PREGNANT PROFESSIONAL PILOTS REPORT

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Executive summary

Objectives

The purpose of this project is to obtain, analyse, and report on the current medical evidence relating to the risks and manifestations of pregnancy that may relate to aviation safety, and that may result in reduced functional capacity, incapacitation, or unsafe behaviour.

Review outcomes

Outcomes of interest were the prevalence and manifestation of the following conditions in pregnancy:

1. Overall symptoms and indications for sick leave
2. Pregnancy complications
3. Fatigue and sleep problems
4. Nausea and vomiting
5. Pelvic and back pain
6. Headache and migraine
7. Urinary and bowel problems
8. Vaginal bleeding
9. Miscarriage
10. Ectopic pregnancy
11. Venous thrombosis
12. Gestational hypertension, pre-eclampsia and eclampsia
13. Preterm birth
14. Cognitive disorders
15. Mental health disorders
16. Girth and mobility problems

Methods

We included studies of the incidence of common effects and complications of pregnancy. Preferred study designs were systematic reviews of population-based studies, and population-based cohort and cross-sectional studies.

The search included seven online databases, the references lists of articles retrieved, and use of online citation-linking tools. We selected relevant studies and extracted data on study characteristics and relevant findings. (See Appendix 1: Methods; Appendix 2: Table of included studies.)

Key findings are summarised in the text and table below (pp. 4-9). A description of the included studies and detailed findings for each review outcome are reported in the Results section (pp. 10-38).

Description of studies

We included 74 studies. They comprised 13 systematic reviews, 42 cohort studies, 16 cross-sectional surveys, one case-control study, one case report and one narrative review. Seventy-one of the studies were at low or moderate risk of bias.

Key findings

- Common symptoms of early pregnancy include (in order of prevalence), exhaustion, morning sickness, back pain and constipation. Headache is also commonly reported, but this may be due partly to high prevalence in the general population rather than the effects of pregnancy. Nearly 20% of women report often having three or more of these symptoms. Average quality of life scores are significantly below population norms, particularly in the areas of vitality and physical function.
- Based on Norwegian data, about 75% of women require sick leave during pregnancy, with absence rates increasing from 29% in the first trimester to 63% in the third. The most common indications for sick leave are fatigue or sleep problems and pelvic girdle pain. These are contributing factors for nearly half of women taking leave. For most indications the duration of sick leave ranges from 8 to 16 weeks, and 31% of women are on sick leave for at least 10% of their scheduled working time. In Sweden one in three women are treated in hospital at some point in their pregnancy.
- Over 36% of healthy New Zealand and Australian women experience a significant complication during their first pregnancy, such as high blood pressure, preterm delivery or a baby that is small for gestational age. Being in paid employment at 15 weeks' gestation is associated with reduced risk of such a complication. There is no good evidence as to whether the prevalence of pregnancy complications differs in any respect between airline pilots and other women.
- Nearly 40% of US women report poor sleep quality at 14 weeks' gestation, and symptoms tend to worsen over time, mainly due to discomfort. In both early and late pregnancy, one third of women report excessive daytime sleepiness, and over 40% of US and NZ women report that they regularly nap during the day in late pregnancy.
- Up to 80% of pregnant women experience nausea or vomiting, which is rated as comparable in severity to moderately nausea-producing cancer chemotherapy. Symptoms are usually limited to the first trimester, but persist for up to 22 weeks in about 10% of cases. Up to one third of pregnant women require sick leave for this indication (usually two to three weeks). Among Australian women with nausea and vomiting in early pregnancy, 4% resigned, 28% adapted their work hours to accommodate their symptoms and 65% reported that it reduced their attentiveness at work.
- Nearly 5% of pregnant women have hyperemesis gravidarum, defined as repeated vomiting in early pregnancy requiring inpatient admission, requiring day stay with IV fluids or nasogastric feeding, or causing loss of over 5% of booking weight. About 2% of pregnant women are hospitalised for hyperemesis gravidarum.
- Lower back or pelvic pain affects about 40% of pregnant women in the first trimester and is even more common in the second and third trimesters. Increased risk of back pain correlates with the need to twist or

bend frequently or to lift hands above shoulder level. Increased risk of pelvic pain correlates with working bent forward. Due to severe pelvic pain nine per cent of Swedish women gave up work during pregnancy and a similar proportion of Norwegian women reported having great difficulty with housework. Women rated pelvic girdle and lower back pain (at its worst) as similar to the worst pain experienced during delivery. Among Norwegian women with pelvic girdle pain, 16% required crutches during pregnancy.

- Headaches and migraine are usually less frequent and less severe in pregnancy than in non-pregnant women. Moreover among women with a history of migraine, attacks are usually less intense and of shorter duration.
- During pregnancy urinary frequency occurs in most women and urinary stress incontinence occurs in 30-45%. Symptoms tend to worsen as pregnancy progresses. However fewer than 3% of pregnant women with urinary incontinence report that it restricts their activities, and only about 1% find it a real problem.
- With regard to bowel symptoms, 13% of women reported that during pregnancy they experienced faecal urgency or incontinence (of flatus or stool).
- At least 20% of pregnant women have vaginal bleeding in the first trimester of pregnancy and up to 6% have bleeding in the second trimester. In about 10% of cases (in either trimester) the bleeding is heavy, and in about 5% of cases it is associated with moderate or severe pain. About 14% of women with first trimester bleeding and 28% of those with second trimester bleeding are admitted to hospital.
- Based on UK data, about 12% of known pregnancies end in clinically–confirmed miscarriage, and in about two thirds of cases women are admitted to hospital and undergo evacuation of the uterus. Nearly all miscarriages occur in the first trimester. In a Hong Kong study, although psychological morbidity decreased over one-year follow-up, 11% of women were still distressed a year after miscarriage. Evidence suggests that the prevalence of miscarriage in female flight crew does not differ from rates in other women.
- Ectopic pregnancy occurs in 1.5% to 2% of pregnancies, most commonly at around 7 weeks' gestation. The most common symptoms are abdominal or pelvic pain, amenorrhea or vaginal bleeding. Suspected ectopic pregnancy requires urgent medical assessment and (if confirmed) may necessitate immediate surgery or medical treatment.
- There is wide variation in reported incidence rates for venous thrombosis in pregnant women, with estimates ranging from 5 to 20 per 10,000 pregnancies. Although antenatal venous thrombosis is a relatively rare event, it is a major cause of preventable maternal death. Management usually involves treatment until the end of the postpartum phase with anticoagulant injections once or twice daily.

- Pre-eclampsia occurs in about 3-4% of pregnancies. It is more prevalent in first pregnancies, and occurs in over 5% of healthy nulliparous women. Pre-eclampsia is a complex, progressive and unpredictable disease with a major functional impact, usually requiring hospital admission. Eclampsia is very rare, occurring in about 0.1% of deliveries, but it is a leading cause of preventable maternal death.
- Approximately 7% of babies in New Zealand are born preterm (before 37 weeks' gestation). The rate of preterm birth among healthy women in their first pregnancy is nearly 5%, with twice the risk in smokers.
- Case-control studies have suggested that pregnancy significantly impairs memory function and/or visuo-spatial ability, though the effects are subtle. However, the only good quality evidence available (from a prospective cohort study) suggests that pregnancy does not impair memory but that there may be a temporary decline in cognitive speed in the second half of pregnancy.
- The prevalence of common mental disorders in pregnant women is comparable with (or lower than) rates in non-pregnant women. The symptoms and course of mental disorders is also similar in pregnant and non-pregnant women. However, the functional impact of such disorders can be especially severe in pregnancy, and anxiety or depression were responsible for longer sick leave (20 weeks) than any other health problem in antenatal women.
- No evidence was found on the effects of increasing girth and potential mobility problems in pregnancy associated with this. The following comment appears on an aviation website (AvWeb); *Interestingly, the airlines do not restrict obese pilots from flying, and their stomachs can be more prominent than a pregnant woman's at term.*

Conclusions

No direct evidence was found on the risks and manifestations of pregnancy in relation to aviation safety. However there was reliable evidence on the prevalence of the most common pregnancy-related conditions among the general female population of various westernised countries. There was limited evidence on the likely occupational effects of such conditions.

It seems reasonable to extrapolate the findings of the current evidence review to female aviators in New Zealand. Risks seem unlikely to be higher in this group than in the included studies, as recent evidence suggests that pilots (at least male pilots) in New Zealand are healthier than the general population in most respects. [1]

Table 1: Summary of key findings

*** Denotes low risk of bias**

Condition	Prevalence	Functional effects
Complications of pregnancy	In the SCOPE study 36.5% of healthy nulliparous New Zealand and Australian women had a complication of pregnancy. [2]*	9% of pregnant Norwegian women require sick leave for a complication of pregnancy, for a median duration of 13 weeks. [3]*
Fatigue	*At mean 14 weeks*: 33% of US women report excessive daytime sleepiness. [4] *At mean 30 weeks*: 38% of US women report excessive daytime sleepiness. [4] *At median 36 weeks*: 33% of NZ women report excessive daytime sleepiness. [5]	35% of pregnant Norwegian women require sick leave for fatigue or sleep problems, for a median duration of 8 weeks. [3]*
Nausea and Vomiting	*First trimester*: 80% of UK women have nausea or vomiting, with symptoms peaking at 9 weeks. [6]* *Second trimester*: 9% of UK women have ongoing nausea or vomiting at 16 weeks. [6]*	23% of pregnant Norwegian women require sick leave for nausea and vomiting (including HG), for a median duration of 16 weeks. [3]*
Hyperemesis Gravidarum (HG)	*First trimester*: 4.8% of women in the SCOPE study had HG. [7]* *Second trimester*: <1% of women in the SCOPE study had ongoing HG at 15 weeks. [7]*	2.1% of women in the SCOPE study required hospitalisation for HG. [7]* Requirement for sick leave in all three trimesters is strongly associated with HG. [3]*
Pelvic or lower back pain	*First trimester*: 40% of Swedish women had back pain by 12 weeks. Worst pain in previous week was rated at 4/10 on VAS scale. Rates included women (20-22%) who had back problems before pregnancy. [8, 9]* *Second trimester*: In the Swedish cohort, prevalence of back pain increased steadily in the second trimester, with a sharp increase in weeks 18-22. Rates levelled off at about 63% of women by week 24. [9]* *Third trimester*: The prevalence remained stable: 63% of Swedish women had back pain at 36 weeks. Worst pain in the previous week was rated at 6.5/10 on VAS scale. [9]*	18% of pregnant Norwegian women require sick leave for lower back pain and 32% require sick leave for pelvic girdle pain. Median duration of leave is 10-12 weeks. [3]* (Some women may be in both groups)
Headache and migraine	Although headaches are reported to be common in early pregnancy it is more common for headaches and migraine to stop during pregnancy than for them to start. [10, 11] Headaches and migraine tend to become less common with increasing gestation and migraines become shorter and less intense. [10]	

Urinary and bowel problems	*First trimester:* 13-19% of women report urinary incontinence. [12] *Second trimester:* About 19% of women report urinary incontinence. [12] *Third trimester:* 30-38% of women report urinary incontinence. [12] *Throughout pregnancy*: Most urinary continence is stress incontinence. About 81% of women report urinary frequency in pregnancy.[13] 13% of women report faecal urgency or incontinence (of faeces or flatus) during pregnancy. [13]	Fewer than 3% of pregnant women with urinary incontinence report that it restricts their activities. [13] Only about 1% of pregnant women report that incontinence is "a hygienic or social problem". [14]
Vaginal bleeding	*First trimester:* 19% of women in the SCOPE study had vaginal spotting or bleeding in the first trimester. [15*] *Second trimester*: 6% of women in the SCOPE study had vaginal spotting or bleeding at 13-20 weeks. [15*] Less than 1% of women had new onset bleeding at 16-20 weeks. [15*] *Both trimesters:* 10% of women with bleeding had one or more episodes of heavy bleeding. [15*]	Among women with bleeding before 20 weeks, about half miscarry. [16*]
Miscarriage	*Before 20 weeks*: In a UK primary care setting, about 12% of clinically confirmed pregnancies end in miscarriage before 20 weeks. [16*] Most miscarriages occur in the first trimester. Up to 7% occur in the second trimester. [16*]	About two thirds of women who miscarry are admitted to hospital, where about 60% of them have evacuation of the uterus. [16*]
Ectopic pregnancy	Nearly all ectopic pregnancies occur early in pregnancy, with mean onset at about 7 weeks(SD ≥2.2) [17] Ectopic pregnancy most commonly presents with abdominal pain, amenorrhoea or vaginal bleeding. [18]	Ectopic pregnancy requires urgent assessment and treatment (surgical or medical). [19]
Venous thrombosis (DVT or PE)	In a recent systematic review the best estimate of the overall incidence of antenatal VT is 118 per 100,000 person-years (0.1%). [20] Most studies report higher risk with increasing gestation. [20]	Pregnancy-related VT is a major cause of preventable maternal death, due to the risk of fatal pulmonary embolism. [21]

Pre-eclampsia	By definition, pre-eclampsia does not occur before 20 weeks' gestation. Pre-eclampsia was diagnosed in the SCOPE study at a mean of 36.9 weeks' gestation (SD 3.3). The prevalence of pre-eclampsia in the SCOPE study was 5.3%. The prevalence of pre-term pre-eclampsia (resulting in delivery before 37 weeks) was 1.3%. [22*]	The standard management of pre-eclampsia is close observation until 37 completed weeks or until the onset of either maternal or fetal complications. Hospital admission is usual. [23*]
Eclampsia	The prevalence of eclampsia in the Western Pacific area is about 0.1% of deliveries. [24*]	Eclampsia is a leading cause of preventable maternal death. [24*]
Preterm birth	The SCOPE study reported a preterm birth rate (<37 weeks) of 4% for non-smokers and 10% for smokers in Australian and New Zealand women. [25, 26*]	
Cognition	*Up to 20 weeks:* There was no difference between pregnant and non-pregnant women in four measures of cognition (cognitive speed, working memory, immediate recall, delayed recall). [27*] *20-40 weeks:* Pregnant women were significantly slower on a test of cognitive speed in later pregnancy (20-40 weeks). There was no difference between the groups for working memory, immediate recall or delayed recall. [27*]	
Mental health	*First trimester:* Estimated prevalence of depressive disorders is 7.4% but confidence intervals are very wide (95% CI 2.2 to 12.6). [28*] *Second trimester*: Estimated prevalence of depressive disorders is 12.8% (95% CI 10.7 to 14.8). [28*] *Third trimester*: Estimated prevalence of depressive disorders is 12% but confidence intervals are very wide (95% CI 7.4 to 16.7). [28*] US epidemiological data indicates that pregnant women are less likely than non-pregnant women to have depression (7.3% vs 11.4%), alcohol abuse or dependence (2.8% vs 8.3%), or any mental disorder (19.2% vs 9.3%). [29]	At least 2% of pregnant Norwegian women require sick leave for anxiety or depression, for a median duration of 20 weeks. [3*]
Girth/Mobility problems	No evidence found	No evidence found

Results

Characteristics of included studies

74 studies were included, comprising 13 systematic reviews, 21 prospective cohort studies, 21 retrospective cohort studies (using registry data), 16 cross-sectional surveys, one case-control study, one case report and one narrative review). Some of the studies had multiple publications, including one (the SCOPE study) that contributed six relevant papers.

