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Differences in post-traumatic stress, anxiety and depression following miscarriage and ectopic pregnancy between women and their partners: a multi-centre, prospective, cohort study

SHORT TITLE

The psychology of early pregnancy loss in partners

Jessica Farren *clinical research fellow*[1,2], Maria Jalmbrant *clinical psychologist*[1], Nora Falconieri *medical statistician*[3], Nicola Mitchell-Jones *clinical research fellow*[1,2,4], Shabnam Bobdiwala *clinical research fellow*[1,2], Maya Al-Memar *clinical research fellow*[1,2], Sophie Tapp *medical student*[2], Ben Van Calster *associate professor*[3,5,6], Laure Wynants *assistant professor*[3,6,7], Dirk Timmerman *professor of obstetrics and gynecology*[3,8], Tom Bourne *professor of gynecology*[1,2,3]

Corresponding author: Professor Tom Bourne, Tommy's National Centre for Miscarriage Research, Imperial College, Queen Charlottes and Chelsea Hospital, Du Cane Road, London W12 0HS

E-mail: t.bourne@ic.ac.uk

Telephone : 07768 076797

Co-author affiliations:

1 Tommy's National Centre for Miscarriage Research, Queen Charlottes and Chelsea Hospital, Imperial College, London W12 0HS, UK

2 Department of Obstetrics and Gynaecology, Imperial College Healthcare Trust, London W2 1NY, UK

3 KU Leuven, Department of Development and Regeneration, Herestraat 49 box 805, 3000 Leuven, Belgium

4 Department of Obstetrics and Gynaecology, Chelsea and Westminster NHS Trust, London SW10 9NH, UK

5 Department of Biomedical Data Sciences, Leiden University Medical Centre (LUMC), Leiden, the Netherlands

6 EPI-centre, KU Leuven, Leuven, Belgium

7 Department of Epidemiology, CAPHRI Care and Public Health Research Institute, Maastricht University, PO Box 616, 6200 MD, Maastricht, The Netherlands

8 Department of Obstetrics and Gynaecology, University Hospitals Leuven, Herestraat 49 box 7003, 3000 Leuven, Belgium

CONTRIBUTION

What are the novel findings of this work?

This was the first study to use a standardised psychometric instrument to assess for symptoms of post-traumatic stress in partners of women after early pregnancy loss. All partners recruited were male. We found a small proportion of men met screening criteria for post-traumatic stress, which was lower than the proportion of women at one month.

What are the clinical implications of this work? –

There is considerable disparity in the emotional response to early pregnancy loss between women and their partners, which may impact relationships. Although less frequent, some partners report clinically relevant levels of anxiety, depression and posttraumatic stress symptoms after a loss. Clinicians should consider onward assessment or treatment.

Abstract

Objectives: To investigate and compare post-traumatic stress, depression and anxiety in women and their partners over a nine-month period following miscarriage or ectopic pregnancy.

Methods: This was a prospective cohort study. Consecutive women and partners were approached in the early pregnancy units of three central London hospitals. One, three and nine months after early pregnancy loss, recruits were emailed links to surveys containing the Hospital Anxiety and Depression Scale (HADS) and Post-traumatic Diagnostic Scale (PDS). The proportion of participants meeting screening criteria for moderate/severe anxiety or depression and post-traumatic stress (PTS) was assessed. Mixed-effects logistic regression was used to analyse differences between women and partners and the evolution over time.

Results: 386 partners were approached after the woman in whom the loss had been diagnosed consented to participate. 192 couples were recruited. All partners were male. Response rates were 57%, 45% and 38% for partners, and 76%, 68% and 57% for women, at month 1, 3, and 9 respectively. For partners, 7% met criteria for PTS at month 1, 8% at month 3 and 4% at month 9, compared to 34%, 26% and 21% for women. Partners also experienced lower rates of moderate-severe anxiety (6% versus 30% at month 1, 9% versus 25% at month 3, 6% versus 22% at month 9) and depression (2% versus 10% at month 1, 5% versus 8% at month 3, 1% versus 7% at month 9). The odds ratio for morbidity in partners versus women after 1 month was 0.02 (95% confidence interval 0.004 to 0.12) for post-traumatic stress, 0.05 (0.01 to 0.19) for moderate/severe anxiety and 0.15 (0.02-0.96) for moderate/severe depression. Morbidity for each outcome decreased modestly over time, without strong evidence of a different evolution for women and partners.

