depression, improved quality of life, and less pregnancy-related anxiety over the same period.

MATERIAL AND METHODS

This longitudinal cohort study was carried out in a large tertiary maternity hospital in Auckland, New Zealand. All eligible women attending the preterm birth clinic over a 12 month period from August 2018 to August 2019 were invited to participate prior to their first appointment. This preterm birth clinic provides care to pregnant women perceived to be at high risk of spontaneous preterm birth and accepts local and regional referrals. Eligibility criteria for the preterm birth clinic include women with a previous spontaneous preterm birth, previous second trimester loss, history of extensive cervical surgery, or congenital uterine anomaly. Care through the preterm birth clinic includes initial assessment, risk factor modification, serial surveillance of cervical length until 24 weeks, and interventions such as vaginal progesterone and cervical cerclage when indicated (Supplementary Table 1). Care in the preterm birth clinic is provided by a specialist obstetric and midwifery team on a weekly basis, and is in addition to routine antenatal care.

Inclusion criteria for the study were gestational age $<24^{+0}$ weeks at first visit; live fetus; eligible for preterm birth clinic review due to $\geq$1 risk factor for spontaneous preterm birth (Supplementary Table 1); written consent obtained; and sufficient English to independently complete questionnaires. Participants completed three sets of questionnaires: prior to their first clinic appointment (baseline, Set 1), after their second appointment (usually 2-3 weeks later, Set 2), and after their last appointment (usually at 23-24 weeks of gestation, Set 3). Three women were seen for only two appointments and returned the Set 3 questionnaires by post two weeks after their last visit. Each set of questionnaires contained three validated measures: the State-Trait Anxiety Inventory (STAI), used under licence from Mind Garden Incorporated[18] which contains two subscales to allow differentiation between temporary 'state-anxiety' and the relatively stable and long-standing aspects of anxiety proneness in 'trait-anxiety';[19] the Edinburgh Postnatal Depression Scale (EPDS) which is validated for antenatal depression;[20] and the RAND 36-Item Short Form Survey (SF-36) to assess health-related quality of life.[21,22] Set 1 and 3 also included a study-specific questionnaire to assess mental health history, social support, pregnancy-related anxiety and perceptions of care. This included free text responses on pregnancy-related anxiety triggers and what helped to relieve it (Supplementary Tables 2 and 3). The study-specific questionnaires were developed by the research team and piloted for the first five women and minor changes made based on feedback.

For the purposes of this study, state-anxiety was considered the most relevant assessment for current levels of anxiety. A screen positive result was defined as a score of >40 on the STAI state-anxiety score. Pregnancy-related anxiety was also assessed using a ten-point visual analogue scale and reported separately. In the assessment of depression, a screen positive result was defined as a score of >12 on the EPDS.

Participants were contacted by telephone prior to their first appointment and invited to participate, and participant information and consent forms were provided in advance to interested women. After consenting, participants completed hard copy questionnaires independently using a private room, just prior to their first clinic consultation. The EPDS self-harm question was reviewed at completion and for any women answering 'yes, quite often' or 'sometimes', further assessment of safety was made and referral to maternal mental health services offered. No other changes were made to clinical care. All other responses were seen only by a single investigator not responsible for decisions about referral for psychological support, until completion of the study. Standard clinic practice is described in Supplementary Table 1. At the last visit, the discharging obstetrician used pre-defined criteria developed for the purposes of this study to classify ongoing preterm birth risk. Women were considered low risk if cervical length was >25 mm with fetal fibronectin <50 ng/ml (if performed), and no intervention with vaginal progesterone or cerclage required; intermediate risk if cervical length was 11-25 mm, and/or fetal fibronectin 50-199 ng/ml, and/or there was need for progesterone or cerclage; or high risk if cervical length was <10 mm, and/or fetal fibronectin ≥200 ng/ml (Supplementary Table 4).

Demographic details, pregnancy characteristics, medical history, and pregnancy outcomes were obtained from electronic medical records. These data, along with questionnaire responses were entered into a password-protected Excel spreadsheet by a single investigator.

The primary outcome was the STAI state-anxiety score. Secondary outcomes were the EPDS score, SF-36 summary quality of life scores, and pregnancy-related anxiety (as continuous measures).

Statistical analyses

A pragmatic sample size was used. We aimed to invite all eligible women over a one year period to participate. Using data from medically high risk women,[23] we estimated a sample size of 60

would provide 80% power, with alpha of 0.05, two-sided test and an estimated within subject correlation of 0.75 to detect a decrease in the mean state-anxiety score from 40.0 (SD 12.0) to 36.9.

Descriptive statistics were calculated using SPSS (version 25.0) and R software (version 3.5.3).[24,25] Thematic analysis was carried out on free-text responses using Braun and Clarke methodology by a single investigator.[26] The mixed model for repeated measures analyses (MMRM) was used to analyse repeatedly measured continuous outcomes and conducted using SAS software (version 9.4).[27] This analyses was used to test for time effect adjusting for prior diagnosis of a mental health condition, gestational age at first visit and obstetric history (categorised by no previous pregnancy beyond 12 weeks; loss/preterm birth at 12-28 weeks; loss/preterm birth at 28-37 weeks; or term birth only), and subject was included as a random effect. Kenward-Roger method was used to estimate the denominator degrees of freedom for fixed effects. Two-sided P-value <0.05 determined statistical significance. All confidence intervals (CI) are given at a two-sided 95% level.

Ethical approval

Ethical approval was granted by the New Zealand Health and Disability Ethics Committees (18/NTA/103) and institutional approval by the Auckland District Health Board Research Review Committee (A+8127) in July 2018.

Patient and public involvement

The study-specific questionnaire was piloted amongst the first five participants, who were asked for feedback on the clarity and importance of the questions. There was no other patient involvement in the study development.

RESULTS

The recruitment rate was 75.3% (73/97), participation is described in Figure 1. Demographics, obstetric characteristics and risk factors for preterm birth are detailed in Table 1. Some women had been seen in the clinic in a previous pregnancy (17/73, 23.3%) and/or for pre-pregnancy review (12/73, 16.4%).