Forty-nine of the studies were clearly population based. Most of the other studies were clinic-based without a clear indication as to whether their clientele were representative of the general population. The majority of systematic reviews included a mixture of population-based and other studies.

The 61 primary studies were set in Australia (n=4), Canada (n=2), Denmark (n=4), Finland (n=3), France (n=1), Hong Kong (n=1), Italy (n=2), Norway (n=9), New Zealand (n=7), Spain (n=1), Sweden (n=6), the UK (n=10), and the USA (n=7). Four were international (two set in in New Zealand and Australia, one in New Zealand, Australia, the UK and Ireland, and one in the USA and Canada)

Seventeen of the studies were rated as at low risk of bias and 54 were rated as at moderate risk of bias. Common study limitations were potential selection bias, low participation rates, retrospective data collection, small samples, uncertain reliability of registry data and (for systematic reviews) failure to explore heterogeneity and suboptimal literature search. Studies at high risk of bias were excluded, with the exception of three studies, which were included because they related to pregnancy in an aviation context.

Findings for each review outcome

1. Overall symptoms and indications for sick leave

Evidence base

- An Australian population-based cross-sectional survey of the general health of nulliparous women in early pregnancy [11]
- A Norwegian longitudinal population survey of indications for sick leave in pregnancy [3]*
- A Danish register-based study of sick leave taken by hospital employees during pregnancy [30]
- A Norwegian population-based cohort study of absence from work and job adjustment in pregnancy [31]
- Swedish National Public Health Reports of indications for absence from work [32, 33]

Prevalence of symptoms

General health

An Australian population-based study [11] reported on the general health of nulliparous women in early pregnancy. Symptoms experienced "occasionally or often" were (in order of frequency) exhaustion (87%), morning sickness (64%), back pain (46%), constipation (44%) and severe headache or migraine (30%). Nineteen percent of women reported often experiencing three or more of these. The authors noted that the impact of common comorbidities was most pronounced for younger women, but was strongly evident for all women in the sample.

Evidence on functional impact

Impact on functional roles

In the Australian study [11] SF-36 status was significantly below population norms for most SF-36 categories. The domains most affected were *vitality* and *physical role*. The authors commented as follows: "These findings highlight the significant impact of early pregnancy symptoms on women's physical and mental health. Although the common pregnancy symptoms reported are often considered 'minor discomforts of pregnancy', these findings suggest that the cumulative effect of experiencing multiple symptoms lasting longer than a few weeks significantly compromises women's health and well-being in early to mid pregnancy".

Sick leave

In the Norwegian studies of sick leave taken during pregnancy, [3, 31] 75% of women took sick leave: 29% in the first trimester, 39% in the second and 63% in the third. [3] Over one third of women took more than 15 days of sick leave between weeks 13 and 28. [31] Absence levels were lower among women whose working conditions were adjusted to allow for pregnancy where (in the woman's view) this was required.

Swedish public health reports noted that a third of women are treated in hospital at some point in their pregnancy. [32, 33]

The most common reasons for sick leave were fatigue or sleep problems (which were an indication for sick leave in 35% of women) and pelvic girdle pain (32%). These conditions were contributing factors in 45-49% of women who took leave. Other common indications for leave were nausea or vomiting, and lower back pain (a contributing factor for 23% and 18% of women respectively). Nine per cent of women required leave for pregnancy complications. [3*]

For most indications the median duration of sick leave ranged from eight to 16 weeks. Anxiety or depression were responsible for the longest median duration of sick leave.

Being on sick leave in all three trimesters was strongly associated with hyperemesis, exercising less than weekly, chronic pain before or during pregnancy, and infertility treatment. [3*]

Summary

Common symptoms in early pregnancy include (in order of prevalence), exhaustion, morning sickness, back pain, constipation and severe headache or migraine. Nearly 20% of women report often having three or more of these symptoms. On average, quality of life is significantly below population norms, particularly in the areas of vitality and physical function.

Several European studies have assessed the need for sick leave during pregnancy. About 75% of women required sick leave during pregnancy, with absence rates increasing from 29% in the first trimester to 63% in the third. The most common reasons for sick leave were fatigue or sleep problems and pelvic girdle pain, which were contributing factors in nearly half of women who took leave. For most indications the duration of sick leave ranged from 8 to 16 weeks, and 31% of women were on sick leave for at least 10% of their scheduled working time

In Sweden a third of women are treated in hospital at some point in their pregnancy.

2. Complications of pregnancy

Evidence base

- A prospective international cohort study with a New Zealand cohort (SCOPE) which reported the overall likelihood of complications in pregnancy [2*]
- New Zealand Ministry of Health reports on hospital-based maternity events in 2006 and 2007 [34, 35]
- A literature review of gestational complications associated with air travel [36]

Incidence of complications

The SCOPE study found that among healthy nulliparous women with a singleton pregnancy 61.3% had an uncomplicated pregnancy, defined as normotensive, delivering a live baby not small for gestational age after 37 weeks, and having no other significant complications of pregnancy. Nearly 39% (2176/5628) had a significant complication. [2*] However, in the New Zealand and Australian cohort the rate of complications was lower (36.5%) than in the UK and Irish cohorts (41.4%).

Complications were defined as follows:

- Gestational hypertension
- Pre-eclampsia
- Gestational proteinuria
- Gestational diabetes
- Antepartum haemorrhage, placenta praevia, or placenta accreta
- Placental abruption
- Chronic hypertension (mild, diagnosed in pregnancy)
- Renal tract complications (e.g. pyelonephritis)
- Gastrointestinal tract or hepatic complications
- Respiratory complications (e.g. pneumonia)
- Other obstetric complications (e.g. obstetric cholestasis)
- Other medical complications (e.g. venous thromboembolism)
- Maternal death during pregnancy
- Small for gestational age infant (<10th customised birthweight centile)
- Spontaneous preterm birth
- Other fetal problems (including severe neonatal morbidity
- Fetal anomalies
- Fetal death in utero or neonatal death
- Miscarriage or abortion

When women with an uncomplicated pregnancy were compared with those without, it appeared that there were a number of factors amenable to individual lifestyle change which would reduce the risk of complications. Beneficial factors included normalising maternal weight, increasing pre-pregnancy fruit intake, reducing blood pressure, stopping misuse of drugs and being in paid employment at 15 weeks' gestation (per 8 hours increase in employment RR 1.02, 95% CI 1.01 to 1.04). [2*]

A literature review of pregnancy complications associated with air travel reported that there was insufficient evidence to reach any conclusions.[36] The review was non-systematic and associated with a high risk of bias, but the authors' conclusions (with respect to lack of evidence) appear justified.

Evidence on functional impact

About 17% of New Zealand of inpatient hospital admissions and 7% of antenatal day stay admissions are for excessive vomiting; over 10% of inpatient hospital admissions and nearly 8% of antenatal day stay admissions are for gestational hypertension (with or without proteinuria); nearly 13% of inpatient hospital admissions and 12% of antenatal day stay admissions are for haemorrhage; and about 7-8% of inpatient hospital admissions and 4% of antenatal day stay admissions are for genitourinary infection. The mean duration of inpatient admission for these indications ranges from one to three days. [34, 35]

A further 28% of New Zealand antenatal day stay admissions and 25% of inpatient hospital admissions are for other (unspecified) maternal diseases complicating pregnancy. The mean duration of inpatient admission for this indication is two days. [34, 35]

Summary of evidence

Among healthy nulliparous women with a singleton pregnancy, over 60% are likely to have an uncomplicated pregnancy, defined as normotensive, delivering a live baby not small for gestational age after 37 weeks, and having no other significant complications of pregnancy (as defined above). Over 36% are likely to experience a significant complication. Being in paid employment at 15 weeks' gestation has been identified as a factor associated with reduced risk of complications.

Complications of pregnancy may require hospital admission or same-day admission to an antenatal unit. The duration of inpatient stay for the most common complications is usually 1-3 days.

There is no evidence as to whether the prevalence of pregnancy complications differs in any respect between airline pilots and other women.

3. Fatigue and sleep problems

Evidence base

- Two population-based surveys of pregnancy-related morbidity in Australia [11] and pregnancy-related sick-leave in Norway [3*]
- A prospective cohort study of sleep disturbances in a 'socioeconomically diverse' US convenience sample of healthy nulliparous women [4]
- A cross-sectional survey of sleep problems in randomly-selected women booked to deliver at an NZ maternity unit [5]

Prevalence of fatigue and sleep problems

Exhaustion was the most common symptom in early pregnancy, experienced by 87% of Australian women "occasionally or often". [11]

The US study compared sleep disturbances at about 14 and about 30 weeks' gestation. Poor sleep quality was reported by 39% of women at 14 weeks and 54% at 30 weeks. Other sleep-related problems that increased during pregnancy included insomnia (38% at 14 weeks and 54% at 30 weeks), short sleep duration (26% and 40% respectively) and restless legs syndrome (18% and 31% respectively). [4]

The NZ study [5] compared self-reported sleep duration and quality at 36 weeks' gestation with (retrospectively recalled) pre-pregnancy values. Women reported deterioration in sleep quality, which was rated as fairly bad or very bad by 4% prior to pregnancy and by 38% in the previous week. The mean duration of sleep was 8.1 hours pre-pregnancy versus 7.5 hours in the previous week. Women reported that the main cause of sleeping problems was discomfort.

Evidence on functional impact

Fatigue or sleep problems were the most common indication for sick leave during pregnancy in the Norwegian study, [3] and such problems were cited as a factor in 49% of sick leave taken. The median length of sick leave for this indication was 8 weeks.

Daytime fatigue was reported by 33% of NZ women in late pregnancy (versus 4% pre-pregnancy), and 41% regularly napped during the day (versus 5% pre-pregnancy). [5] Similarly, excessive daytime sleepiness was reported by nearly 33% of US women at 14 weeks gestation and by 38% at 30 weeks. [4]

Summary of evidence

Fatigue and sleep problems are the most frequently-reported symptom in early pregnancy, and are the most common indication for sick leave during pregnancy. Poor sleep quality is common in the first trimester (reported by 39% of US women at 14 weeks) and appears to get worse during pregnancy, mainly due to discomfort.

Over one third of women reported excessive daytime sleepiness in the first trimester and also in the third trimester. Over 40% of women in both early and late pregnancy reported that they regularly napped during the day.

4. Nausea and vomiting

Evidence base:

- A Canadian systematic review of NVP incidence rates [37]
- An Australian systematic review of 38 studies of the impact of NVP [38]
- A prospective study of NVP in UK primary care setting [6]*
- A prospective study of NVP in Canadian tertiary care setting [39]* (included in Einarson 2013 [37])
- Two population-based surveys of pregnancy-related morbidity [11] and pregnancy-related sick-leave [3]*
- An Australian cross-sectional survey of the impact of nausea and vomiting [40] (included in Wood 2013 SR [38])
- A prospective international population-based cohort study with an NZ cohort (SCOPE), which reported the incidence of hyperemesis gravidarum [7]*
- New Zealand Ministry of Health reports on hospital-based maternity events in 2006 and 2007 [34, 35]

Prevalence of nausea and vomiting

Nausea and vomiting

In an urban UK primary care setting, 52% of women had both nausea and vomiting during pregnancy, and a further 28% had nausea only. [6]* Onset was usually at 5-6 weeks, peaking at 9 weeks. Symptoms often stopped abruptly at about 12 weeks, but 9% of women had ongoing symptoms at 16 weeks and beyond. Nausea most commonly occurred between 6 am and midday, but could occur at any time of day.