Conclusions: Partners experience far lower levels of post-traumatic stress, anxiety and depression than women after early pregnancy loss.

Introduction

Both partners may grieve the loss of a wanted pregnancy. However, differences in emotional responses are to be expected. There may be underlying differences in attachment to an unborn child relating to the lack of any physical experience in one partner. The majority of partners are male, and there may also be psychological differences between men and women, and societal pressures for men not to grieve, or to support the woman [1].

Qualitative studies have shown that partners may feel burdened by the grief or depressive reactions of the person physically experiencing the loss [2], or feel inadequate and frustrated by their inability to influence the outcome [3]. There is often a lack of regard for their own bereavement by family or friends, and they may feel marginalized [4]. Support from healthcare professionals may be suboptimal [5]. They may also be traumatised by seeing the physical pain experienced during the loss, by perceiving a life-threatening situation, or by directly witnessing the miscarriage itself.

Quantitative data to date has suggested higher anxiety and depression scores in women experiencing a miscarriage than in their partners at multiple time points: a significant difference persisted to 13 months in Cumming's study but not in two others [2, 6, 7]. No studies to date have compared post-traumatic stress symptoms. One small study comparing 68 partners after miscarriage to 210 partners after a live birth showed higher traumatic impact (higher scores on the Impact of Events Scale) within three weeks and at one year after miscarriage [8]. Depression scores were also higher at one year. There is no published evidence on the emotional reaction of partners to ectopic pregnancy (EP). There has also been no published quantitative data of any kind on partners for the last decade [9].

The aim of this analysis was to assess the psychological morbidity of partners in the nine months after both miscarriage and EP, including post-traumatic stress symptoms. A further aim was to compare this to the reactions of women in whom the loss was diagnosed.

Methods

Design

This is the second report from the Psychological Impact of Early Pregnancy Events (PIEPE) prospective cohort study. The first report focused on the morbidity in all women experiencing loss: in this report we include only the subsection of women whose partners were recruited. Ethical approval of the study protocol was granted by the NRES committee of South-West Exeter, reference 11/SW/0052. The sample size of women was calculated based on a further aim of PIEPE to investigate for potential risk factors for psychological morbidity (see [10]): the sample size was not adapted to this research.

Recruitment took place via Early Pregnancy Assessment Units (EPAUs) at three central-London hospitals (Queen Charlottes and Chelsea, St Mary's, and Chelsea and Westminster Hospitals) between 13/11/13 and 11/2/16. Recruitment was consecutive on the days on which an investigator was available, and could take place on the day of diagnosis of an early pregnancy loss, or at any subsequent follow-up within one month of diagnosis. If present at the consultation, partners were approached along with the woman experiencing the loss. Partners were only recruited if the index woman consented to take part. Although recruitment was open to same-sex couples and transgender individuals, only cisgender opposite-sex couples were encountered (thus 'woman' refers to the person physically experiencing the loss, and 'partner' he who would be assumed to take on the role of the father had the pregnancy been successful).

Clinical management was unaltered by involvement in the study, and in line with national guidance. Women with a miscarriage were offered expectant, medical or surgical management. Depending on symptoms, ultrasound findings and serum hormone levels, women with EP were offered expectant management, methotrexate or surgical intervention (usually laparoscopic salpingectomy).

All women and partners were separately e-mailed a link to a survey one, three, and nine months after the diagnosis of loss. E-mail communication always included a reminder that they were free to withdraw from the study. A lack of response without active withdrawal prompted up to two reminder emails at weekly intervals.