Table 1. Demographic details, obstetric characteristics and risk factors for preterm birth

Characteristic	Number (%) or mean (SD), n=73
Ethnicity	
European	36 (49.3)
Māori	7 (9.6)
Pacific	5 (6.8)
Asian	11 (15.1)
Indian	9 (12.3)
Other	5 (6.8)
Age (years)	
Mean	34.0 (5.1)
Range	22-45
Body mass index (kg/m^2) [a]	
Mean	26.3 (6.4)
Range	19-57
Current smoker	5 (6.8)
Has a current partner	72 (98.6)
Previous diagnosis of a mental health condition (non-exclusive) [b]	
Depression	10 (13.7)
Postnatal depression	4 (5.5)
Generalised anxiety disorder	2 (2.7)
Panic disorder	1 (1.4)
Social anxiety disorder	1 (1.4)
Post-traumatic spectrum disorder	3 (4.1)
None	58 (79.4)
Currently taking medication for a mental health condition?	4 (5.5)
Currently under the care of a psychiatrist/psychologist	1 (1.4)
Nulliparous	16 (21.9)
Previous stillbirth or neonatal death ≥20^{+0} weeks	22 (30.1)
Current twin pregnancy	1 (1.4)
Reasons for preterm birth clinic referral (non-exclusive)	
Previous spontaneous preterm birth/PPROM (24^{+0} to 36^{+0} weeks) [c]	30 (41.1)
Previous second trimester loss (16^{+0} to 23^{+6} weeks)	23 (31.5)

Previous extensive cervical surgery [d]	21 (28.8)
Congenital uterine anomaly	1 (1.4)
Short cervix in current pregnancy <25 mm	5 (6.8)
≥2 surgical terminations and/or other uterine instrumentations	14 (19.2)
Other risk factors for spontaneous preterm birth	4 (5.5)
Multiple reasons for referral to the preterm birth clinic	23 (31.5)

SD, standard deviation; mm, millimetres; PPROM, pre-labour premature rupture of membranes; LLETZ, large loop excision of the transformation zone.

[a] Missing data n=2.

[b] Self-reported.

[c] Includes survivors born at 23 weeks of gestation.

[d] LLETZ with depth of excision ≥10 mm or >1 procedure, or knife cone biopsy.

The mean gestational ages at questionnaire completion were 13^{+4} weeks (SD 3^{+3}), 16^{+2} weeks (SD 3^{+2}) and 23^{+6} weeks (SD 1^{+2}). Anxiety, depression and quality of life scores and proportion of screen positive results (defined as >40 on the STAI state-anxiety scale and >12 on the EPDS) are shown in Table 2. MMRM analyses, adjusting for gestation at first visit, prior mental health condition and obstetric history (fixed effects), are described in Table 3. The primary outcome of the adjusted mean state-anxiety score was 39.0 at baseline and decreased to 36.5 after the second visit (least square means difference -2.5, 95% CI -5.5 to 0.5, *P=0.1*), with a further reduction to 32.6 after the last visit (least squares means difference -3.9 from the second visit, 95% CI -6.4 to -1.5, *P=0.002*). Adjusted secondary outcomes are reported in Table 3.

Table 2. Anxiety, depression and quality of life scores (unadjusted)

	Set 1 (baseline), n=73 [a]		Set 2, n=69 [a]		Set 3, n=63 [a]	
	Mean (SD) or proportion (%)	95% CI	Mean (SD) or proportion (%)	95% CI	Mean (SD) or proportion (%)	95% CI
STAI state-anxiety score	38.6 (11.9)	36.8 – 41.3	36.2 (11.6)	33.5 – 38.9	32.0 (9.8)	29.6 – 34.4
STAI state-anxiety positive screen [b]	28/73 (38.4)	27.2 – 49.5	24/69 (34.8)	23.5 – 46.0	12/63 (19.0)	9.4 – 28.7
STAI trait-anxiety score	37.3 (10.1)	35.0 – 39.6	36.5 (9.6) [c]	34.2 – 38.8	34.9 (10.8)	32.2 – 37.6
STAI trait-anxiety positive screen [b]	28/73 (38.4)	27.2 – 49.5	23/68 (33.8) [c]	22.6 – 45.1	15/63 (23.8)	13.3 – 34.3
EPDS score	7.3 (4.6)	6.2 – 8.4	6.0 (4.5)	4.9 – 7.1	5.4 (5.1)	4.1 – 6.6
EPDS positive screen [d]	10/73 (13.7)	5.8 – 21.6	6/69 (8.7)	2.0 – 15.3	6/63 (9.5)	2.3 – 16.8
Summary mental health score [e]	63.8 (15.9) [e]	60.0 – 67.8	65.7 (17.0) [g]	61.5 – 69.9	72.4 (17.9) [f]	67.8 – 77.0
Summary physical health score [e]	69.3 (21.5) [d]	64.3 – 74.3	66.0 (24.1) [i]	60.2 – 71.8	71.3 (22.7) [d]	65.6 – 77.0
Pregnancy-related anxiety [j]	4.9 (2.5) [d]	4.3 – 5.5	-	-	2.7 (2.5)	2.1 – 3.3

STAI, State Trait Anxiety Inventory; SD, standard deviation; CI, confidence interval; EPDS, Edinburgh Postnatal Depression Scale.

[a] Set 1 questionnaires were completed prior to the women's first clinic appointment (baseline); Set 2 after their second appointment (usually 2-3 weeks later); Set 3 after their last appointment (usually at 23-24 weeks of gestation).

[b] Positive screen defined as STAI score >40.

[c] Missing score for one woman as one incomplete question.

[d] Positive screen defined as EPDS >12.

[e] Using the RAND 36-Item Short Form Survey. Higher scores associated with better quality of life.

[f] Missing scores for nine women as one or more incomplete questions.

[g] Missing scores for five women as one or more incomplete questions.

[h] Missing scores for four women as one or more incomplete questions.

[i] Missing scores for three women as one or more incomplete questions.

[j] Visual analogue scale, 0 = not at all anxious, 10 = extremely anxious.