A prospective Canadian study [39]* reported very similar findings: 74% of women had nausea during pregnancy, and half also had vomiting. The mean time of onset was 5.7 weeks' gestation. Nausea resolved in 50% of cases by 14 weeks and in 90% by 22 weeks. It usually lasted throughout the day. Nausea ratings were rarely extreme, but were comparable in severity to those reported in a study of moderately nausea-producing cancer chemotherapy.

A recent systematic review [37] reported widely varying rates of nausea and vomiting in pregnancy (55 studies, median rate in early pregnancy 69%, range 35% to 91%). Symptoms were reported as mild in 40% of cases, moderate in 46% and severe in 14%. The variation in rates may relate to differing definitions used by the included studies, and possibly also to ethnic differences in incidence. Rates were generally higher in Asian than in non-Asian countries.

In an Australian survey 'morning sickness' was the most common symptom in early pregnancy, experienced by 64% of women "occasionally or often". [11]

Hyperemesis gravidarum (HG)

In the SCOPE study [7] HG was defined as repeated vomiting in early pregnancy requiring inpatient admission, day stay with IV fluids, nasogastric feeding (at home or in hospital) or vomiting associated with loss of over 5% of booking

weight. Among healthy nulliparous women the incidence of HG was 4.8%, and the incidence of severe HG requiring hospitalization was 2.1%. The mean incidence of HG in the Canadian systematic review was 1% (range 0.3% to 3.6%).[37] The authors noted that there is no standard definition of HG but that hospitalization is often a requirement. Use of a wider definition of HG in the SCOPE study may account for the discrepancy in findings between the SCOPE study and the systematic review.

Evidence on functional impact

Among UK women in paid employment, 35% required time off due to nausea or vomiting. Mean time off was 62 hours. The likelihood of taking time off correlated with the severity of symptoms.[6]* NVP was an indication for sick leave in 23% of antenatal women in a Norwegian survey, and was the third most common indication for sick leave during pregnancy.[3]* Median duration of leave for this indication was 16 weeks.

Hyperemesis gravidarum is strongly predictive of being on sick leave in all trimesters[3]* and 2.1% of pregnant women require hospitalization for HG.[7]*

A systematic review of 38 studies[38] assessed the impact of NVP on quality of life, including the ability to maintain professional commitments. It included an Australian study of 593 volunteers with nausea and vomiting in early pregnancy,[40] in which over half the participants were in paid employment. In the early weeks of pregnancy, 14 women (4%) resigned from work, 95 women (28%) made changes to their work schedule, coming in later or leaving earlier, and 221 women (65%) thought they were less attentive at work. In this study SF-36 scores were lower on all dimensions than in healthy non-pregnant controls, especially for energy and physical functioning; scores for women in early pregnancy were comparable to published data for chronic illness.

Another prospective study[41] in the systematic review[38] administered questionnaires to 4041 pregnant women in Sweden. Women who took sick leave due to NVP took on average 13 days of leave, comprising 28% of all sick leave taken up to week 28. Other studies in the review reported a decline in work productivity among women with NVP, especially those with severe symptoms.

About 17% of New Zealand antenatal inpatient hospital admissions and 7% of daystay admissions are for excessive vomiting.[34, 35]

Summary of evidence

Up to 80% of pregnant women experience nausea or vomiting. It is usually limited to the first trimester, but persists for up to 22 weeks in about 10% of cases. Women's' ratings of nausea in pregnancy suggest that it is comparable in severity to moderately nausea-producing cancer chemotherapy.

About 23-35% of pregnant women require time off work (usually two to three weeks) due to nausea and vomiting.
Among women with nausea and vomiting in early pregnancy, 4% resign, 28% adapt their work hours to accommodate their symptoms and 65%

report that it reduces their attentiveness at work. Quality of life scores for women in early pregnancy with nausea and vomiting are comparable to scores in people with chronic illness.
Nearly 5% of women have hyperemesis gravidarum, defined as repeated vomiting in early pregnancy requiring inpatient admission, day stay with IV fluids, nasogastric feeding (at home or in hospital) or vomiting causing a loss of over 5% of booking weight. Women with HG often require sick leave in all three trimesters. About 2% of women have HG severe enough to require hospitalisation.

5. Pelvic and back pain

Evidence base

- A systematic review [42] of pelvic girdle pain in pregnancy (in a guideline on pelvic girdle pain). It included four prospective studies. [8, 43-45]
- A prospective Swedish population-based cohort study of back pain in pregnancy [9*]
- A cross sectional Swedish population-based survey of pelvic girdle and lumbar pain [46*]
- A population-based longitudinal survey of pregnancy-related sick-leave [3*]
- Five population-based cross-sectional surveys of pelvic and/or lower back pain in pregnancy, conducted in Spain [47], Norway [48-50] and Sweden [51]
- A cross-sectional analysis of baseline data from an Australian prospective cohort study of pregnancy-related morbidity [11]

Prevalence of pelvic and back pain

Most studies reported high rates of pelvic and /or back pain during pregnancy, though estimates varied widely.

Pelvic girdle pain

Pelvic girdle pain is a specific form of low back pain, which occurs separately or in conjunction with other types of back pain. [50] The systematic review [42] estimated a point prevalence of pelvic girdle pain of about 20%. However there was variation between the four included studies: two [8, 43] found that 19-20% of women had pelvic girdle pain at 30-33 weeks, while the other two reported rates 'in pregnancy' of 14% [44] and 49%. [45]

Any type of back pain

First trimester:

The Swedish cohort study [9*] reported that 40.5% of women had any type of back pain in early pregnancy (before week 12), but that only 19.5% had *new onset* pain, as 21.5% of women had back pain before pregnancy. The mean score for the worst pain in the previous week was rated at 4/10 on a VAS scale.

Similarly, Ostgaard et al [8] noted that prevalence rates of back pain in pregnancy were influenced by the large number of women (22%) who already had ongoing pain before they became pregnant.

In an Australian study [11] 'back pain' was the third most common symptom in early pregnancy, experienced by 46% of women "occasionally or often".

Second trimester

The Swedish cohort study [9*] reported that there was a steady increase in all types of back pain from early pregnancy up to week 18. The incidence increased sharply from weeks 18-22 then levelled off. Prevalence at week 24 was 63.1%.

The Swedish cross-sectional study [46*] reported that 62% of women had pelvic girdle or lumbar pain at 12-18 weeks, among whom over half had pelvic girdle pain, 29% had lumbar pain and 29% had both. In the Norwegian retrospective

cohort study,[49] 23% of women had moderate or severe pelvic or lower back pain at 5 months' gestation.

Third trimester

The Swedish cohort study[9*] reported that 63.3% of women had back pain (of any type) at 36 weeks' gestation, among whom 16% had pain pre-dating pregnancy. The mean score for the worst pain in the previous week was rated at 6.5/10 on a VAS scale.

A Spanish study[47] reported that 71% of women had lower back pain and 65% had pelvic girdle pain at a median of 35 weeks' gestation (range 31-35). By the end of pregnancy (at 9 months) about 42% of women had moderate or severe pelvic and/or lower back pain in the Norwegian retrospective cohort study.[49]

Throughout pregnancy (no specific trimester)

Other studies reported rates of pelvic or back pain occurring at any stage of pregnancy. Robinson et al[50] reported that 46% of women had experienced pelvic girdle pain in their most recent pregnancy, while Endresen et al[48] reported that 49% of postpartum women had either pelvic or back pain or both during pregnancy. In the Swedish survey[51] 72% of women had lower back or pelvic pain (most commonly both), which started at a mean of 22 weeks' gestation (range 1-39 weeks).

The Swedish cohort study[9*] noted that back pain was usually short term and that long-term pain was rare. Pain intensity increased over pregnancy.

Evidence on functional impact

Studies used a variety of measures to assess the functional impact of pelvic and back pain, including pain scores,[51] disability scores,[9, 46, 49] need for treatment,[49] need for crutches,[50] waking at night,[50] difficulty with housework or with occupation[45, 48] and requirement for sick leave.[3] Their findings varied widely.

Mogren et al[51] reported that the worst back or pelvic pain experienced during pregnancy (mean pain score for worst pain 5.8, SD 2.2) was comparable with the worst pain during delivery (mean pain score for worst pain 5.4, SD 3.8).

Kristiannson et al[9*] noted that the quartile with the worst back pain had difficulty with normal activities, such as walking up or down stairs, leaning over a sink, running, heavy work or lifting. Gutke et al[46*] found that 15% of women with pelvic girdle or lumbar pain at 12-18 weeks were not functionally affected. Most of the other women in this study reported only minimal disability and only 6% reported moderate disability (Oswestry Disability Index >40%). A third study[49] which assessed functional impairment related to pelvic or lower back pain reported that among women with moderate to severe pain (57% of the total sample), the mean score Oswestry disability index score indicated moderate disability. In this study 27% of women received treatment for lower back or pelvic pain during pregnancy.

Waking up at night with pelvic girdle pain (PGP) was reported by 15% of women in the Norwegian survey.[50] This comprised 33% of women with PGP. In this

study 7% of pregnant women (16% of those with PGP) required crutches in their most recent pregnancy as a result of PGP.

Another Norwegian study [48] reported that 9% of women had serious difficulty with housework due to pelvic pain and that among women in paid employment the risk of pelvic pain was increased by working with the body bent forward. The risk of lower back pain was increased by occupations requiring frequent twisting or bending, or lifting the hands above shoulder height.

Ostgaard et al [8] also reported occupational factors that increased the prevalence of back pain during pregnancy; these included physically heavy work, lifting, twisting, bending forward, poor work satisfaction, post-work fatigue, inability to take rest breaks and constrained working postures.

One of the studies in the systematic review [45] reported that for 9% of women, the severity of pelvic pain necessitated giving up work.

Pelvic pain was the second most common indication for sick leave during pregnancy in the Norwegian study, and was an indication for sick leave in 32% of women. Median duration of leave for this indication was 10-12 weeks. Lower back pain was an indication for sick leave in 18% of women, for a median duration of 10 weeks. [3*] In another Norwegian study, [50] 67% of all pregnant women were "sicklisted" during pregnancy, among whom 41% reported that the indication was PGP.

Summary of evidence

Pelvic and back pain are very common during pregnancy. This is partly because over 20% of women with back pain in early pregnancy already have back pain before they become pregnant.

Nearly half of pregnant women have lower back or pelvic pain occasionally or often in the first trimester and 50-72% have this type of pain in the second or third trimester.

Assessment of the functional impact of back pain varied widely, but nearly 60% of women in one study reported some functional impairment during pregnancy (such as more pain and difficulty with sitting, lifting and standing). Nearly 10% of women with pelvic pain reported a high degree of functional impairment, resulting in giving up work or having difficulty with housework.

Pelvic girdle pain was an indication for sick leave during pregnancy in 32% of women, median duration of leave being 10-12 weeks. The worst pain associated with pelvic girdle and lower back pain was rated as similar to pain during delivery. Among women with pelvic girdle pain, 16% reported that they required crutches during their most recent pregnancy.

6. Headaches and migraine

Evidence base

- Two population-based Norwegian studies of the prevalence of headaches and migraine in pregnancy, one prospective cohort study [52] and one cross-sectional survey [10]
- An Australian population-based cross-sectional survey of the general health of nulliparous women in early pregnancy [11]

Prevalence of headaches and migraine

The Norwegian cross-sectional survey [10] found that overall migraine and non-migrainous headache were less prevalent overall among nulliparous pregnant women than among non-pregnant women (One year prevalence: OR 0.5, 95% CI 0.4 to 0.7). The same trend was seen for multiparous pregnant women but the difference was not significant (OR 0.8, 95% CI 0.7 to 1.0). There was no difference in headache prevalence during the first and second trimester between pregnant and non-pregnant women, but headache was significantly less prevalent in the pregnant women in the third trimester than in non-pregnant women (OR 0.4, 95% CI 0.3 to 0.6). This applied to all pregnant women and to both migraine and non-migrainous headache.

Similarly, the prospective study noted a gradual decrease during pregnancy in the frequency of headaches and migraine in general. [52]

The prospective study [52] also found that more women changed during pregnancy from having headaches to not having headaches (248/1,618 = 15%) than the other way around (101/1,618 = 6%) ($p< 0.001$). Overall there was no significant difference in the prevalence of headaches and migraine (combined) between pregnant and pre-pregnant women. Among women who reported migraine, the intensity and duration of headaches was significantly reduced during pregnancy.

In the Australian survey, [11] 30% of women reported having a severe headache or migraine during early pregnancy either occasionally or often.

Evidence on functional impact

The evidence suggests that for most women, pregnancy is not associated with increased headaches or migraine and that it is more likely to reduce their impact, especially in the second and third trimester.

Summary of evidence

Headaches and migraine are usually less frequent and less severe in pregnant women than in non-pregnant women, especially in the later stages of pregnancy and especially in nulliparous women. Moreover among women with a history of migraine, attacks are likely to be less intense and of shorter duration. However some women develop new symptoms in pregnancy, and an Australian survey reported that 30% of women experience severe headache or migraine 'occasionally or often' in early pregnancy.