Participants

Couples eligible for participation had received a diagnosis of a miscarriage (a small number of which were later confirmed to be molar pregnancies), a resolving or persistent pregnancy of unknown location (PUL), or an ectopic pregnancy (EP) at a gestation <20 weeks. Exclusion criteria were: participant age <18 years, lack of proficiency in the English language, inability to give informed consent and voluntary termination of pregnancy.

Clinical, demographic and background information

Information regarding the clinical encounter, including the diagnosis and management, were prospectively recorded.

The participant's age, and number of past pregnancy losses or live births, among other details, were asked at the start of the first questionnaire.

Measures

The participants were asked to complete a number of psychometric screening questionnaires presented in the same order. For the purposes of this paper, we have limited our analysis to anxiety and depression (using the Hospital Anxiety and Depression Scale (HADS)) and post-traumatic stress (using the Post-traumatic stress Diagnostic Scale (PDS)). Both are well-validated scales that have been previously used in the pregnancy loss population [11,12]. Since the start of this study, post-traumatic stress disorder (PTSD) diagnostic criteria have changed: DSM-IV was updated to DSM-5 in 2013. The PDS screens according to pre-2013 criteria. Evidence however suggests that DSM-IV criteria can be used to closely approximate the new

criteria [13].

HADS comprises 14 questions: seven related to each of anxiety and depression [14]. Each subscale measures symptom severity, scoring out of a total of 21, with ≥11 indicating moderate or severe symptoms. PDS contains 17 items, with an overall symptom severity score out of 51. Questions mainly relate to the specific trauma identified, in this case the pregnancy loss – for example asking whether the participant is reliving the loss, or feeling it is actually happening again. A number of scoring criteria have been proposed: we used criteria involving endorsement of each symptom cluster (re-experiencing, avoidance and hyper-arousal clusters), as well as a total severity score cut-off of ≥18, as this has been found to maximise accuracy in the diagnosis of PTSD in victims of motor vehicle accidents, and physical and sexual assault [15]. Consistent with our previous publication, we use the term 'post-traumatic stress' (PTS) rather than 'post-traumatic stress disorder' (PTSD), to acknowledge that our criteria focus on screening for probable PTSD [10].

Statistical analysis

We compared women and their partners in terms of anxiety, depression and PTS after early pregnancy loss using descriptive statistics. Furthermore, the miscarriage and ectopic group were investigated separately regarding the prevalence of anxiety, depression and PTS in partners (see Supplementary Table 3).

We fitted a mixed effects logistic regression model for moderate/severe depression and anxiety and for post-traumatic stress: a simple model including a main effect of exact time since loss (continuous), a main effect of parent (woman vs partner) and an interaction effect between time and gender. Apart from these fixed effects, two random intercepts are included: a random intercept per couple and a random intercept per individual within a couple.

When fitting the model, all available observations were used. No further actions were taken with regard to missing values due to incomplete follow-up, since the estimation method used to fit the mixed effects logistic regression model automatically handles incomplete follow-up under missing at random (MAR), conditional on the covariates in the model.

All statistical analyses were performed using R software version 3.4.3 (www.r-project.org) and SAS v9.4 (SAS Institute Inc, Cary, NC, USA).

Results

Recruitment and response rates

1201 women who experienced early pregnancy losses were approached for participation across three sites. In just over half of the women (386/737, 52%) who consented to participate, their partners were present at the consultation. Of these partners who were approached, all were male, and 192/386 (50%) were eligible and agreed to participate. This was lower than the participation rate in all women (737/1098 (67%) for the first aim of the PIEPE study [10]. Of 13 partners who volunteered a reason for non-participation, nine reported time constraints.