Table 3. Mixed model for repeated measures analyses for anxiety, depression and quality of life scores

	STAI state-anxiety score			EPDS score			Summary physical health score [a]			Summary mental health score [a]		
Fixed effect	**P value** [b]			**P value** [b]			**P value** [b]			**P value** [b]		
Questionnaire set number	<0.0001			0.0001			0.3			<0.0001		
Gestation at first visit [c]	0.7			0.4			0.2			0.2		
Prior mental health condition [c]	0.7			0.09			0.6			0.006		
Obstetric history [c, d]	0.4			0.04			0.8			0.3		
Least squares means	**Estimate**	**95% CI**		**Estimate**	**95% CI**		**Estimate**	**95% CI**		**Estimate**	**95% CI**	
Set 1	39.0	35.6 – 42.4		7.5	6.1 – 8.9		70.9	63.9 – 77.8		60.7	55.8 – 65.6	
Set 2	36.5	33.0 – 40.0		6.3	4.9 – 7.7		67.2	60.1 – 74.4		62.5	57.5 – 67.4	
Set 3	32.6	29.1 – 36.1		5.7	4.3 – 7.1		71.5	64.3 – 78.6		69.5	64.6 – 74.5	
Least squares means difference	**Estimate**	**95% CI**	**P value** [e]	**Estimate**	**95% CI**	**P value** [e]	**Estimate**	**95% CI**	**p value** [e]	**Estimate**	**95% CI**	**P value** [e]
Set 2 - 1	-2.5	-5.5 – 0.5	0.1	-1.2	-2.3 – -0.2	0.02	-3.7	-10.1 – 2.8	0.3	1.8	-3.1 – 6.6	0.5
Set 3 - 1	-6.4	-8.8 – -4.0	<0.0001	-1.8	-2.6 – -1.0	<0.0001	0.6	-4.6 – 5.8	0.8	8.9	4.7 – 13.0	<0.0001
Set 3 - 2	-3.9	-6.4 – -1.5	0.002	-0.6	-1.4 – 0.2	0.2	4.2	-1.1 – 9.6	0.1	7.1	-3.0 – -11.2	0.001

STAI, State Trait Anxiety Inventory; EPDS, Edinburgh Postnatal Depression Scale; CI, confidence interval.

[a] RAND 36-Item Short Form Survey. Higher scores associated with better quality of life.

[b] Pr > F. Type 3 tests of fixed effects.

[c] Analysis adjusted for these factors.

[d] Categorised by no previous pregnancy beyond 12 weeks; loss/preterm birth at 12-28 weeks; loss/preterm birth at 28-37 weeks; or term birth only.

[e] Pr > |t|

One woman was referred to maternal mental health services following review of the EPDS self-harm question. Preterm birth clinic clinicians referred six women to the women's health social work for psychological support and two to maternal mental health services as part of routine practice. None of the women who completed the Set 3 questionnaires reported having a new diagnosis of a mental health condition during the study period made by a health practitioner. One woman declined to complete the last set of questionnaires after a diagnosis of severe depression.

Women had mixed feelings about referral to the clinic prior to review, but following their last visit 56/63 (88.9%) reported care in the preterm birth clinic made them significantly or somewhat less anxious. The majority (55/63, 87.3%) would want to be cared for in a preterm birth clinic again in another pregnancy. The seven women who did not, had already had a term birth since their prior early birth, or were referred for cervical surgery or multiple uterine instrumentations only (and only one required an intervention greater than surveillance in their current pregnancy) (Supplementary Table 5).

The predominant themes causing pregnancy-related anxiety at baseline were preterm birth, pregnancy loss, and concern for the baby's health. Many women were anxious about extremely early birth – *"being born too early to do anything about it,"* and were worried about reaching milestones – *"getting to 24 weeks to be deemed to have a 'viable' pregnancy."* Women were worried about history repeating itself – *"I am scared that it might happen again,"* and how they would cope if it did – *"my ability to manage emotions associated with NICU [neonatal intensive care unit] if this baby is early."* Fewer women were anxious about the risks of chromosomal or fetal anomalies.

When asked at clinic discharge what they found most helpful to relieve pregnancy-related anxiety, the main theme was medical support, including close monitoring, the preterm birth clinic, regular ultrasound scans, and support and communication from doctors – *"the fortnightly visits have really helped me! Lots of reassurance," "follow up from the preterm birth clinic," "the weekly check-ups and reassurance from the doctors and how quickly they acted when there was an issue,"* and *"the support of specialists who are willing to listen."* Other themes included support from family and friends, distraction, relaxation techniques and prayer.

The mean number of clinic visits was 5.4 (SD 2.1), range 1-11. Clinic interventions and pregnancy outcomes are reported in Table 4. Elective cervical cerclage is reserved for the highest risk women, and was performed in 17/72 cases (23.6%, excludes one women with local follow up after the first visit as no further data collected), usually at 12-14 weeks gestation. The remaining women had ultrasound surveillance of cervical length as their primary management. The overall rate of birth <37 weeks was 17/72 (23.6%), including two spontaneous second trimester losses. One extremely early preterm birth followed pre-labour fetal demise, all other preterm births occurred following spontaneous labour or preterm pre-labour rupture of membranes. Of pregnancies that reached ≥20^{+0} weeks 67/69 (97.1%) babies were alive at hospital discharge.

Table 4. Preterm birth clinic interventions and pregnancy outcomes [a]

Characteristics	**Proportion (%) or mean (SD)**
Shortest transvaginal cervical length measurement	
Mean (SD) (in mm)	27.0 (9.1)
Range (in mm)	0-39
Number <25 mm (threshold for intervention)	21/72 (29.2)
Treatments given to reduce the risk of preterm birth	
Cervical cerclage only	16/72 (22.2)
Vaginal progesterone only	4/72 (5.6)
Both cervical cerclage and vaginal progesterone	10/72 (13.9)
No treatment	40/72 (55.6)
Antenatal hospital admission from clinic due to preterm birth risk	2/72 (2.8)
Risk of preterm birth for those who had an exit visit [b]	
Low	45/66 (68.2)
Intermediate	18/66 (27.3)
High	3/66 (4.5)
Pregnancy outcome	
Termination of pregnancy for fetal anomalies	2/72 (2.8)
First trimester miscarriage (<13^{+0} weeks)	1/72 (1.4)
Second trimester loss (13^{+1} to 22^{+6} weeks)	2/72 (2.8)
Extremely early preterm birth (23^{+0} to 27^{+6} weeks) [d]	3/72 (4.2)
Very early preterm birth (28^{+0} to 31^{+6} weeks)	1/72 (1.4)

Moderate to late preterm birth (32^{+0} to 36^{+6} weeks)	11/72 (15.3)
Term birth ($\geq 37^{+0}$ weeks)	52/72 (72.2)
Mode of birth for pregnancies that reached $\geq 20^{+0}$ weeks [e]	
Normal vaginal birth	44/68 (64.7)
Instrumental birth	7/68 (10.3)
Caesarean section	17/68 (25.0)
Neonatal outcome for pregnancies that reached $\geq 20^{+0}$ weeks [e f]	
Alive at hospital discharge	67/69 (97.1)
Early neonatal death	1/69 (1.4)
Stillbirth	1/69 (1.4)

[a] Excluding one with all follow up at local hospital after first visit as no further data collected.