7. Urinary and bowel problems

Evidence base

- A systematic review of studies of the prevalence of urinary incontinence in pregnancy [12]
- A prospective Danish longitudinal study of urinary symptoms in pregnancy (and postpartum) [14] (included in Sangsawang et al [12])
- A prospective UK longitudinal study of urinary and faecal incontinence in pregnancy (and postpartum) [13]
- An Australian population-based cross-sectional study on the general health of nulliparous women in early pregnancy [11]
- New Zealand Ministry of Health reports on hospital-based maternity events in 2006 and 2007 [34, 35]

Prevalence of urinary and bowel problems

Urinary symptoms

A prospective UK study [13] reported that among nulliparous women with a singleton pregnancy at a London hospital, 81% reported urinary frequency, 44% reported urinary incontinence, and 9.3% had urinary incontinence at least daily.

The systematic review [12] found a wide disparity in estimates of the prevalence of urinary incontinence in pregnancy. Overall stress incontinence rates ranged from 19% to 60%, incontinence with urgency from 2% to 35% and mixed incontinence from 4% to 13%. Variation in rates appeared to relate partly to study setting. In most European and Australian studies, between 30% and 45% of women reported urinary incontinence at some stage during pregnancy, with higher rates in multiparous women.

The risk of urinary incontinence increased with gestational age, with a rate of 13% to 19% reported in the first trimester. The rate in the second trimester was 19.2 %, and in the third trimester was 30-37.5 %. [12]

Bowel symptoms

The UK study [13] reported that 9% of pregnant women experienced faecal urgency, 6% incontinence of flatus and nearly 1% incontinence of liquid stool. Thirteen per cent reported *any* urgency or incontinence of flatus or stool.

The Australian study [11] reported that 44% of women experienced constipation occasionally or often in early pregnancy.

Evidence on functional impact

A Danish population-based study [14] in the systematic review [12] reported that the prevalence of urinary stress incontinence in pregnancy was 32%, but that the prevalence of such incontinence "causing a hygienic or social problem" (the definition used by the International Continence Society) was only 1%. The authors concluded that the psychosocial impact of symptoms is modest.

Among women in the UK study who had urinary incontinence, 10.2% wore

sanitary protection. Only 2.8% felt that the symptoms restricted their activities. [13]

About 4% of New Zealand antenatal day stay admissions and 7-8% of inpatient hospital admissions were for genitourinary infection. The mean duration of inpatient admission for this indication was two days. [35, 34]

Summary

During pregnancy urinary frequency occurs in most women. Urinary incontinence (usually stress incontinence) occurs in 30-45%. Rates of incontinence are higher in multiparous women and with increasing gestational age. Fewer than 3% of women with urinary incontinence in pregnancy report that it restricts their activities. Only about 1% of pregnant women find it problematic ('a hygienic or social problem').

Genitourinary infections are the fourth most common indication for antenatal hospital admission in New Zealand, responsible for about 8% of such admissions.

With regard to bowel symptoms, 44% of Australian women reported occasional or frequent constipation in early pregnancy, while in a UK study 13% of women reported that during pregnancy they experienced faecal urgency or incontinence (of flatus or stool).

8. Vaginal bleeding

Evidence base:

- A systematic review of abnormal bleeding in the second half of pregnancy [53]
- A prospective UK population-based primary care cohort study of bleeding early in pregnancy [16*]
- Three prospective population-based cohort studies of first or second trimester bleeding reported by women with pregnancies ongoing at 20-28 weeks. They were set in Finland, [54*] Denmark [55*] and internationally (SCOPE study) [15*]
- Two prospective cohort studies in US hospital settings, describing first or second trimester bleeding reported by women with pregnancies ongoing at 20-29 weeks [56, 57]
- A retrospective hospital registry-based Australian study of bleeding occurring after 24 weeks' gestation [58]
- Two New Zealand Ministry of Health reports on Hospital-based Maternity Events in 2006 and 2007 [34, 35]

Prevalence of vaginal bleeding

Estimates of the incidence of bleeding in pregnancy vary according to the definition of bleeding and measures used. Most studies [15, 54-56] only included women with pregnancies ongoing at 20-29 weeks. These studies did not include women who miscarried prior to 20-29 weeks. Moreover data on early bleeding were subject to potential recall bias in most studies.

First trimester bleeding

In a recent international study with a New Zealand cohort 19% of nulliparous women had bleeding in the first trimester, including any event from spotting to heavy bleeding. [15*] Other studies using a similar definition of bleeding reported rates of 16%, [55*] 19% [57] and 23%. [56] All these studies only included women with ongoing pregnancy at 20-29 weeks.

In most cases first trimester bleeding consisted of a single episode of light spotting lasting from 1-3 days. [15, 55, 57] However about 10% of women reported moderate to heavy bleeding. [15*] Onset of bleeding was most commonly at six to eight weeks' gestation. [15, 55*]

Second trimester bleeding

Vaginal bleeding was less common in the second trimester, with estimated rates ranging from 2% to 6%. [15, 54-56] Fewer than 1% of women had new-onset bleeding in weeks 16-20. [15*] A systematic review [53] reported that the incidence of bleeding of unknown origin in the second half of pregnancy was 2%.

As in the first trimester, bleeding was moderate to heavy in about 10% of cases. [15*]

Bleeding in either first or second trimester

The only population-based study that has prospectively collected data on bleeding from conception onwards reported a bleeding rate of 21% in the first

20 weeks in a semirural UK primary health setting.[16]* It was unclear whether this study included spotting in the definition of bleeding.

Among women with bleeding, nearly two thirds reported that it was not associated with pain, while 31% reported light pain. Pain was more common among women with heavy bleeding, of whom 50%-54% reported pain. Five per cent of women with bleeding reported moderate or severe pain which lasted more than a day.[55]*

Evidence on functional impact

Among women with first trimester bleeding, about 14% were admitted to hospital, usually for fewer than 7 days. Among women with second trimester bleeding, about 28% were admitted to hospital for up to 13 days. [55]*

Antepartum haemorrhage accounted for about 13% of antenatal hospital admissions and 12% of same-day antenatal admissions in NZ in 2006 and 2007. These figures include about 3% of antenatal admissions and 7% of same-day admissions which were specifically reported as being in *early* pregnancy. The average length of overnight stay was under 2 days.[34, 35]

Summary of evidence

The evidence suggests that at least 20% of pregnant women have vaginal bleeding in the first trimester of pregnancy and at least 5% have bleeding in the second trimester.

Bleeding most commonly occurs around weeks 6-8, and often consists of a single episode of light bleeding or spotting, lasting for up to three days. In about 10% of cases, vaginal bleeding is heavy. The bleeding is usually painless, but in about 5% of cases it is associated with moderate or severe pain.

About 14% of women with first trimester vaginal bleeding and 28% of women with second trimester vaginal bleeding are admitted to hospital. This indication accounts for 12-13% of day and inpatient antenatal hospital admissions in New Zealand.

Bleeding rates are probably higher than reported in these studies, as most did not include women with vaginal bleeding related to miscarriage.

9. Miscarriage

Evidence base

- A systematic review of population-based cohort studies of miscarriage rates at up to 20 weeks gestation [59]
- A prospective UK population-based primary care cohort study of miscarriage [16*]
- Two prospective cohort studies of miscarriage rates in the general population, conducted in Sweden [60*] and Denmark [61*]
- Three cross-sectional surveys of miscarriage rates in the general population conducted in Finland [62], the UK [63] and New Zealand [64]
- A retrospective cohort study of first-trimester miscarriage rates among Finnish flight attendants [65]
- A retrospective analysis of baseline data from a multicentre US cohort study [66]
- Two New Zealand Ministry of Health reports on miscarriages occurring in hospital in 2006 and 2007 [34, 35]
- A longitudinal hospital–based cohort study of psychological morbidity after miscarriage, conducted in Hong Kong [67]
- A UK case-control study comparing miscarriage rates in female flight crew with those in female air-traffic controllers [68]
- A UK cohort study of registry data, reporting the annual incapacitation rate of commercial pilots [69]

Incidence of miscarriage

Miscarriage was defined in these studies as spontaneous pregnancy loss before 20-28 weeks. As with bleeding, reported incidence rates for miscarriage are likely to be underestimates. Studies noted the potential for confounding related to unsuspected pregnancy loss, early miscarriage for which women do not seek medical help or are not hospitalised [16, 61*] and high rates of legal abortion. [60*] The likely effect of such confounding is that miscarriage rates may be over 30% higher than official statistics suggest. [16*]

In most studies the miscarriage rate was between 11% and 13% of all pregnancies, [16, 60, 62, 63] though a systematic review reported estimates ranging across studies from 11% to 22%. [59] In one study [61*] the self-reported miscarriage rate was 21%, but based on hospital registry data for the same cohort of women the rate was only 16%.

Most miscarriages occur in the first trimester: one study reported that 88% of miscarriages occurred at 6-14 weeks and about 7% of miscarriages at 16-18 weeks' gestation (data were missing for 5%). [16*] Two studies estimated the risk of miscarriage in the second trimester (up to 20-24 weeks) at 0.5% to <1%. [24, 66]

A New-Zealand population-based study [64] reported that about one third of women have at least one miscarriage in their lifetime, at a conservative estimate. Other estimates were 25% (by age 39) in Sweden [60*], and 50% (by age 44) in Finland. [62]

A study of first trimester miscarriage among flight attendants reported a rate of 12%.[65] The UK case-control study of flight crew[68] found that the risk of miscarriage among flight crew was similar to that of air-traffic controllers (OR 1.39, 95% CI 0.58 to 3.33 (adjusted for maternal age, BMI and smoking history)), suggesting that the risk of miscarriage is not increased by flight-crew related exposures.

Evidence on functional impact

In the UK primary care study, about two thirds of women who miscarried were admitted to hospital. About 63% of women who miscarried underwent evacuation of the uterus.[16]*

In New Zealand rates of referral to hospital for miscarriage are around 5% per pregnancy for European and Asian women, and around 6-7% among Pacific and Maori women.[34, 35] These figures are not overall population rates, as they do not include miscarriages occurring elsewhere. The above-mentioned UK study estimated that at least a quarter of all known miscarriages are treated at home by general practitioners and not recorded in any published statistics.[16]*

A cohort study of psychological morbidity among women admitted to a Hong Kong Hospital for management of miscarriage found that although scores for distress and depression decreased over one-year follow-up, 11% of women were still distressed (compared to a control group) after 1 year.[67]

A UK study reported the prevalence of incapacitations in commercial pilots in 2004. The cohort included 617 female pilots. The sole incapacitation among the female pilots was a spontaneous abortion at 22 weeks in a pilot who was already deemed temporarily unfit, due to pregnancy.[69]

Summary of evidence

Between 11% and 22% of known pregnancies end in miscarriage (spontaneous pregnancy loss before 20-28 weeks). Data on early miscarriages are unreliable, partly due to the high proportion of miscarriages for which women do not seek medical help. Around 90% of miscarriages occur in the first trimester.

In New Zealand, rates of referral to hospital for miscarriage are about 5% for European and Asian women and 6-7% for Pacific and Maori women. Based on UK population data, about 12% of pregnancies end in clinically–confirmed miscarriage, and in about two thirds of cases women are admitted to hospital after miscarriage and undergo evacuation of the uterus.

A cohort study of women admitted to a Hong Kong Hospital for management of miscarriage found that although psychological morbidity decreased over one-year follow-up, 11% of women were still distressed one year later.

There is some evidence to suggest that the prevalence of miscarriage in female flight crew is similar to rates in other women.

10 Ectopic pregnancy

Evidence base

- Six retrospective population-based cohort studies set in Norway, [70] Australia, [71] France, [72] the UK, [73] Sweden, [74] and Italy [75]
- One large North American retrospective cohort study of women with ectopic pregnancy [17]
- Two clinical guidelines [18, 19]

Incidence of ectopic pregnancy

All the population-based cohort studies aimed to evaluate changes in the annual incidence of ectopic pregnancy over periods of 8-15 years. Older studies tended to report a declining rate, [70, 71] while more recent studies reported stable or increasing rates. [72, 73, 75] In the most recent year reported in each study (which ranged from 1995 to 2010), the rate of ectopic pregnancies per 10,000 women-years ranged from 5.1 to 10, and the rate per 1000 pregnancies or deliveries ranged from 6.3 to 16.

The population-based cohort studies did not report gestational age at presentation in their samples. However a large North American chart review[17] described the characteristics of 693 consecutive ectopic pregnancies. The mean gestational age for diagnosis of unruptured ectopic pregnancy was 6.9 weeks (SD 1.9), and of ruptured ectopic pregnancy was 7.2 weeks (SD 2.2). [17]

Evidence on functional impact

Clinical presentation of ectopic pregnancy ranges from a missed period or pelvic tenderness to (rarely) shock and collapse. The most common symptoms are abdominal or pelvic pain, amenorrhea or vaginal bleeding. Women with suspected ectopic pregnancy require immediate referral to an early pregnancy assessment unit or gynaecology clinic. [18] Management usually involves laparotomy, operative laparoscopy or medical treatment. [19]

Summary of evidence

Ectopic pregnancy occurs in about 1.5% to 2% of pregnancies. It usually presents in early pregnancy, most commonly at around 7 weeks' gestation. Clinical presentation varies but the most common symptoms are abdominal or pelvic pain, amenorrhea or vaginal bleeding. Suspected ectopic pregnancy requires urgent medical assessment and (if confirmed) may necessitate immediate surgery or medical treatment.