Partners were less likely to respond than their female counterparts at every time point. Response rates were 57%, 45% and 38% for partners, and 76%, 68% and 57% for women at month 1, 3 and 9, respectively (see Figure 1). Overall 152/192 (79%) women responded at least once, compared to 125/192 (65%) of their partners. In total there were 652 observations (at 1, 3 or 9 months) from 277 individuals in 170 couples. Women in the subgroup whose partners were recruited were more likely to respond at every time point than the group of women whose partners were not recruited (147/192 (77%) vs 349/545 (64%) at month one).

There was no evidence of selective drop out in women or partners according to background clinical data, or according to baseline psychological response (see Supplementary Tables 1 and 2).

Post-Traumatic Stress

At month one, 7/107 (7%) of partners met screening criteria for PTS, 7/83 (8%) at month three and 3/70 (4%) at month nine (Table 1, Figure 2). This compares to 49/145 (34%), 33/129 (26%) and 23/109 (21%) respectively in women.

The most commonly endorsed symptom cluster at all three time points for both women and partners was re-experiencing (endorsed by 79% of partners at month one, and 95% of women) (see Table 2). In partners, approximately one third of participants met criteria for the avoidance and hyper-arousal clusters at month 1; in women, proportions were closer to two thirds. A high proportion of both women and partners reported interruption of activity relating to the symptoms they endorsed: at one month, 62% of partners and 78% women reported at least one interruption (Table 2). 44% partners and 53% women reported at least one interruption at nine months.

Based on the mixed effects logistic model (supplementary table 3), the odds ratio for post-traumatic stress in partners compared to women at one month was 0.02 (95% CI 0.004 to 0.12). The interaction between time and parent was weak, although sample size is small for a definitive evaluation. The odds ratio for time was 0.81 (0.79 to 0.93) for women and 0.84 (0.64 to 1.10) for partners, suggesting a modest decrease of the proportion meeting screening criteria for PTS over time. Proportions tended to decrease over time in women and partners, but were clearly lower for partners throughout. The proportion of women and partners meeting criteria for PTS over time estimated by the model is shown in Figure 3.

In the group of partners following miscarriage, proportions were 6/80 (8%) at month one, 5/58 (9%) at month three and 1/47 (2%) at month nine (supplementary table 4). In the group of partners following ectopic pregnancy, proportions were 1/16 (6%), 1/16 (6%), and 1/13 (8%), but numbers were small.

Anxiety and depression

In partners (irrespective of the type of pregnancy loss) 7/109 (6%) met criteria for moderate/severe anxiety at month one, 8/87 (9%) at month three, and 4/72 (6%) at month nine (Table 1, Figure 2). In women, proportions were 44/145 (30%), 32/130 (25%) and 24/109 (22%) respectively. For depression, proportions were 2/109 (2%), 4/87 (5%) and 1/72 (1%) in partners, and in women 15/145 (10%), 11/130 (8%) and 8/109 (7%) respectively.

Based on the mixed effects logistic model, the odds ratio for anxiety in partners compared to women at month one is 0.05 (95% CI 0.01 to 0.19). For depression it is 0.15 (95% CI 0.02 to 0.96). Again, the interactions between time and parent were modest, although uncertainty due to low sample size is considerable. The odds ratio of time for women was 0.89 (0.79 to 0.99) for anxiety and 0.92 (0.79 to 1.08) for depression; for partners the odds ratios were 0.98 (0.79 to 1.20) and 0.91 (0.65 to 1.27), respectively. These results suggest modest decrease in morbidity over time. Figure 3 shows clearly lower proportions for partners versus women across follow-up.

Following miscarriage, partners met criteria for moderate/severe anxiety in 5/81 (6%) at month one, 5/62 (8%) at month three and 1/49 (2%) at month nine (supplementary table 3). They met criteria for moderate/severe depression in 2/81 (2%) at month one, 3/62 (5%) at month three and 0/49 (0%) at month nine. Following an ectopic pregnancy, moderate/severe anxiety was observed in 2/17 (12%) partners at month one, 2/16 (13%) at month three, and 2/13 (15%) at month nine. None of the partners (0/17, 0/16, 0/13, respectively) met criteria for moderate/severe depression after an ectopic pregnancy.