[b] Risk assessment defined in Supplementary Table 4. Quantitative fetal fibronectin was included in 29/66 (44%) cases. Excludes six women who did not have an exit appointment. Includes three women who did not complete Set 3 questionnaires – for two the exit visit was their second visit, both were high risk and delivered prior to planned completion of the Set 3 questionnaires by post; and one who declined.

[d] Includes one pre-labour fetal demise.

[e] Excluding one termination of pregnancy >20 weeks.

[f] Includes one set of twins.

DISCUSSION

This is the first study to assess the psychological wellbeing of women receiving care in a specialised preterm birth clinic. It identifies high rates of psychological distress, with 38.4% and 13.7% of women having significant symptoms of anxiety and depression, respectively, at the beginning of the second trimester. Whilst the change in mean state-anxiety scores after two clinic visits did not reach statistical significance, improvement may still be clinically important. Adjusted mean state-anxiety scores were significantly improved by clinic discharge, with rates of anxiety half that of baseline. Although depression was less common than anxiety, the adjusted mean EPDS score improved by the second clinic visit and this was sustained to the end of the second trimester. Quality of life improved with regard to mental health, but not physical health. Pregnancy-related anxiety scores also improved and women perceived care in the preterm birth clinic to be a significant factor in relieving anxiety.

A number of studies have reported rates of anxiety and depression in pregnancy, with a wide range of estimates.[1,2] In systematic review, the overall prevalence of a clinical diagnosis of an anxiety disorder in pregnancy was 15.2%, with rates of self-reported anxiety of 18.2%, 19.1% and 24.6% in the first, second and third trimesters respectively.[2] Women with high risk pregnancies have higher rates of anxiety than low risk women; 45.0% vs 16.7% in one study.[23] Rates of depression were 7.4%, 12.8% and 12.0% in the general pregnant population in the first, second and third trimesters,[1] and ranged from 11% to 28% in studies on high risk pregnancies.[3,4,23,28,29] The higher rates of anxiety seen in our study are consistent with published literature for high risk pregnancies with rates of depression in the lower range of those previously reported.

Although we do not have data for the whole pregnancy, it seems that gestational changes in rates of anxiety in women at high risk of spontaneous preterm birth may not follow the same trends as in the general pregnant population in which rates rise throughout pregnancy.[2] In our study, anxiety was highest at the beginning of the second trimester and then decreased to levels similar to those seen in general pregnant populations by the end of the second trimester. This may be due to reduced anxiety over second trimester loss once this gestational time period is complete (31.5% of our cohort had experienced a second trimester loss previously). However, advancing gestation is unlikely to be the sole factor in anxiety levels returning to those of the general pregnant population, as the risk of early preterm birth was still ongoing at the time of last clinic visit. This, along with women's perception of care, suggests that preterm birth clinic care may have had a role in improving psychological wellbeing. The provision of an overall ongoing risk assessment at the final clinic visit is likely to be beneficial; the majority of women were considered to have a relatively low ongoing risk of preterm birth and encouraged to return to a low risk model of maternity care.

Whilst there is some evidence that simply labelling a pregnancy 'high risk' may increase anxiety and fear, other studies identified that women embrace this label in a positive way.[10,11] A qualitative study has assessed women's perceptions of care in a preterm birth clinic in the United Kingdom, with all women viewing their high risk status positively.[11] These women reported that regular reassurance from the clinic was a helpful coping strategy and that other health professionals were not always sensitive to their worries about having another preterm birth.[11] Our results are consistent with these findings.

Preterm birth clinics offer individualised, coordinated and evidence-based care with the aim of reducing spontaneous preterm birth and improving perinatal outcome. Any potential to reduce psychological distress is an additional benefit. Further research should aim to include a comparison group to more directly quantify the effect of preterm birth clinics in improving psychological wellbeing. A larger sample size would also be required to direct practice change if considering the psychological, as well as clinical, benefit of preterm birth clinics. However the new knowledge from our study should reassure clinicians and policy makers that preterm birth clinics do not seem to cause psychological harm.

Symptoms of anxiety and depression were under-recognised by clinicians in this study, with low referral rates for psychological support or maternal mental health review based on usual indications. Early recognition of anxiety and depression with provision of support or referral for other interventions may reduce maternal morbidity and improve pregnancy outcomes, and is likely to reduce the risk of postnatal depression.[30] Our findings suggest there are currently missed opportunities for care and preterm birth clinics should ensure they have referral pathways and access to psychological assessment and support, or should incorporate this into part of standard care within the clinic.

The main limitations of our study are the lack of a comparison group and modest sample size. The most appropriate comparison is with women of similar preterm birth risk who do not receive care in a preterm birth clinic; however, withholding clinic care is not possible when a clinic is well established within an area and available to all. Use of the general population or a medically high risk group as a comparator is not appropriate as background anxiety levels for these women may increase over gestation due to increasing risk of other pregnancy complications, whereas the risk of preterm birth decreases with advancing gestation. Sample size was directed by the duration of the study and the number of women referred to the preterm birth clinic over the 12 month period. We are aware that not all women eligible for the clinic (and therefore for the study) were referred during this time period, and the women seen may have a higher risk profile than those who were eligible but not referred.

A further limitation is the use of screening tests rather than diagnostic criteria for anxiety and depression. Whilst diagnostic interviews are the gold standard, they are time consuming, require special training and are expensive.[31] Screening tests are reliable and have been validated for use in pregnancy.[28,32-38] The STAI with a cut-off >40 has a sensitivity of 81% and specificity of

80% for diagnosis of an anxiety disorder in pregnancy when compared to DSM-IV criteria.[39] The EPDS is also accurate, with a cut-off of >12 used in pregnancy, giving a sensitivity of 83% and specificity of 90% for detection of major depression.[40] Participant dropout may have influenced the study outcome as the majority were due to pregnancy loss or extremely early preterm birth, and these women may have had the highest risk pregnancies and hence highest levels of psychological distress. However, unadjusted analysis of only the 63 women who completed all assessments showed similar results to those presented here.

Strengths of this study include longitudinal assessment of a high risk cohort with a high recruitment rate in an ethnically diverse group of women. Although undertaken at a single site, referrals are accepted from the wider region, improving generalisability of results. There were multiple clinicians working in the clinic over the study period (two lead obstetricians, three senior obstetric trainees, and three specialist midwives), so an individual clinician is unlikely to have had significant influence over outcomes. Variation in practice between preterm birth clinics has been recognised as an issue,[41,42] however the general principles of care identified by women as factors that reduced anxiety i.e. close surveillance and regular ultrasound scans, are similar across clinics globally.