11. Venous thrombosis

Evidence base

- A systematic review of DVT rates in pregnancy [76]
- A population-based retrospective cohort study of the incidence of VT in England, which was accompanied by a comparative systematic review of 21 other VT incidence studies [20]
- A retrospective population-based cohort study of the incidence of VT in a US County over 30 years. [77] (included in Abdul Sultan 2013 SR [20])
- A population-based retrospective cohort study of the incidence of VT in Scotland [78]
- A retrospective chart review of VT rates at two hospitals, one in New Zealand and one in Australia [21]
- A literature review of gestational complications associated with air travel [36]

Incidence of venous thrombosis

Venous thrombosis (VT) was defined in the included studies as deep vein thrombosis (DVT) or pulmonary embolism (PE) diagnosed using objective clinical criteria (need for anticoagulants, imaging tests) or by ICD-10 codes. All relevant studies were retrospective or cross-sectional analyses of data from national registries or hospital discharge databases.

The incidence of antenatal VT in England was estimated at 99 per 100, 000 person-years in the primary study conducted by the authors of one of the systematic reviews. [20] The rate in their accompanying meta-analysis ranged from 53 to 144 per 100,000 woman-years. The authors addressed heterogeneity by limiting analysis to post-2005 studies which conducted a form of case validation (n=4), a process which resulted in a pooled estimate of 118 per 100, 000 years.

Other studies also reached widely varying estimates: the recent Scottish study [78] estimated a rate of 136 per 100,000 deliveries, whereas the rate in a small New Zealand-Australian chart review was only 40 to 59 per 100,000 deliveries. [21]

Most VT events were DVTs: in Heit et al [77] the overall incidence of antenatal VT was 96 events per 100,000 years, of which 85 events were DVT and 11 were PE.

The two SRs reported increasing risk of VT with increasing gestation. One [20] estimated incidence rates of VT at 46, 58 and 182 per 100, 000 woman-years in the first, second and third trimesters respectively (though with wide variation between studies). The other [76] reported that 22% of DVTs occur in the first trimester, 34% in the second and 48% in the third. In the small NZ/Australian study [21] there was no difference between the rates in different trimesters, with 14, 7 and 10 events occurring in the first, second and third trimesters respectively.

The incidence of VT peaked around the time of delivery [20] and was fivefold higher during delivery and the postpartum period than in the antenatal period [77]. A similar trend was noted in the NZ study. [21] Rates of VT in pregnancy and post-

partum were over four times greater than among non-pregnant women in the same population. [77]

Although it is recognised that both air travel and pregnancy increase the risk of VT, there appears to be no evidence about their combined risk. [36, 79]

Evidence on functional impact

Pregnancy-related VT is a major cause of preventable maternal death (associated with fatal pulmonary embolism). Women diagnosed with antenatal VT are generally treated with short-acting anticoagulants given subcutaneously once or twice daily, and monitored with regular blood tests for the remainder of the pregnancy and post-partum period. [21]

Summary of evidence

There is wide variation in estimated incidence rates for venous thrombosis (deep vein thrombosis (DT) and pulmonary embolism (PE)) among pregnant women. This may relate to differences in data sources, coding practices and in the use of different diagnostic tools, such as imaging.

Estimated rates of VT during pregnancy range from 50 to 200 per 100, 000 pregnancies. Ninety per cent of antenatal VTS are DVT rather than PE.

Although VT is a rare event in pregnancy, it is a major cause of preventable maternal death and requires treatment until the end of the postpartum phase, usually by means of anticoagulant injections once or twice daily.

12. Pre-eclampsia and eclampsia

Evidence base

- A systematic review of worldwide incidence rates of pre-eclampsia and eclampsia [24*]
- A prospective international cohort study with a New Zealand cohort (SCOPE) [22*]
- A prospective population-based NZ cohort study of BP in pregnancy [80*]
- An NZ population-based retrospective cohort study [81]
- A retrospective NZ/Australian cohort study [82]
- A retrospective population-based Norwegian cohort study [83]
- New Zealand Ministry of Health reports on hospital-based maternity events in 2006 and 2007 [34, 35]
- A New Zealand Health Quality and Safety Commission report [84]

Australian and New Zealand guidelines [23] use the following definitions for hypertensive disorders arising in pregnancy:

- Gestational hypertension: new onset hypertension at >20 weeks' gestation, without proteinuria or other features of pre-eclampsia
- Pre-eclampsia: hypertension with proteinuria (or other organ involvement) at >20 weeks' gestation
- Eclampsia: pregnancy-related seizures

Incidence of pre-eclampsia

The systematic review [24*] estimated that in the Western Pacific area (Australia, Japan, Korea, New Zealand and Singapore) 3.9% of women giving birth have pre-eclampsia. However confidence intervals were very wide (95% uncertainty range 1.8 to 9.2). Eclampsia (pregnancy-related seizures) occurred in about 0.1% of deliveries.

The SCOPE study, an international population-based prospective cohort study with an NZ cohort [22*] reported a 5.3% prevalence of pre-eclampsia in healthy nulliparous women, including 1.3% who had *pre-term* pre-eclampsia, defined as eclampsia resulting in delivery before 37 weeks. Pre-eclampsia developed at a mean of 36.9 (SD 3.3) weeks' gestation.

A prospective population-based NZ cohort study of BP in pregnancy [80*] reported a 3.2% rate of antenatal pre-eclampsia. Incidence of eclampsia was 0.05%. In addition 10.8% of participants had antenatal gestational hypertension (hypertension without proteinuria).

Retrospective registry-based cohort studies conducted in Australia and New Zealand [82], New Zealand only [81] and Norway [83] estimated pre-eclampsia rates at 3.3% to 4.2% per birth. Nearly 10% of women had *any* gestational hypertension [82].

The New-Zealand registry study [81] identified independent risk factors for preeclampsia which included Maori ethnicity (50% higher risk), and being overweight or obese. The risk was 50% lower in Chinese women.

Evidence on functional impact

The usual management of gestational hypertension is ongoing monitoring to facilitate early detection of pre-eclampsia or severe hypertension. [23]

Preeclampsia is a progressive disorder that worsens as pregnancy continues. The standard management is close observation of mother and fetus until 37 completed weeks or until the onset of either maternal or fetal complications. This usually involves hospital admission. [23]

As noted above, in about 1.3% of first pregnancies in the SCOPE study, pre-eclampsia was associated with delivery before 37 weeks' gestation. [22]

As also noted above, eclampsia is very rare, affecting only about 0.1% of deliveries. However it is a leading cause of preventable maternal death. [84]

In New Zealand, nearly 8% of antenatal daystay admissions and over 10% of inpatient hospital admissions are for gestational hypertension (with or without proteinuria). [34, 35]

Summary of evidence

Pre-eclampsia occurs in about 3-4% of pregnancies overall. It is more prevalent in first pregnancies, and occurs in about 5.3% of healthy nulliparous women in their first pregnancy. About 1.3% of first pregnancies (in healthy women) result in delivery before 37 weeks' gestation due to pre-term pre-eclampsia.

By definition pre-eclampsia does not occur before 20 weeks. Median gestation at time of diagnosis in the SCOPE study was 36.9 weeks.

Pre-eclampsia is a complex, progressive and unpredictable disease with a major functional impact, usually requiring hospital admission.

Eclampsia is very rare, occurring in about 0.1% of deliveries, but it is a leading cause of preventable maternal death.

13. Pre-term birth

Preterm birth is defined as birth before 37 weeks' gestation.

Evidence base:

- A systematic review of 92 studies of pre-term birth rates worldwide [85]*
- Two publications from a prospective international cohort study with a New Zealand cohort (SCOPE) [25, 26]*
- A New Zealand Ministry of Health report, based on data from hospitals and lead maternity carers [86]

Incidence of pre-term birth

The New Zealand Ministry of Health reported [86] that in 2010 7.4% of all live born babies in New Zealand were born preterm. Rates varied by ethnicity and socioeconomic status. The systematic review [85]* reported a rate of 6.4% in Australasia (Australia and New Zealand), for all preterm births.

The SCOPE study [25]* reported that among healthy nulliparous Australian and New Zealand women (n=2535), the preterm birth rate was 4% in non-smokers and 10% in smokers. In the wider international study population (n=3234) [26]* the overall rate was 4.9%.

Summary of evidence

Approximately 7% of babies in New Zealand are born preterm (before 37 weeks' gestation), with individual risk varying according to demographic and behavioural factors. The rate in healthy women in their first pregnancy is 4-5%, with twice the risk in smokers.

14. Cognitive disorders

Evidence base

- A prospective Australian cohort study of cognition in pregnancy and motherhood [27*]
- A systematic review of 14 small case-control studies of the effects of pregnancy (and the post-partum) on memory [87]
- A case-study of a pregnant pilot tested for mental rotation ability [88]

Prevalence of cognitive disorders

The systematic review [87] found that pregnant women (n=412) were significantly impaired on measures of short-term memory, working memory, free recall and delayed free recall, compared to non-pregnant controls (n=386). There was no significant difference between the groups in measures of recognition, implicit memory or subjective memory.

The Australian study [27] recruited women prior to pregnancy and compared cognitive changes in women who subsequently became pregnant with changes in those who did not, using four measures of cognition (cognitive speed, working memory, immediate recall, delayed recall). Pregnant women were categorized into early and late pregnancy (pre 20 weeks and 20-40 weeks gestation, respectively). There was no difference between the groups for any measure except cognitive speed in the later stages of pregnancy; and the difference was no longer significant when all pregnant women were considered as a group. For this outcome, non-pregnant women recorded an improvement or stability between measures, whereas performance fell in pregnant women, with a significant difference between the groups. However the difference did not persist: there were no differences between non-pregnant women and mothers.

Evidence on functional impact

The authors of the systematic review [87] concluded that "memory measures that place relatively high demands on executive cognitive control may be selectively disrupted in pregnancy". However they noted that in all cases the effects were small and that "the observed impairment may be regarded as relatively subtle".

The authors of the prospective cohort study[27*] stated that "Except in a brief period in later pregnancy, (our) findings challenge the common myth that women develop 'placenta brain' ".

The authors of the case-study of mental rotation ability in a female pilot [88] concluded that there was an effect of pregnancy on visuo-spatial ability that can last for some time after delivery. As no baseline (pre-pregnancy) measures were taken in this study and the pilot's performance did not vary significantly between pregnancy, post-partum or one year after delivery, these conclusions appear unreliable.

Summary of evidence

The evidence of case-control studies suggests that pregnancy significantly impairs short-term memory, working memory, free recall and delayed free recall, though differences are relatively subtle.

However, the only evidence from a prospective well-controlled cohort study (which tested cognitive speed, working memory, immediate recall and delayed recall in early and late pregnancy) suggests that pregnancy does not affect memory. However there may be a temporary decline in cognitive speed in the second half of pregnancy.

A recent case-study suggested that mental rotation ability may be impaired in female pilots during pregnancy, but this evidence does not appear reliable.

15. Mental health disorders

Evidence base

- Three systematic reviews of depression rates [28, 89, 90] with differing inclusion criteria but considerable overlap between studies
- A study of US epidemiological survey data [29]
- A Norwegian population-based study of sick leave taken during pregnancy [3]*
- A systematic review of studies of the prevalence of obsessive compulsive disorder in pregnancy [91]

Prevalence of mental health disorders

All mental disorders

A cross-sectional studies of US epidemiological survey data from 2001-2 [29] compared the prevalence of mental disorders in currently pregnant women compared to non-pregnant, non post-partum women. It assessed DSM-IV-diagnosed disorders including major depression, dysthymia, bipolar disorder, social phobia, specific phobia, generalized anxiety disorder, panic disorder, alcohol abuse or dependence and drug abuse or dependence. Pregnant women were less likely than non-pregnant women to have depression (7.3% vs 11.4%), alcohol abuse or dependence (2.8% vs 8.3%), or any mental disorder (19.2% vs 29.3%) There was no difference between pregnant and non-pregnant women in the prevalence of dysthymia, manic episodes, phobias, or drug abuse or dependence. Pregnancy per se was not associated with increased risk of the most prevalent mental disorders (although the risk of major depressive disorder appeared to increase postpartum).

Depressive disorders

Three systematic reviews reported the prevalence of antenatal depressive disorders, measured either by diagnostic interview [90] and/or by validated self-screening tools. [28, 89] Chatillon et al [89] estimated a rate of 5 to 15%. Bennett et al [28]* estimated rates as follows: first trimester 7.4% (95% CI 2.2 to 12.6), second trimester 12.8% (95% CI 10.7 to 14.8) and third trimester 12.0% (95% CI 7.4 to 16.7). Gavin et al [90]estimated that during pregnancy up to 12.7% of women have an episode of major depression, up to 18.4% have either major or minor depression, and up to 14.5% of pregnant women have a *new* episode of major or minor depression.

Confidence intervals were wide for all estimates. Review authors explored possible reasons for the disparity between reported rates, but were unable to suggest an explanation. [28, 90] Differences in findings between the systematic reviews may relate to their population differences, as only one [28]* was clearly restricted to population-based studies. It was unclear whether women experience depression on a continued or intermittent basis throughout pregnancy, and moreover disease severity was not well documented [28]*.

Obsessive compulsive disorder (OCD)

A systematic review [91] reported a mean prevalence of OCD in pregnancy of 1.64% (95% CI 1.23% to 2.2%). However there was huge variability in estimates

across the 12 relevant studies (from 0.20% to 29%). Comparison with 'matched' studies with non-pregnant controls suggested an increased risk in pregnant women (RR 1.45, 95% CI 1.07 to 1.96).