Discussion

We have found that one, three and nine months following an early pregnancy loss, women display a higher level of symptoms suggestive of post-traumatic stress, and of moderate-severe anxiety and depression than their partners.

Normative population data from a study published in 2001 suggests that in the background UK population of men, 8% meet criteria for moderate or severe anxiety according to HADS, and 2% for depression [16]. Our sample of partners after pregnancy loss does not have appreciably different rates to this. PTSD is a diagnosis specific to a particular stressor, and thus background rates are dependent on trauma exposure. Seven percent of partners in this study met screening criteria for PTS relating to the loss at one month, and four percent at nine months. Although this is a much smaller proportion than in women, in view of the high frequency of losses, and the seriousness of this condition, this is an important finding. Men are generally less likely to seek support for mental health and may have poorer peer support. It is also important to recognise that, although symptomatology may usually fall shy of the threshold to suggest PTS, there is still an appreciable impact as indicated by endorsement of individual symptom clusters and the impact of the symptoms on their lives. It is also relevant to note that 86% partners reported the loss making them feel helpless after 1 month: a similar proportion to that in women.

A strength of this study is that it is large compared to previous studies in the literature, and incorporates a demographically and ethnically diverse sample from three areas of London. Women and partners were recruited consecutively: the results from the larger group of women were analysed in our team's first publication, whereas this analysis focuses only on those women whose partners consented to participate [10]. Details of the clinical encounter were prospectively collected from hospital records. It is the first study to assess for symptoms

of post-traumatic stress in partners. It is also the first study to include partners following ectopic pregnancy, although the small numbers preclude subgroup analysis.

A limitation of the study is that only a minority of women's partners were present at the appointment to be approached for participation, and, of those approached, only 50% agreed. This may introduce selection bias, and increased uncertainty in the statistical analysis. Moreover, the attrition rate was high in both groups, but higher for partners, and thus the potential for non-response bias must be considered. It is conceivable that a) unaffected individuals are less likely to take part, or b) highly affected individuals may avoid reminders of the event; both may co-exist at the highest and lowest extremes of symptomatology. We found no clear evidence of selective drop-out based on psychological response, in those that responded to the first part of the questionnaire.

It is not clear whether the partner's experience of early pregnancy loss always fulfils strict criteria of a 'traumatic event' necessary for diagnosis of PTSD. Exposure to real or threatened death or serious injury must be directly witnessed. Learning about death or serious injury is not included if from 'natural causes'[17]. Medical incidents may qualify if they involve 'sudden, catastrophic events' only. Clearly some pregnancy loss situations will involve critical situations risking the life of the woman, as well as the perceived sudden death of an unborn child. In less acute situations, the interpretation of whether they fulfil criteria is subjective. This study does not take into account an objective classification of the individual participants' pregnancy loss along those criteria when reporting on their PTS symptoms.

We used screening questionnaires, rather than the gold standard of individualised assessment by a professional: the large size of the study was at the cost of reduced sensitivity and specificity. Validation of the results with comprehensive psychometric assessment would be beneficial. It was not feasible to use validated translations of the questionnaires, and thus the exclusion of those who did not speak English was necessary. Whilst participants were asked

to complete the PDS specifically in relation to the experience of the pregnancy loss, we are unable to exclude the presence of psychological morbidity prior to the diagnosis of a loss.

Our findings relating to anxiety and depression are similar to previous studies, including one large study in the UK from 2007 [6]. Our first publication, which analysed all women recruited to the study, showed similar proportions meeting screening criteria of all three disorders to this subgroup of women whose partners were recruited [10]. Kessler's national comorbidity survey published in 1995 showed the risk of developing PTSD after a traumatic event was 8.1% for men and 20.4% for women: this is consistent with the disparity we have seen in relation to pregnancy loss.