CONCLUSION

Women at increased risk of spontaneous preterm birth are more likely to have higher levels of anxiety in early pregnancy. Improvements in psychological wellbeing were seen during the time these women were cared for in a specialised preterm birth clinic through the second trimester. Women's perceptions of a preterm birth clinic were favourable and they attributed the care received as being a significant factor in reducing pregnancy-related anxiety. Findings of this study support the ongoing use and development of these specialised clinics.

FIGURE LEGEND

Figure 1. Participant recruitment and study flow diagram

TOP, termination of pregnancy.

[a] Reasons not eligible: 19 were pre-pregnancy consultations, 2 had previously participated in study (both with pregnancy losses), 9 had insufficient English (including one who provided consent but was then identified to have insufficient written English when attempted first set of questionnaires and was withdrawn from the study), 3 were >24 weeks at first visit, and 12 had a single visit planned only.

[b] Distressed with new diagnosis of severe hypertension and fetal growth restriction, subsequently had fetal demise before last visit.

[c] Gestational ages at delivery 16^{+1}, 22^{+3}, 23^{+4} and 24^{+4} weeks.

[d] Recent diagnosis of severe depression with acute distress.

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Competing interests statement

None of the authors have any competing interests to declare.

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Data sharing statement

Not applicable.

Contribution to authorship

All authors fulfil the authorship requirements described by the International Committee of Medical Journal Editors. LD was the lead investigator and was responsible for writing the first draft of the study protocol, obtaining ethical approval, the majority of data collection and analysis and wrote the first draft of the manuscript. KG was the supervising investigator, she conceived the idea for the study and provided substantial contribution to the study protocol, ethical approvals, analysis and interpretation of results. AL made substantial contributions to the statistical analyses and interpretation of results. JW made substantial contributions to the study design and interpretation of results. All authors critically reviewed the manuscript and approved the final version of the manuscript submitted for publication.

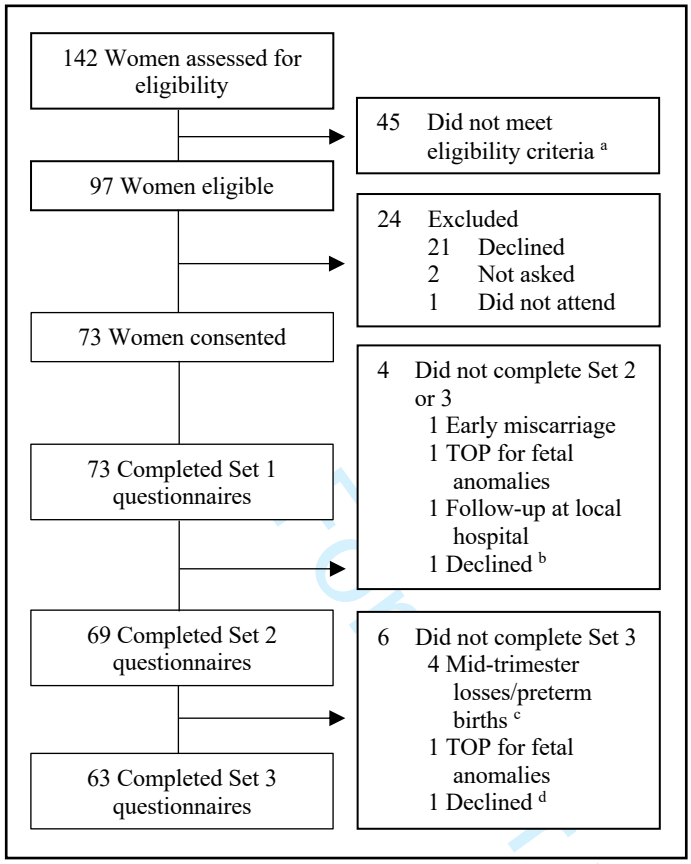
References

1. Bennett HA, Einarson A, Taddio A, et al. Prevalence of depression during pregnancy: Systematic review. *Obstet Gynecol*. 2004;103(4):698-709.
2. Dennis C-L, Falah-Hassani K, Shiri R. Prevalence of antenatal and postnatal anxiety: Systematic review and meta-analysis. *Br J Psychiatry*. 2017;210(5):315-23.
3. Dagklis T, Tsakiridis I, Chouliara F, et al. Antenatal depression among women hospitalized due to threatened preterm labor in a high-risk pregnancy unit in Greece. *J Matern Fetal Neonatal Med*. 2018;31(7):919-25.
4. Thiagayson P, Krishnaswamy G, Lim ML, et al. Depression and anxiety in Singaporean high-risk pregnancies: Prevalence and screening. *Gen Hosp Psychiatry*. 2013;35(2):112-6.
5. Fairbrother N, Young AH, Zhang A, et al. The prevalence and incidence of perinatal anxiety disorders among women experiencing a medically complicated pregnancy. *Arch Womens Ment Health*. 2017;20(2):311-9.
6. Vernet G, Watson H, Ridout A, et al. The role of PTB clinics: A review of the screening methods, interventions and evidence for preterm birth surveillance clinics for high-risk asymptomatic women. *Womens Health Bulletin*. 2017;4(4):2-9.
7. National Institute for Health and Care Excellence. Preterm Labour and Birth 2015. Available from: https://www.nice.org.uk/guidance/ng25/resources/preterm-labour-and-birth-pdf-1837333576645.
8. Jin W, Hughes K, Sim S, et al. The contemporary value of dedicated preterm birth clinics for high-risk singleton pregnancies: fifteen-year outcomes from a laeding maternal centre. *J Perinat Med.* Published online first: 20 May 2021. doi:10.1515/jpm-2021-0020.
9. Stahl K, Hundley V. Risk and risk assessment in pregnancy; do we scare because we care? *Midwifery*. 2003;19(4):298-309.
10. Simmons HA, Goldberg LS. 'High-risk' pregnancy after perinatal loss: Understanding the label. *Midwifery.* 2011;27(4):452-7.
11. O'Brien ET, Quenby S, Lavender T. Women's views of high risk pregnancy under threat of preterm birth. *Sex Reprod Healthc*. 2010;1(3):79-84.
12. Malouf R, Redshaw M. Specialist antenatal clinics for women at high risk of preterm birth: A systematic review of qualitative and quantitative research. *BMC Pregnancy Childbirth*. 2017;17(1):51.