Evidence on functional impact

Mental health disorders can cause substantial disruption to daily functioning. However, NICE guidelines state that the nature and course of such disorders occurring in pregnancy does not substantially differ from such disorders at any other time, though they may necessitate more urgent intervention. [92]

A Norwegian population-based study [3]* of sick leave during pregnancy reported that anxiety or depression, were responsible for the longest median duration of sick leave (20 weeks), but only 2% of women reported this as an indication for leave. The study authors suggested that this is probably an underestimate, as the questionnaire response rate was lower in this group.

Summary of evidence

Estimated rates for specific mental health disorders in pregnancy varied widely across studies. Evidence from population-based studies suggested that about 7% of women have depressive disorders in the first trimester, rising to 12-13% in the second and third trimesters. However, there was a high degree of uncertainty for all estimates. US survey data suggested that about 19% of women have any type of DSM-IV psychiatric disorder in pregnancy.

There was some suggestion of an increased rate of obsessive compulsive disorder in pregnancy, but the evidence did not appear robust.

Rates for the most prevalent mental health disorders in pregnant women are similar to, or lower than, rates in other women.

The symptoms and course of mental disorders in pregnancy are similar to those experienced by non-pregnant women, though they may require more urgent intervention. The functional impact of such disorders can be severe: anxiety or depression were responsible for longer sick leave (20 weeks) than any other health problem.

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Appendix 1: Methods

Inclusion criteria

Included:

- Studies of the incidence of common effects and complications of pregnancy.
- Systematic reviews, population-based cohort and cross-sectional studies (in order of preference)

Excluded:

- Lower-level studies (e.g. retrospective, case-control) unless no data were available from studies with higher level of evidence.
- Unpublished and ongoing studies, studies without at least abstract in English

Review outcomes

The prevalence and manifestation of the following conditions in pregnancy:

1. Overall symptoms and indications for sick leave
2. Complications of pregnancy
3. Fatigue and sleep problems
4. Nausea and vomiting
5. Pelvic and back pain
6. Headaches and migraine
7. Urinary and bowel problems
8. Vaginal bleeding
9. Miscarriage
10. Ectopic pregnancy
11. Venous thrombosis
12. Pre-eclampsia and eclampsia
13. Pre-term birth
14. Cognitive disorders
15. Mental health disorders
16. Abdominal girth and mobility

Search

The search was designed in consultation with a Cochrane Collaboration information specialist. We searched the following sources:

- MEDLINE/PubMed
- The Cochrane Library
- CINAHL
- PsycINFO
- Web of Science
- TRIP
- EMBASE
- Google
- Reference lists of articles retrieved

We also made extensive use of the citation-linking tools on Medline and Web of Science.

The basic MEDLINE search was as follows. We added keywords (e.g. *fatigue, nauesa, vomiting, back pain*) to search within the results for the outcomes of interest. The search was adapted for other databases:

1. Epidemiologic studies/
2. exp case control studies/
3. exp cohort studies/
4. Case control.tw.
5. (cohort adj (study or studies)).tw.
6. (Follow up adj (study or studies)).tw.
7. (observational adj (study or studies)).tw.
8. Longitudinal.tw.
9. Retrospective.tw.
10. Cross-sectional.tw.
11. Cross-sectional studies/
12. Cohort analy$.tw.
13. Questionnaires/
14. systematic review.tw.
15. or/1-14
16. *Pregnancy Complications/
17. 15 and 16

Study selection, data extraction and quality assessment

Relevant studies were selected and data were extracted on their characteristics, risk of bias and findings of the included studies (see Appendix 2). The risk of bias assessment took into account to what extent studies met the following criteria:

Reporting
- methods described in sufficient detail
- findings clearly expressed, with measures of variability
- authors' conclusions well-supported by evidence

Study design
- data-collection prospective

Sample:
- population-based
- applicable to a New Zealand setting
- appropriate control group used
- adequately powered to answer study question

Outcome measures
- valid measures used
- low risk of recall bias

Completeness of data
- high participation rate
- high follow-up rate

For systematic reviews
- rigorous search
- heterogeneity adequately addressed
- risk of bias in primary studies adequately addressed

Appendix 2: Table of included studies

Studies with low risk of bias have *

Study ref	Study characteristics	Stated objective	Methodological characteristics	Outcomes of interest (definition)	Findings
Abalos 2013 [24]* SR (WHO)	• Systematic review • Included studies of incidence of hypertensive disorders of pregnancy (HDP) (74 reports, 78 datasets) • Searched MEDLINE and EMBASE 2002-2010 and reference lists • Weighted average calculated	To evaluate the magnitude of hypertensive disorders of pregnancy, globally and in different regions and settings	Low risk of bias • Review processes conducted in duplicate • Searched 2 databases and references • Assessed quality of included studies (definition of outcomes, use of controls, whether national or whether regional/hospital, sample size) Overall study quality rated average to good	• pre-eclampsia • eclampsia (For aggregated data - model-based incidence: combines national and sub-national datasets plus modelled estimates using pre-specified predictor variables; for individual country data - crude incidence)	*Model-based incidence of pre-eclampsia in Western Pacific region* (i.e. Australia, Japan, Korea, NZ, Singapore): 3.9% (95% uncertainty range 1.8 to 9.2%) *Model-based incidence of eclampsia in Western Pacific region*: 0.1% (95% uncertainty range 0% to 0.1%) *Crude incidence of pre-eclampsia in NZ*: 14.4% [single dataset of women with type 2 diabetes: Hughes 2006 – not likely to be representative] Authors comment: "Eclampsia is a leading cause of preventable maternal death"
Abdul Sultan 2013 [20] UK	• Population-based retrospective cohort study • Linkage of two UK health databases (Clinical Research Practice Datalink and English Hospital Episode	1. To estimate the incidence of first VT in and around pregnancy; 2. To systematically review studies on perinatal VT incidence and compare our	Moderate risk of bias • Primary study based on population registry data • Systematic review only searched 2 databases • Post-hoc subgroup analysis was used in SR, restricting analysis to post 2005 studies	Antepartum and postpartum venous thromboembolism (Used 3 definitions, the most stringent included heparin prescription, death from VT Less stringent definition: Signs or symptoms of VT, diagnostic tests (e.g. imaging) or recorded in both datasets	*1. Primary study* Rate of antepartum VT per 100,000 person-years for pregnancies leading to live or stillbirth, and using a stringent definition of VT: Antepartum: 99 (95% CI 85-116)

	Statistics Database) • Plus meta-analysis of earlier incidence studies • Primary study included all women on relevant databases 1997-2010 (n=1,117,691 women, 248,953 pregnancies leading to live or stillbirth) • Systematic review included 21 cohort and cross-sectional studies • Searched MEDLINE and EMBASE to Jan 2013 • Excluded studies that did not report incidence data on VT suitable for meta-analysis	estimates.		Least stringent definition: Other VT diagnoses in databases, not included above)	*2. Systematic review:* Rate of antepartum VT per 100,000 person-years for pregnancies leading to live or stillbirth, and using a stringent definition of VT: Trimester 1: 46 (95% CI 31-70) Trimester 2: 58 (95% CI 41-83) Trimester 3: 182 (95% CI 150-221) Rates were about 50% higher using a less stringent definition, and were more than twice as high using the least stringent definition. Authors described limitations of using less stringent definitions and/or only primary or only secondary data source. They noted that leg swelling and calf pain are common in pregnancy, without DVT In the meta-analysis, there was high heterogeneity with antenatal incidence rates ranging from 53 to 144 per 100, 000 years . When meta-analysis was restricted to studies conducted after 2005 and those using

					case-validation for VT, the pooled estimates for antenatal incidence of VT were similar to those calculated in the primary study. The rate of VT peaked around the time of delivery and the first week of postpartum period (AR = 991 per 100,000 person years) after which the rates showed a graded decline throughout the remaining postpartum period
Aegidius 2009 [10] Norway	• Cross-sectional population-based survey • Included all women who responded to questions on headache in a county-wide survey of residents aged over 20 • 27,700/46,506 (60%) participation rate • Survey consisted of 2 questionnaires and a clinical examination • Non-pregnant	To evaluate the impact of pregnancy and parity on the 1-year headache prevalence in a large population-based study	Moderate risk of bias • Population based • 60% participation rate • Some risk of recall bias: participants were asked about headache during the last 12 months, rather than per trimester • Used validated self-report measures • Some potential for selection bias: participants were younger and had higher socioeconomic status than the non-responders • Comparison group were non-pregnant women rather than pre-pregnancy values in same women	Impact of pregnancy on the prevalence of headache and migraine (Used International Headache Society classifications)	*One-year headache prevalence*: Both migraine and non-migrainous headache were less prevalent among nulliparous pregnant women than among non-pregnant women (One year prevalence: OR 0.5, 95% CI 0.4 to 0.7) The same trend was seen for other pregnant women but the difference was not significant (OR 0.8, 95% CI 0.7 to 1.0) There was no difference in headache prevalence during the first and second trimester compared with non-pregnant women but headache was significantly less prevalent in the third trimester. (OR 0.4, 95% CI 0.3 to 0.6) This was seen for all

	women of the same age used as reference.				pregnant women and both migraine and non-migrainous headache.
Ammon Avalos 2012 [59]	• Systematic review • Searched MEDLINE to 2009, plus references • Included population-based studies that reported gestational age at study entry, pregnancy outcome and gestational age at outcome (n=4 studies, 58,462 pregnancies) • All included studies were conducted by the same US health care consortium (Kaiser Permanente) • Used life table (=survival) analysis methods	To calculate: (1) the expected rates of miscarriage by gestational week; (2) the cumulative risk of miscarriage; (3) the remaining risk of miscarriage for gestational weeks five through 20, through a systematic review of the literature	Moderate risk of bias • Only one database searched • Studies varied in gestational age at recruitment, and miscarriage rate in early weeks varied widely across studies • Applicability uncertain – all samples drawn from same US health provider, studies published 1970 to 2002.	Miscarriage (Pregnancy loss before 20 weeks gestation)	• Weekly miscarriage rates varied in the early gestational weeks with the highest rate documented at > 20 miscarriages per 1000 women-weeks at each week of gestation prior to week 13. • By week 14, the rate for all studies became relatively comparable and fell below 10 miscarriages per 1000 woman-weeks at risk and fell even lower through week 20. • The cumulative risk of miscarriage for weeks 5 through 20 of gestation ranged from 11 miscarriages per 100 women to 22 miscarriages per 100 women (11%–22%).
Anderson 2012 [81] NZ	• Retrospective population-based cohort study of registry data • Included women	To assess independent pre-eclampsia risk factors in a multiethnic New	Moderate risk of bias • Retrospective analysis of hospital database "albeit with robust data cleaning"	• Pre-eclampsia • Risk factors for pre-eclampsia	*Incidence of pre-eclampsia*: 3.3% Independent risk factors for preeclampsia included

	with singleton pregnancies delivered at 20+ weeks' gestation at National Women's Hospital, Auckland, from 2006-2009 (n=26,254) • Excluded infants with major congenital abnormalities ,and cases with missing data (n=3049)	Zealand population.	• Event rates higher in excluded women (those with missing data)		overweight/obesity, nulliparity, diabetes, chronic hypertension, preexisting medical conditions, Maori ethnicity (50% higher risk), and overweight/obesity. Risk 50% lower in Chinese women. 25.8% of infants of pre-eclamptic women were born <37 weeks 28.5% of infants of pre-eclamptic women were small for gestational age (versus 10.8% for non-pre-eclamptic women) The rate of pre-eclampsia in women excluded for missing data was higher than in the study population (4.5%, n = 130/2904 compared with 3.3%, P < 0.01). These excluded women were at greater risk of pre-eclampsia than the general population, as they included a high proportion of women transferred for tertiary care or unbooked (n = 676, 23%).
Aspholm 1999 [65] Finland	• Retrospective cohort • Included female Finnish flight attendants born	To investigate whether work as a cabin attendant is related to an increased risk for	Moderate risk of bias • Sample representative of (Finnish) flight attendants • Reliability of registry	Miscarriage in first 12 weeks of pregnancy	• The rate of spontaneous abortion among all flight attendants was 12.1% from 1973 to 1994. • The rate of spontaneous

	since 1932 who worked for Finnish commercial airlines • Only included women aged 24-39 at beginning of pregnancy • Excluded women who had induced abortions • n=1751 pregnancies in 967 women) • Employment records linked to data from hospital discharge register on pregnancy outcomes 1973-1994 • Compared flight attendants with and without exposure to work during first trimester of pregnancy	spontaneous abortion.	data uncertain		abortions in the pregnancies exposed to work in first trimester was 11.5% and was 9.2% in the unexposed pregnancies • The results suggest a slightly increased risk of spontaneous abortion among female cabin crew members exposed to work during early pregnancy. • The overall rate of spontaneous abortion among flight attendants is of the same magnitude as that among the general population (when overall rate compared with official population stats)
Axelsen 1995 Denmark [55]*	• Prospective population-based cohort study • All Danish-speaking women	To evaluate characteristics of vaginal during pregnancies that led to childbirth	Low risk of bias • Population sample • Participation rate: 67% • First trimester bleeding assessed retrospectively	Self-reported bleeding in pregnancies ongoing at 28 weeks	• Overall bleeding rate in first and second trimesters: 19% • First trimester bleeds: 16% (vast majority just

	having antenatal care at study centre (n=8714) • Estimated as likely to include >97% local women		at 16 weeks		spotting) • Second trimester bleeds: 5% • Median occurrence of first bleeding = 8 weeks (range 4-20) • Median duration of bleeding: 2 days (range 1-12) *Among women with bleeding*: • 55% had one episode of short duration (i.e. bleeding for 1-3 days, lighter than normal period) • 64% had no pain • 31% of bleeders felt light pain • 5% had moderate or severe pain for more than one day • 19% of women with bleeding admitted to hospital, comprising 14% of women with first-trimester bleeding and 28% of women with second-trimester bleeding • Hospitalisation was usually for <7 days for first trimester bleeding, <13 days for second trimester bleeding.
Bakken 2003	• Retrospective	To investigate the	Moderate risk of bias	Ectopic pregnancy	*Annual incidence of ectopic*