Although we planned to include partners in same-sex relationships, none were recruited during this study. There is an increase in same-sex couples seeking to achieve pregnancy with assisted reproduction, and the emotions are likely to be particularly hard to navigate in the context of already 'marginalised maternal roles', in which society questions their entitlement to motherhood [18]. Further research focused on same-sex couples is needed to address this.

A previous study has reported a marriage dissolution hazard ratio of 1.22 (95% CI 1.08-1.38) following miscarriage (mostly occurring 1.5 to 3 years later) [19]. The stress on a relationship is likely to be more significant where reactions are incongruous or conflicting [2]. In this context, the substantial differences we have found between responses to pregnancy loss in women and partners overall is concerning. The untreated burden of psychological distress following miscarriage may be a modifiable factor that may reduce the likelihood of marital breakdown in these circumstances. It will be important to address whether treatment of individuals, or couples, can reduce marital conflict. While awaiting such research, couples might consider accessing therapy together to talk about the event and how to support and communicate with each other.

Overall, these results point to a generally more pervasive and severe psychological impact of early pregnancy losses in women. This may be due to the differences in physical experiences, attachment, or the emotional makeup of partners. However, although many partners do not reach the threshold for being classified as having post-traumatic stress or moderate to severe anxiety or depression, many partners endorsed a number of symptoms clusters in the PDS without passing the threshold for PTS. These individuals are likely to be suffering from a level of adjustment disorder that may well be distressing and impact day to day life. Clinicians, and indeed society at large, should be encouraged to acknowledge this, such that the long-held taboos surrounding both pregnancy loss and mental health can be broken, and both women and their partners may find it easier to access the treatment that they need.

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TB and MJ devised the original study protocol, which was amended by JF. JF, NMJ, ST, SB and MA were responsible for recruiting participants. NF, LW and BVC performed the statistical analysis of the results. JF wrote the first draft of the manuscript that was then critically reviewed and revised by the other co-authors. DT commented on the drafts of the paper.

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Conflict of Interest

There are no conflicts of interest

Tables

Table 1 *Mean and standard deviation (SD) of anxiety, depression (according to HADS) and PDS scores, and the percentage of participants with moderate-severe symptoms (HADS) or meeting criteria for cases (PDS), following early pregnancy loss*

	Women			Partners		
	Month 1	**Month 3**	**Month 9**	**Month 1**	**Month 3**	**Month 9**
Number of HADS respondents	145	130	109	109	87	72
Mean Anxiety score (SD)	7.43 (4.52)	7.73 (4.20)	6.75 (4.41)	4.81 (3.62)	4.85 (3.77)	4.90 (3.97)
Moderate/severe anxiety (%)	44 (30%)	32 (25%)	24 (22%)	7 (6%)	8 (9%)	4 (6%)
Mean depression score (SD)	4.23 (4.33)	4.35 (4.01)	3.80 (3.82)	2.29 (2.73)	2.80 (3.55)	2.65 (3.21)
Moderate/severe depression (%)	15 (10%)	11 (8%)	8 (7%)	2 (2%)	4 (5%)	1 (1%)
Number of PDS respondents	144	129	108	107	83	70
Mean PDS score (SD)	14.1 (10.3)	11.8 (9.4)	10.4 (10.5)	7.1 (7.1)	6.7 (8.0)	5.2 (6.0)
Screening criteria for PTS	49 (34%)	33 (26%)	23 (21%)	7 (7%)	7 (8%)	3 (4%)

Table 2 *Mean score, and proportion of partners meeting overall criteria, and criteria of each symptom cluster (subdivided by severity), according to the Post-traumatic Diagnostic Scale (PDS), in partners of women with losses, at three time points following early pregnancy loss*