13. Grigoriadis S, VonderPorten EH, Mamisashvili L, et al. The impact of maternal depression during pregnancy on perinatal outcomes: A systematic review and meta-analysis. *J Clin Psychiatry*. 2013;74(4):e321-41.
14. Grote NK, Bridge JA, Gavin AR, et al. A meta-analysis of depression during pregnancy and the risk of preterm birth, low birth weight, and intrauterine growth restriction. *Arch Gen Psychiatry*. 2010;67(10):1012-24.
15. Field T. Prenatal anxiety effects: A review. *Infant Behav Dev*. 2017;49:120-8.
16. Robertson E, Grace S, Wallington T, et al. Antenatal risk factors for postpartum depression: A synthesis of recent literature. *Gen Hosp Psychiatry*. 2004;26(4):289-95.
17. Giardinelli L, Innocenti A, Benni L, et al. Depression and anxiety in perinatal period: Prevalence and risk factors in an Italian sample. *Arch Womens Ment Health*. 2012;15(1):21-30.
18. Mind Garden. State-Trait Anxiety Inventory for Adults: Mind Garden; 2018 [Available from: https://www.mindgarden.com/145-state-trait-anxiety-inventory-for-adults.
19. Spielberger C, Gorsuch R, Lushene R. STAI: Manual for the State-Trait Anxiety Inventory (STAI). California: Consulting Psychologists Press; 1970.
20. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression: Development of the 10-item edinburgh postnatal depression scale. *Br J Psychiatry*. 1987;150(6):782-6.
21. Ware JE, Sherbourne CD. The MOS 36-Item Short-Form Health Survey (SF-36): I. Conceptual framework and item selection. *Med Care.* 1992;30(6):473-83.
22. RAND Corporation. 36-Item Short Form Survey (SF-36) 2018 [Available from: https://www.rand.org/health/surveys_tools/mos/36-item-short-form.html.
23. King NMA, Chambers J, O'Donnell K, et al. Anxiety, depression and saliva cortisol in women with a medical disorder during pregnancy. *Arch Womens Ment Health*. 2010;13(4):339-45.
24. IBM Corp. IBM SPSS Statistics for Windows. 25.0 ed. New York: IBM Corp; 2017.
25. R Core Team. R: A language and environment for statistical computing. 3.5.3 ed. Vienna, Austria: R Foundation for Statistical Computing; 2019.
26. Braun V, Clarke V. Using thematic analysis in psychology. Qualitative Research in *Psychology.* 2006;3(2):77-101.
27. SAS Institute. SAS Software. 9.4 ed. Cary, NC: SAS Institute; 2017.
28. Adouard F, Glangeaud-Freudenthal NMC, Golse B. Validation of the Edinburgh Postnatal Depression Scale (EPDS) in a sample of women with high-risk pregnancies in France. *Arch Womens Ment Health*. 2005;8(2):89-95.

29. Brandon AR, Trivedi MH, Hynan LS, et al. Prenatal depression in women hospitalized for obstetric risk. *J Clin Psychiatry*. 2008;69(4):635-43.
30. Austin M. Antenatal screening and early intervention for "perinatal" distress, depression and anxiety: where to from here? *Arch Womens Ment Health*. 2004;7(1):1-6.
31. Evans K, Spiby H, Morrell CJ. A psychometric systematic review of self-report instruments to identify anxiety in pregnancy. *J Adv Nurs.* 2015;71(9):1986-2001.
32. Gunning MD, Denison FC, Stockley CJ, et al. Assessing maternal anxiety in pregnancy with the State-Trait Anxiety Inventory (STAI): Issues of validity, location and participation. *J Reprod Infant Psychol.* 2010;28(3):266-73.
33. Grant N, Raouf S. A prospective population-based study to investigate the effectiveness of interventions to prevent preterm birth. *BJOG.* 2016;123:96.
34. Murray D, Cox JL. Screening for depression during pregnancy with the Edinburgh Depression Scale (EPDS). *J Reprod Infant Psychol.* 1990;8(2):99-107.
35. Bunevicius A, Kusminskas L, Pop VJ, et al. Screening for antenatal depression with the Edinburgh Depression Scale. *J Psychosom Obstet Gynecol.* 2009;30(4):238-43.
36. Gibson J, McKenzie-McHarg K, Shakespeare J, et al. A systematic review of studies validating the Edinburgh Postnatal Depression Scale in antepartum and postpartum women. *Acta Psychiatr Scand*. 2009;119(5):350-64.
37. Adewuya AO, Ola BA, Dada AO, et al. Validation of the Edinburgh Postnatal Depression Scale as a screening tool for depression in late pregnancy among Nigerian women. *J Psychosom Obstet Gynecol*. 2006;27(4):267-72.
38. Felice E, Saliba J, Grech V, et al. Validation of the Maltese version of the Edinburgh Postnatal Depression Scale. *Arch Womens Ment Health*. 2006;9(2):75-80.
39. Grant K, McMahon C, Austin M-P. Maternal anxiety during the transition to parenthood: A prospective study. *J Affect Disord*. 2008;108(1):101-11.
40. National Institute of Health and Clinical Excellence. Antenatal and Postnatal Mental Health: Clinical Management and Service Guidance 2014. Available from: https://www.nice.org.uk/guidance/cg192.
41. Care A, Ingleby L, Alfirevic Z, et al. The influence of the introduction of national guidelines on preterm birth prevention practice: UK experience. *BJOG.* 2019;126(6):763-9.

42. Dawes L, Groom K, Jordan V, et al. The use of specialised preterm birth clinics for women at high risk of spontaneous preterm birth: a systematic review. *BMC Pregnancy Childbirth*. 2020;20(1):58.