[70] Norway	cohort study • Population data from national registry of hospital discharges and outpatient records • In Norwegian, only abstract available in English. • Full text unavailable– sample size not stated in abstract • Included all Norwegian women aged 15-44	incidence and treatment of ectopic pregnancy in Norway 1990-2001	• Retrospective s=analysis of registry data • Potential for data entry or coding errors • Unclear whether most recent data (from 2001) is applicable, as rates appear to be changing	(Cases defined by ICD-9 and ICD-10 codes)	*pregnancy from 1990 to 2001*: • Incidence rate decreased from 17.3 per 10,000 women-years to 9.5 per 10,000 women –years • Ratio of ectopic pregnancies to live births decreased from 26.4 per 1000 to 14.9 per 1000
Beck 2010 [85]* Systematic review	• Systematic review • Update of previous WHO review. • Search included 10 databases, to 2007 • Included studies reporting maternal mortality and morbidity with clear reporting of methods and sample >200	To analyse preterm birth rates worldwide to assess the incidence of this public health problem, map the regional distribution of preterm births and gain insight into existing assessment strategies	Low risk of bias • 80% of European and North American samples were population-based • Rigorous search • Data available for 91% of births in Oceania (which includes NZ and Australia)	Preterm birth (childbirth occurring at less than 37 preterm birth or 259 days of gestation)	Pre-term birth rates: • Australia/NZ: 6.4% (95% CI 6.3 to 6.6) • Europe: 6.2% (95% CI 5.8 to 6.7) • North America (excluding Mexico): 10.6% • Africa: 11.9% Highest rates were in Africa and North America – attributed respectively to infection and unavailability of drugs, and to advanced maternal age and high twin rate

	• (n= 35 studies in developed countries, including NZ) • Population-based data preferred				
Bennett 2004 [28] * Systematic review	• Systematic review • Five databases searched to 2003 • Included 21 cohort studies, surveys, or database analyses of pregnant women recruited through general obstetric and • prenatal units and to population surveys • Studies required to report gestation use specified tools • Study quality assessed	To estimate the prevalence of depression during pregnancy by trimester, as detected by validated screening instruments (i.e., Beck Depression Inventory, Edinburgh Postnatal Depression Score) and structured interviews, and to compare the rates among instruments.	Low risk of bias • Included population-based studies • Rigorous search • Explored heterogeneity • Review processes conducted in duplicate • Assessed quality of included studies • Overall study quality rated 62% • Sensitivity analysis by quality did not influence results	Antenatal depression (Diagnosed by structured interview or by self-report using Edinburgh Postnatal Depression or Scale, the Beck Depression Inventory)	*Prevalence of depression* Trimester 1: 7.4% (95% CI 2.2 to 12.6) Trimester 2: 12.8% (95% CI 10.7 to 14.8) Trimester 3: 12.0% (95% CI 7.4 to 16.7) High heterogeneity with no clear explanation Unclear whether women experience depression on a continued or intermittent basis throughout pregnancy, or in subsequent pregnancies. Disease severity was not well documented.
Blohm 2008 [60]* Sweden	• Prospective population-based cohort study • Cross-sectional and longitudinal comparisons • Random sample of all women aged 19 living in	To evaluate incidence of miscarriage and assess pregnancy outcomes	Low risk of bias • Population sample • High response rate o 95% in 1981 o 82% in 1991 o 77% in 1998 • 52% of women assessed in 1981 followed up for 20 years	Spontaneous abortion rate as a proportion of all pregnancies intended to be carried to term	• Miscarriage rate = 12% • Clinical miscarriage constituted 12% of all pregnancies • One in four women had experienced a miscarriage by age 39 years. • Three or more miscarriages were

	Gotenborg in 1981 (n=656), 1991 (n=780) and 1982 n=666) • Participants surveyed every 5 years • Data cross-checked with hospital records				reported by 7.4% of women. Miscarriage was not influenced by order of pregnancy. • Relatively low miscarriage rate may relate to high rate of legal abortion in Sweden (20%)
Boufous 2001 [71] Australia	• Retrospective cohort study • Population data from hospital registries (New South Wales Inpatient Statistics collection) • Included 11,531 records of discharges, deaths or transfers for ectopic pregnancy	To provide a more current assessment of the incidence of ectopic pregnancy in Australia by reporting rates for New South Wales between 1990 and 1998	Moderate risk of bias • Retrospective analysis of registry data • Potential for data entry or coding errors • Unclear whether most recent data (from 1998) is applicable, as rates appear to be changing • Potential for double-counting, as all hospital discharges, transfers etc. recorded separately	Ectopic pregnancy (as per UCD-9 coding)	*Annual incidence of ectopic pregnancy from 1990 to 1998*: • Rate per 10,000 women declined from 11.1 (95% CI 10.5 to 11.7) to about 10 per 10,000 women in 1997-8 • Incidence rate decreased from 17.4 per 1000 births (95% CI 16.5 to 18.3) in 1990-91 to 16 per 1000 births (95% CI 15.2 to 16.8) in 1997-8 (as per abstract)
Buss 2006 [61]* Denmark	• Prospective population-based cohort study • Random sample of women in Copenhagen aged 20-29 (n= 11088 women, 2433 pregnancies)	To measure rate of incident spontaneous abortion	Low risk of bias • Population sample • 68% participation • 80% follow up at 2 years	Spontaneous abortion rate as a proportion of all pregnancies intended to be carried to term (Spontaneous pregnancy loss up to 28 weeks)	Based on interview data: • 339 pregnancies (20.9%) of the pregnancies ended as spontaneous abortions • 1,247 pregnancies (76.9%) resulted in childbirth Based on registry data: • On the basis of the Hospital Discharge Register data, the spontaneous abortion rate

	• Follow up by interview • Data linkage to Hospital Discharge register to compare with interview findings • Secondary analysis of data from study of HPV infection and cervical neoplasia				was 16.3%. More than 25% of the spontaneous abortions were only reported by the women, and this could not be explained by erroneously reported induced abortions, and may be early, non-hospitalized abortions.

Chaliha 1999 [13]
UK
	• Prospective cohort study
	• Included consecutive nulliparous women with singleton pregnancies in the third trimester (n=549), at a London teaching hospital
	• Excluded women with current or chronic past urinary tract problems
		To investigate the effect of pregnancy and delivery on continence and to assess whether physical markers of collagen weakness can predict postpartum urinary and fecal incontinence (including incontinence of flatus).	Moderate risk of bias
			• Prospective, consecutive recruitment
			• London teaching hospital sample
			• Participation rate unclear
			• 100% follow-up
			• Characteristics similar to overall nulliparous population delivered over the same period (n=2211)
			• Ethnic distribution similar to rate in the whole institution
			• Generalisability unclear
			• Mean gestation at interview =37 weeks: potential recall bias
				1. Urinary frequency, nocturia, urgency, and stress and urge incontinence.
				
				(self-reported voiding seven or more times per day or more than once every 2 hours; voiding on two or more occasions during the night; loss of urine on physical effort or coughing; loss of urine with a strong desire to void, respectively)
				
				2. Faecal urgency and incontinence.
				
				(inability to defer defecation for longer than 5 minutes, incontinence of flatus and liquid and solid stool and soiling of underwear, respectively)
				
				Severity of incontinence was
					Urinary symptoms during pregnancy:
					• Urinary frequency 81.1%
					• Nocturia 67.6%
					• Urgency 22.9%
					• Stress incontinence 35.7%
					• Urge incontinence 8.0%
					• Urinary incontinence (total) 43.7%
					• Incontinence frequency
					  ○ Once per week: 24.9%
					  ○ No more than daily, but more than once per week: 9.5%
					  ○ Daily leakage or more 9.3%
					• Need for protection: 10.2%
					• 51 women (21.3%) had episodes of incontinence at least once per day. All of these women required sanitary protection and

				assessed by the degree and frequency of incontinence, pad usage, and the effect on daily activities.	seven (13.7%) felt that it restricted their activities. *Bowel symptoms during pregnancy:* • Faecal urgency: 8.7% • Flatus incontinence 6% • Soiling of underwear 0.5% • Liquid stool incontinence 0.9% • Solid stool incontinence 0.2% • Any incontinence 6% • Urgency or incontinence 12.7% Authors' comment: None of these women complained voluntarily or sought medical help, which is not surprising because these symptoms are embarrassing and known to be underreported
Chan 2012 [21] Australia and New Zealand	• Retrospective chart review • Included pregnant women with objectively diagnosed VT at a hospital in Melbourne and one in Auckland (n=60) • Included women identified by ICD	To define the epidemiology, management and adverse effects of pregnancy-related VT in Australia and New Zealand.	Moderate risk of bias • Relied on registry data and medical charts – possibility of missing data • Small sample	Venous thrombosis objectively diagnosed (e.g. by imaging)	*Rate of antenatal VT*: • There were 31 antepartum events, giving an incidence rate of 40 to 59 per 100,000 deliveries. • The rate did not differ across trimesters, with 14, 7 and 10 events occurring in the first second and third trimester respectively. • Three women with first-

	codes on hospital database (Australia), or on a database of consecutive VT referrals (NZ)				trimester VT had a history of unprovoked VT. Management: Women were treated initially with either enoxaparin, dalteparin or intravenous unfractionated heparin at diagnosis. Forty-six (77%) received twice-daily weight-adjusted enoxaparin, whereas only nine (15%) received daily enoxaparin at diagnosis
Chappell 2013 [93]* SCOPE study NZ, Australia, UK, Ireland	• International population-based prospective cohort study • Includes NZ cohort • Included healthy nulliparous women with singleton pregnancy (Exploration dataset = 2129 NZ/Australian women; replication dataset=1067 NZ/Australian women; confirmation dataset= 2432 European women)	To identify factors at 15 and 20 weeks' gestation associated with a subsequent uncomplicated pregnancy.	Low risk of bias • Prospective, population based • 76% of potentially eligible women agreed to participate (3780/4961)	Uncomplicated pregnancy, (normotensive pregnancy delivered at >37 weeks' gestation, resulting in a liveborn baby not small for gestational age, and the absence of any other significant pregnancy complications) Definition of complications: • Gestational hypertension • Pre-eclampsia • Gestational proteinuria • Gestational diabetes • Antepartum haemorrhage, placenta praevia, or placenta accreta • Placental abruption • Chronic hypertension (mild, diagnosed in pregnancy)	*Incidence of uncomplicated normotensive pregnancy:* Overall: 61.3% (3452/5628) Australasia: 63.5% UK and Ireland: 58.6% *Incidence of significant complication of pregnancy or baby small for dates*: 39% *Modifiable risk factors:* Factors that reduced the likelihood of an uncomplicated pregnancy included increased body mass index (relative risk 0.74, 95% confidence intervals 0.65 to 0.84), misuse of drugs in the first trimester (0.90, 0.84 to 0.97), mean diastolic blood pressure (for each 5 mm Hg increase 0.92, 0.91 to 0.94), and mean systolic blood

	• Uncomplicated pregnancy compared with complicated pregnancy, by stepwise logistic regression			• Renal tract complications (e.g. pyelonephritis) • Gastrointestinal tract or hepatic complications • Respiratory complications (e.g. pneumonia) • Other obstetric complications (e.g. obstetric cholestasis) • Other medical complications (e.g. venous thromboembolism) • Maternal death during pregnancy • Small for gestational age infant (<10th customised birthweight centile) • Spontaneous preterm birth • Other fetal problems (including severe neonatal morbidity¶ • Fetal anomalies • Fetal death in utero ≥20/40 or neonatal death • Fetal death in utero <20/40 • Miscarriage or abortion	pressure (for each 5 mm Hg increase 0.95, 0.94 to 0.96). Beneficial factors were pre-pregnancy fruit intake at least three times daily (1.09, 1.01 to 1.18) and being in paid employment (per eight hours' increase 1.02, 1.01 to 1.04).
Chatillon 2010 [89] Systematic review (in French)	• Systematic review • Searched 2 databases • Included prevalence studies, epidemiological studies, clinical	To provide SR of data on prevalence, risk factors and adverse outcomes of antepartum depression	Moderate risk of bias • Full text in French, • Limited search • Methods not described in detail • Characteristics of included studies not reported – unclear	Antepartum depression	*Prevalence of depression in pregnancy:* 5-15% The lower figure relates to major depression, as opposed to any depressive disorder. Pregnancy is not protective against depression.