	Partners			Women		
	Month 1 N=107	Month 3 N=83	Month 9 N=70	Month 1 N=144	Month 3 N=129	Month 9 N=108
Helpless	92/107 (86%)	69/83 (83%)	62/70 (89%)	121/144 (84%)	109/129 (84%)	89/108 (82%)
Terrified	34/107 (32%)	28/83 (34%)	30/70 (43%)	82/144 (57%)	70/129 (54%)	63/108 (58%)
Helpless OR Terrified	93/107 (87%)	70/83 (84%)	64/70 (91%)	124/144 (86%)	111/129 (86%)	93/108 (86%)
Proportion meeting each symptom cluster*:						
Re-experiencing	84/107 (79%)	60/83 (72%)	46/70 (65%)	137/144 (95%)	115/129 (89%)	85/108 (79%)
Avoidance	38/107 (36%)	28/83 (34%)	22/70 (31%)	93/144 (65%)	64/129 (50%)	46/108 (43%)
Hyper-arousal	42/107 (39%)	31/83 (37%)	21/70 (30%)	89/144 (62%)	74/129 (57%)	60/108 (56%)
All three clusters	24/107 (22%)	17/83 (20%)	13/70 (19%)	76/144 (53%)	51/129 (40%)	40/108 (37%)
Interruption of activities						
Work	32/107 (30%)	18/83 (22%)	14/70 (20%)	74/144 (51%)	54/129 (42%)	38/108 (35%)
Household chores	18/107 (17%)	11/83 (13%)	7/70 (10%)	54/144 (38%)	42/129 (33%)	31/108 (29%)
Relationships with family	20/107 (19%)	16/83 (19%)	13/70 (19%)	45/144 (31%)	44/129 (34%)	29/108 (27%)
Relationships with friends	22/107 (21%)	14/83 (17%)	15/70 (21%)	50/144 (35%)	56/129 (43%)	33/108 (31%)
Fun and leisure activities	27/107 (25%)	16/83 (19%)	12/70 (17%)	68/144 (47%)	51/129 (40%)	33/108 (31%)
Sex life	48/107 (45%)	30/83 (36%)	19/70 (27%)	70/144 (49%)	52/129 (40%)	39/108 (36%)
General satisfaction with life	36/107 (34%)	33/83 (40%)	21/70 (30%)	79/144 (55%)	74/129 (57%)	46/108 (43%)
Overall level of functioning	18/107 (17%)	19/83 (23%)	14/70 (20%)	63/144 (44%)	51/129 (40%)	35/108 (32%)
Any interruption of activities	66/107 (62%)	47/83 (57%)	31/70 (44%)	112/144 (78%)	88/129 (68%)	57/108 (53%)
>= 2 activities interrupted or interruption of overall level of functioning	48/107 (45%)	29/83 (35%)	24/70 (34%)	96/144 (67%)	76/129 (59%)	52/108 (48%)
Post traumatic Diagnostic Scale Score						
Score >=18	8/107 (7%)	10/83 (12%)	3/70 (4%)	51/144 (35%)	34/129 (26%)	25/108 (23%)
Total proportion meeting Ehring screening criteria:						
Post-traumatic stress	7/107 (7%)	7/83 (8%)	3/70 (4%)	49/144 (34%)	33/129 (26%)	23/108 (21%)

*endorsed so as to meet criteria i.e. Re-experiencing – one or more positive responses to 5 questions, Avoidance – three or more positive responses to 7 questions, Hyper-arousal – two or more positive responses to 5 questions

Figure legends

Figure 1 *Flowchart of recruitment and response rates for couples*

Abbreviations: HADS – Hospital Anxiety and Depression Scale; n- total number; P –Partners; W – women

Figure 2 *Bar chart demonstrating proportions of women and partners meeting criteria for PTSD, moderate or severe anxiety or depression at one-, three- and nine-month assessments*

Abbreviations: M1 – one month questionnaire; M3 – three month questionnaire, M9 – nine month questionnaire, P – partners; PTSD – post-traumatic stress disorder, W – women A: Anxiety D: Depression

Figure 3 *Average evolution for anxiety, depression and post-traumatic stress over time for women and partners after pregnancy loss based on the mixed-effects model, with 95% confidence intervals (dotted lines).*