Supplementary Information

Supplementary Table 1. Standard practice in the preterm birth clinic

Clinic referral criteria	At least one of the following risk factors for spontaneous preterm birth: ▪ Previous spontaneous preterm birth or PPROM <36 weeks of gestation ▪ Previous spontaneous second trimester loss at 16^{+0} to 24^{+0} weeks of gestation ▪ Previous LLETZ with >10 mm depth of excision or ≥2 procedures of any depth ▪ Previous knife cone biopsy or trachelectomy ▪ Congenital uterine and/or cervical anomaly ▪ Short cervix detected on transvaginal ultrasound scan in current pregnancy of <25 mm at $<24^{+0}$ weeks of gestation ▪ Other risk factors e.g. ≥2 surgical termination of pregnancy and/or evacuation of retained products of conception procedures, complicated caesarean section at full dilatation, history of diethylstilboestrol exposure (woman or her mother), known collagen or connective tissue disorders
Initial consultation at around 12 weeks	Obstetric and medical review is undertaken to identify risk factors for preterm birth, along with vaginal examination, microbiological swabs, midstream urine for culture and transvaginal ultrasound assessment of the cervix.[1] Women are provided with information regarding their individualised risk for preterm birth and counselled on potential interventions including lifestyle and behaviour change (including support for smoking cessation), serial cervical length assessment, cervical cerclage and progesterone therapy, and an individualised plan of care is made. History-indicated (elective) cervical cerclage is generally reserved for women with multiple second trimester miscarriages or spontaneous preterm births, in line with current evidence.[2] Progesterone is not offered as prophylactic treatment and use is considered only in women who develop a short cervix.
Psychological support	Clinician assessment of psychological wellbeing was performed during routine clinical assessment. Referral to women's health social work or maternal mental health services was offered to women identified as needing additional psychological support.
Subsequent reviews	In the majority of cases, subsequent visits are fortnightly from 14 to 24 weeks and include a review of pregnancy progress and transvaginal ultrasound assessment of the cervix. Ultrasound-indicated cervical cerclage or vaginal progesterone are recommended if the cervix shortens to <25 mm. Decisions regarding these interventions are made on an individual basis including further review of risk factors, other signs and symptoms and cervical length.
On-going care	Women are discharged back to their lead maternity carer at 23 to 25 weeks. An overall risk assessment for very early preterm birth is

	made at the final visit and includes the selective use of quantitative fetal fibronectin and the QUiPP App for those thought at highest risk. The QUiPP App[3] combines history, cervical length and fetal fibronectin to predict spontaneous preterm birth within certain timeframes and is used to guide decisions on hospital admission and antenatal corticosteroid use.

LLETZ, large loop excision of the transformation zone; PPROM, preterm pre-labour rupture of membranes.

Supplementary Table 2. Study specific questionnaires from Set 1

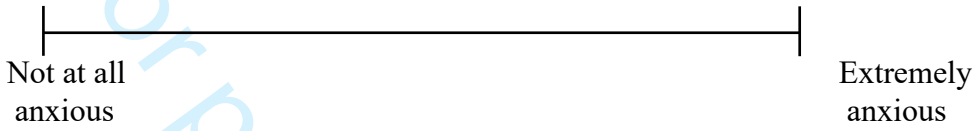
Study specific questionnaire Set 1
1. Which ethnic group do you belong to? Mark the space or spaces which apply to you. ☐ New Zealand European ☐ Māori ☐ Samoan ☐ Cook Island Māori ☐ Tongan ☐ Niuean ☐ Chinese ☐ Indian ☐ Other such as Dutch, Japanese, Tokelauan. Please state: _____
2. Were you aware that you had an increased risk of your baby being born early in this pregnancy before you got pregnant? ☐ Yes If yes, please go to question 3 ☐ No If no, please go to question 4
3. Did you contemplate not getting pregnant prior to this pregnancy because you were worried about your increased chance of having a baby born early? ☐ Yes ☐ No
4. Once you were pregnant, did your lead maternity carer (midwife, GP or obstetrician) identify that there was an increased chance of your baby being born early in this pregnancy? ☐ Yes If yes, please go to question 5 ☐ No If no, please go to question 6
5. How did you feel when your lead maternity carer (midwife, GP or obstetrician) identified that there was an increased chance of your baby being born early in this pregnancy? ☐ Very anxious ☐ Somewhat anxious ☐ No different / the same ☐ Somewhat reassured ☐ Very reassured
6. How did you feel after your maternity care provider (midwife, GP or obstetrician) suggested you come to the Preterm Birth Clinic? ☐ Significantly more anxious ☐ Somewhat more anxious ☐ No different / the same ☐ Somewhat more reassured ☐ Significantly more reassured
7. How did you feel after you read the pamphlet about what to expect in the Preterm Birth Clinic that was included with your appointment details? ☐ Significantly more anxious ☐ Somewhat more anxious ☐ No different / the same ☐ Somewhat more reassured

- ☐ Significantly more reassured

8. Do you have a partner?
   - ☐ Yes
   - ☐ No

9. How would you describe your social support network (for example your partner, whānau/family, friends)?
   - ☐ Very unsupportive
   - ☐ Somewhat unsupportive
   - ☐ Neither supportive nor unsupportive
   - ☐ Somewhat supportive
   - ☐ Very supportive

10. Note how anxious (on average) you have felt about your pregnancy over the past 7 days with a mark (|) on the line below.



11. What are you most anxious about in this pregnancy? *(space for response)*

12. What do you find most helpful to relieve any pregnancy-related anxiety? *(space for response)*

13. Have you ever been diagnosed with any of the following mental health conditions?
   - ☐ Depression
   - ☐ Postnatal depression
   - ☐ Generalised anxiety disorder
   - ☐ Post-traumatic stress disorder
   - ☐ Social anxiety disorder
   - ☐ Panic disorder
   - ☐ Obsessive-compulsive disorder
   - ☐ Bipolar disorder
   - ☐ Schizophrenia
   - ☐ Borderline personality disorder
   - ☐ Other, please name _____
   - ☐ None

14. Are you currently taking any prescribed medication for a mental health condition?
   - ☐ Yes. If so, what is the name of this medication? _____
   - ☐ No

15. Have you ever taken any prescribed medication for a mental health condition?
   - ☐ Yes. If so, what is the name of this medication? _____
   - ☐ No

16. Are you currently under the care of a psychiatrist or psychologist?
   - ☐ Yes. If so, what is this for? _____
   - ☐ No

17. Have you ever been seen by a psychiatrist?
   - ☐ Yes. If so, when was this and what was it for? _____
   - ☐ No

18. Are you taking any pregnancy supplements or probiotics, other than folic acid, Elevit or iodine?

☐ Yes. If so, what is the name of the supplement/s? _____ ☐ No

Supplementary Table 3. Study specific questionnaires from Set 3

Study specific questionnaire Set 3
1. How have you found the quality of your general pregnancy care? ☐ Very low quality ☐ Low quality ☐ Neither high or low quality ☐ High quality ☐ Very high quality
2. How have you found the quality of your care through the Preterm Birth Clinic? ☐ Very low quality ☐ Low quality ☐ Neither high or low quality ☐ High quality ☐ Very high quality
3. Do you think that being seen in a preterm birth clinic made you more or less anxious about your pregnancy? ☐ Significantly more anxious ☐ Somewhat more anxious ☐ Neither more or less anxious ☐ Somewhat less anxious ☐ Significantly less anxious
4. If you have another pregnancy, would you want to be cared for through a preterm birth clinic again? ☐ Yes ☐ No ☐ Unsure
5. Note how anxious (on average) you have felt about your pregnancy over the past 7 days with a mark (|) on the line below. Not at all anxious ——— Extremely anxious
6. What are you most anxious about in this pregnancy? *(space for response)*
7. What do you find most helpful to relieve any pregnancy-related anxiety? *(space for response)*
8. Have you been diagnosed with a mental health condition since you were first seen in the Preterm Birth Clinic this pregnancy? ☐ Yes, if so please provide details_____ ☐ No

Supplementary Table 4. Criteria for risk classification for study purposes at discharge from the preterm birth clinic

Risk classification	Criteria
Low	Cervical length >25 mm, AND Quantitative fetal fibronectin level of <50 ng/ml if performed (based on usual clinical indications), AND No intervention (progesterone or cerclage) required during the current pregnancy due to cervical change
Intermediate	Shortened cervical length to 11-25 mm, AND/OR Quantitative fetal fibronectin level of 50-199 ng/ml if performed (based on usual indications), AND/OR Need for progesterone and/or cerclage during the current pregnancy due to cervical change
High	Shortened cervical length to <10 mm, AND/OR Quantitative fetal fibronectin level of ≥200 ng/ml if performed (based on usual indications)

Supplementary Table 5. Women's knowledge of their preterm birth risk and their perceptions of preterm birth clinic care

Question and response	Number (%)
Set 1 (baseline)	
1. Were you aware that you had an increased risk of your baby being born early before you got pregnant?	
Yes	59/73 (80.8)
No	14/73 (19.2)
2. Did you contemplate not getting pregnant because you were worried about your increased chance of having a baby born early? [a]	
Yes	19/59 (32.2)
No	40/59 (67.8)
3. Once you were pregnant, did your lead maternity carer (midwife, GP or obstetrician) identify that there was an increased chance of your baby being born early?	
Yes	51/71 (71.8)
No	20/71 (28.2)
4. How did you feel when your lead maternity carer (midwife, GP or obstetrician) identified that there was an increased chance of your baby being born early? [b]	
Very anxious	11/51 (21.6)
Somewhat anxious	20/51 (39.2)
Neither anxious nor relieved	12/51 (23.5)
Somewhat relieved	5/51 (9.8)
Very relieved	3/51 (5.9)
5. How did you feel after your maternity care provider (midwife, GP or obstetrician) suggested you come to the Preterm Birth Clinic?	
Significantly more anxious	8/71 (11.3)
Somewhat more anxious	12/71 (16.9)
Neither more or less anxious	11/71 (15.5)
Somewhat less anxious	24/71 (33.8)
Significantly less anxious	16/71 (22.5)
6. How did you feel after you read the pamphlet about what to expect in the Preterm Birth Clinic that was included with your appointment details?	
Significantly more anxious	1/69 (1.4)
Somewhat more anxious	13/69 (18.8)
Neither more or less anxious	30/69 (43.5)
Somewhat less anxious	20/69 (29.0)
Significantly less anxious	5/69 (7.2)
8. How would you describe your social support network (for example your partner, whānau/family, friends)?	
Very unsupportive	7/72 (9.7)
Somewhat unsupportive	1/72 (1.4)
Neither supportive nor unsupportive	2/72 (2.8)
Somewhat supportive	6/72 (8.3)
Very supportive	56/72 (77.8)
Set 3 (after last visit)	

1. How have you found the quality of your general pregnancy care?	
Very low quality	0/63 (0.0)
Low quality	1/63 (1.6)
Neither high or low quality	4/63 (6.3)
High quality	13/63 (20.6)
Very high quality	45/63 (71.4)
2. How have you found the quality of your care through the Preterm Birth Clinic?	
Very low quality	0/63 (0.0)
Low quality	1/63 (1.6)
Neither high or low quality	1/63 (1.6)
High quality	12/63 (19.0)
Very high quality	49/63 (77.8)
3. Do you think that being seen in a preterm birth clinic made you more or less anxious about your pregnancy?	
Significantly more anxious	2/63 (3.2)
Somewhat more anxious	2/63 (3.2)
Neither more or less anxious	3/63 (4.8)
Somewhat less anxious	14/63 (22.2)
Significantly less anxious	42/63 (66.7)
4. If you have another pregnancy, would you want to be cared for through a preterm birth clinic again?	
Yes	55/63 (87.3)
No	7/63 (11.1)
Unsure	1/63 (1.6)

GP, general practitioner.

Denominator reflects numbered of respondents that answered each individual question.

[a] Only answered if responded 'Yes' to question 1.

[b] Only answered if responded 'Yes' to question 3.

References for Supplementary Material

1. Auckland District Health Board. Referral to the National Women's Health Preterm Birth Clinic Auckland: Auckland District Health Board; 2019. Available from: http://nationalwomenshealth.adhb.govt.nz/assets/Uploads/PTB-Clinic-Referral-Guidelines-ACH-May2019.pdf
2. Vernet G, Watson H, Ridout A, Shennan A. The Role of PTB Clinics: A Review of the Screening Methods, Interventions and Evidence for Preterm Birth Surveillance Clinics for High-Risk Asymptomatic Women. Women Health Bull. 2017;4(4):e12667.
3. Kuhrt K, Smout E, Hezelgrave N, Seed PT, Carter J, Shennan AH. Development and validation of a tool incorporating cervical length and quantitative fetal fibronectin to predict spontaneous preterm birth in asymptomatic high-risk women. Ultrasound in Obstetrics & Gynecology. 2016;47(1):104-9.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6-7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5,8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	7-8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	N/A
		(*c*) Explain how missing data were addressed	19
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed	19
		(*e*) Describe any sensitivity analyses	N/A

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Fig 1
		(b) Give reasons for non-participation at each stage	Fig 1
		(c) Consider use of a flow diagram	Fig 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9-10
		(b) Indicate number of participants with missing data for each variable of interest	9-10
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	10
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	11-12
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11-12
		(*b*) Report category boundaries when continuous variables were categorized	11
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	16-17
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18-19
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	18-19
Generalisability	21	Discuss the generalisability (external validity) of the study results	19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	20