	trials, case reports, reviews and meta-analyses • Excluded studies solely of manic depression or bipolar disorder		whether studies of prevalence were all population-based		For the mother, adverse outcomes are those of any depression and are potentially serious. Antepartum depression is associated with an increased risk of delivery complications and of postpartum depression
Chen 2012 [82] Australia and New Zealand	• Retrospective cohort study • Included women who gave birth in NSW hospitals <21 weeks' gestation during 2007–8 and had both birth records and hospital admission data (n=185,416) • Antenatal hospital records also linked, to check consistency	To investigate strategies for ascertaining pre-eclampsia, pregnancy hypertension and gestational diabetes mellitus from birth records and / or hospital discharge data	Moderate risk of bias • Relied on registry data • Unclear how many women otherwise eligible were excluded because they did not have records in both datasets • Multiple datasets cross-checked	• Preeclampsia • Gestational hypertension	*Prevalence of preeclampsia using all data:* 3.4% *Prevalence of gestational hypertension using all data:* 9.7%
Christensen 2010 [27] Australia*	• Prospective cohort study • Population-based • Recruited 20-24 year old women from electoral roll in 1999, 2003 and 2007 (n=2404) • Compared	To determine whether pregnancy and motherhood are associated with brief or long-term cognitive deterioration using a representative sample and measuring cognition	Low risk of bias • Women recruited prior to pregnancy and cognition measured • Recruitment rate 58.6% • Follow-up rate 85% fully followed up • Controlled for education, depression, anxiety, and	Cognition: cognitive speed, working memory, immediate and delayed recall (Cognitive speed was measured with the Symbol–Digit Modalities Test (SDMT), which asks the participant to substitute as many digits for symbols as possible in 90	*Differences between women at up to 20 weeks gestation, women at 20-40 weeks' gestation and non-pregnant women:* The only effect found was on the SDMT for women in the later stages of pregnancy. Performance on this test fell from the previous wave by

	cognitive change in pregnant women (from their pre-pregnant state) versus changes over the same time-span in non-pregnant women. • Included only primagravidae	during and before the onset of pregnancy and motherhood.	other predictor variables • Part of larger study: survey did not provide cues that cognition in pregnancy was a focus of attention	seconds. Working memory was assessed with the Digits Backwards subtest of the Wechsler Memory Scale. Immediate and delayed recall were assessed with the first trial of the California Verbal Learning Test)	2.60 points and 2.79 points for women pregnant at waves two and three respectively, whereas non-pregnant women recorded an improvement (2.23 points at wave two) or stability (0.13 point drop at wave three). These contrasts were significant (P=0.046 and P= 0.033). There were no effects for working memory or immediate or delayed recall. There was no difference between the groups for any measure when non-pregnant women were compared with mothers (categorised in two groups: babies under one year and infants over one year) Authors' comment: Except in a brief period in later pregnancy, these findings challenge the common myth that women develop 'placenta brain' … our results challenge the view that mothers are anything other than the intellectual peers of their contemporaries.
Coste 2004 [72] France	• Retrospective cohort study • Population data from registry	To assess recent incidence trends of ectopic pregnancies in France (1992–	Moderate risk of bias • Retrospective analysis of registry data • Potential for data entry	Ectopic pregnancy 1. Overall rate 2. Rate associated with contraceptive failure	*Overall annual incidence of ectopic pregnancy 1992-2002:* Remained stable at 96.4 to 95.3 per 100,000 women

	(Auvergne ectopic pregnancy register) and population register for same geographical area • Included women aged 15-44 • Catchment area pop=750,000	2002).	or coding errors	(woman using a contraceptive method) 3. Rate associated with reproductive failure	When stratified into 'contraceptive failure (EP-CF) reproductive failure'(EP-RF), the EP-CF incidence decreased and the EP-RF incidence increased (from about 56 per 100,000 women in 1992 to about 63 per 100,000 women in 2002)
De Rosnay 2004 [73] UK	• Retrospective cohort study • Population based • Histopathology and birth data from all hospitals in West Hertfordshire, plus national demographic data • Included women aged 15-44 • Catchment area pop=108,000 females		Moderate risk of bias • Retrospective analysis of registry data • Potential for data entry or coding errors	Ectopic pregnancy (histologically proven)	*Incidence of ectopic pregnancy per 1000 deliveries:* 6.5 in 1993, 11 in 1998, 10.7 in 2007 *Incidence of ectopic pregnancy per 10,000 women in 1993-2007:* ranged from 3.5 to 6.3 *Rate in 2007 (most recent*): 5.1 Authors' note: The data from our study do not support our clinical impression that ectopic pregnancy rates in West Hertfordshire have increased over the last 15 years.
Dorheim 2013 Norway [3]*	• Longitudinal survey • Questionnaires at 17 weeks and 32 weeks • Included women at 17 weeks	To describe the prevalence of, reasons given for, and factors associated with, sick leave during pregnancy.	Low risk of bias • Population sample • Response rate to questionnaires: 80.5% (1st), 63% (2nd) • First trimester data	Indications for sick leave during pregnancy Reports incidence of: 1. Fatigue/sleep problems 2. Nausea or vomiting 3. Lower back pain	*Incidence of leave:* No sick leave: 20% Any sick leave: 75% No paid work: 5% Sick leave by trimester: 1st trimester: 29% 2nd trimester: 39%

	gestation scheduled to give birth at the study centre (n=2918) • Measures at 17 weeks included insomnia, depression and pelvic girdle pain, using validated scales • Multiple logistic regression used to identify factors associated with sick leave		retrospective	4. Pelvic girdle pain 5. Anxiety or depression 6. Pregnancy complications No distinction between full time and part time work (to obtain sick leave in Norway, a medical certificate from a doctor is needed,)	3rd trimester: 63% All trimesters: 14% *Indications for sick leave and median duration:* 1. Fatigue or sleep problems: 34.7%, 8 weeks (cited as a factor in 49.3% of leave) 2. Nausea or vomiting: 23.1%, 16 weeks (cited as factor in 32.8% of leave) 3. Lower back pain: 17.7%, 10 weeks (cited as a factor in 25.1% of leave) 4. Pelvic girdle pain: 31.8%, 12 weeks (cited as a factor in 45.3% of leave) 5. Anxiety or depression: 2.1%, 20 weeks * (associated with longest duration of sick leave) (cited as a factor in 2.1% of leave) 6. Pregnancy complications: 9.2%, 13 weeks (cited as a factor in 13.1% of leave)] *May be an underestimate, as significantly lower response rate in women scoring high on depression scale at 17 weeks (70% versus 79%) Being on sick leave in all trimesters was strongly

					associated with hyperemesis, exercising less than weekly, chronic pain before or during pregnancy, and infertility treatment (all P < 0.001), younger maternal age, and conflicts in the work place (both P < 0.01), multiparity, previous depression, insomnia and lower education (all P < 0.05). A majority of women (60.1%) reported having had some adjustment of their work situation because of pregnancy. Most of the women who stayed in work throughout pregnancy without job adjustments responded that their work was not strenuous. (73.9%).
dos Santos Silva 2009 [68] UK	• Case-control study • Questionnaire completed by flight crew members (cases) and air traffic controllers (controls) (n= 641 women, 325 cases and 316 controls) • Conducted 2001-2004	To examine reproductive outcomes among flight crew.	Moderate risk of bias • 53% response rate overall • Response rate in women not reported • Potential for recall bias • Air traffic controllers used as controls: authors comment that "*they are known to have similar socioeconomic*	Miscarriage rate (and other reproductive outcomes not relevant to current review)	No difference in risk of miscarriage between female air crew and female air traffic controllers (Adjusted for maternal age, BMI and smoking history: OR 1.39, 95% CI 0.58 to 3.33)

			characteristics to the flight crew and are subject to the same rigorous medical surveillance while in employment" • Small event rate, wide confidence intervals		
Egger 1998 [74] Sweden	• Retrospective cohort study • Utilised 1985-1995 data from Hospital discharge registry, official population demographic data and Uppsala chlamydia database • Included women aged 15-39 (n=40,106, among whom there were 51630 pregnancies)	To analyse trends in rates of genital chlamydial infection and ectopic pregnancy between 1985 and 1995 in a county in Sweden.	Moderate risk of bias • Retrospective analysis of registry data • Potential for data entry or coding errors	Rate of ectopic pregnancy Rates of chlamydia	*Overall ectopic pregnancy rate 1985-1995*: 1.8% of pregnancies • Rates of ectopic pregnancy strongly linked to prevalence of Chlamydia, especially in younger women • Rates of both ectopic pregnancy and chlamydia dropped during study period
Einarson 2013 [37], SR	• Lit search of 3 databases to Nov 2012 plus reference lists • Included peer-reviewed published studies (n=79) reporting incidence of	To summarize global rates of NVP using meta-analysis.	Moderate risk of bias • No good indication of design or quality of included studies • High heterogeneity: varying definitions of outcomes in primary studies.	Incidence of nausea and vomiting (any type of NVP from retching to severe) Incidence of hyperemesis (as defined by included studies)	*Incidence of nausea and/or vomiting:* • Median 69% (overall range 35% to 91%) had N&V in pregnancy Among women with N&V: • 40% had mild N&V in early pregnancy (range 32-54) • 46% of women had mod

	nausea and vomiting in pregnancy (NVP) (59 studies) or hyperemesis gravidarum (27 studies) • Excluded studies with selected (symptomatic) populations • Study settings: N America 47% Europe 36% Asia 8% Australasia 5% Africa 3% • Also has economic analysis (Piwco 2012)		• Authors appear to have strong drug- company links		N&V in early pregnancy (range 30-57) • 14% had severe N&V in early pregnancy (range 2-30) • 24% had N&V continuing into 3rd semester (range 8-45) • 32.7% had nausea without vomiting • NVP was rated as mild in 40%, moderate in 46% and severe in 14% of cases • Asian countries tended to have higher rates • *Incidence of hyperemesis gravidarum in pregnancy:* Mean 1% (range 0.3% to 3.6%)
Endresen 1995 [48] Norway	• Population-based cross-sectional survey • Women who gave birth in Norway in 1989 (n=5,438 participants) • Data collected in maternity ward post delivery	To analyze the occurrence of pelvic pain (PPP) and lower back pain (LBP) in pregnancy	Moderate risk of bias • Retrospective data collection, post delivery • Response rate 87%	Pelvic and lower back pain (severity: degree of difficulty doing housework(!); incidence: quite often/rarely/never)	• 9% of women had high degree of difficulty with housework due to pelvic pain • 42% of women had some pelvic pain • 21% of women had both pelvic and lower back pain • 51% of women had neither Work which necessitates bending or twisting several times an hour, or frequently lifting the hands to shoulder

					height or above, was significantly associated with LBP. Working with the body bent forward was significantly associated with PPP.
Eskild 2009 [83] Norway	• Population-based retrospective cohort study • Utilised registry data • Included singleton births on Norwegian birth registry 1999-2004 (n=315, 085)	To study the association of preeclampsia with abnormal bleeding in the first trimester and after delivery.	Moderate risk of bias • Retrospective data collection • National population sample	Pre-eclampsia Defined as an increase in blood pressure to at least 140/90 mmHg after the 20th week of pregnancy, alternatively an increase in diastolic blood pressure of at least 15 mmHg, or an increase in systolic blood pressure of at least 30 mmHg compared to the level measured before the 20th week, in addition to presence of proteinuria	*Prevalence of preeclampsia:* 4.2%
Evans 2012 [69] UK	• Retrospective cohort study of three data sources (statutory notifications of illness or injury, reports of in-flight medical incidents, and death certificates) • Included all UK professional pilots holding a class 1 medical certificate and license in 2004 (n=617	To determine the annual incapacitation rate of the UK commercial pilot population	Moderate risk of bias • Registry data – potential for recording error	Prevalence of incapacitations (for the purpose of this review, only pregnancy-related events considered) (Incapacitation = a medical event that resulted, or would have had the propensity to result, in an inability to act as flight crew for at least 10 min)	Prevalence of incapacitations in 2004 in female pilots related to pregnancy: Single event: spontaneous abortion at 22 weeks. This was the only incapacitation of any kind that occurred in a female pilot in 2004. The event did not occur in flight or in the simulator; the pilot was already classified as temporarily unfit.

	female)				
Everett 1997 UK [16]*	• Prospective primary care cohort study • Included consecutive women aged 15-44 with positive pregnancy test (n=657) attending primary care health centre (base pop 21448)	To estimate the miscarriage rate in a cohort of pregnant women (from conception) and the final outcome of pregnancy.	Low risk of bias • Population sample • Complete primary care cohort • 95% follow-up rate (626/657) • Outcomes assessed prospectively from conception • Smallish sample	Vaginal bleeding in first or second trimester, from conception (bleeding not further defined) Miscarriage (as a proportion of all pregnancies)	• Bleeding rate <20 weeks: 21% • Spontaneous miscarriage rate 12% • 57% of women with bleeding miscarried by 20 weeks (67/117) • At least a quarter of all miscarriages were treated at home by general practitioners and would therefore not be recorded in any published statistics • 88% of miscarriages occurred at 6-14 weeks 7% occurred at 16-18 weeks' gestation • For 5%, data were missing on gestational age at miscarriage • About two thirds of women who miscarried were admitted to hospital (46/67); 63% (42/67) had evacuation of the uterus. • The risk of miscarriage was not significantly increased after a miscarriage in the previous pregnancy • At least a quarter of all miscarriages were treated at home by general

					practitioners and would therefore not be recorded in any published statistics • Data do not include reports of unsuspected early pregnancy loss, which vary from 8% to 22% or the further 10% of women who do not contact any health professional after a miscarriage. Authors suggest that true rate may therefore be 18-32% higher with addition of unsuspected early loss and women who do not seek medical help • Termination rate: 11.7%
Facco 2010 [4] USA	• Prospective cohort • Included healthy nulliparous women attending health providers affiliated to a US hospital • Recruited at 6-20 weeks' gestation • 224 women invited, 90% participated (n=202) • Convenience sample	To estimate the prevalence of sleep disturbances among healthy nulliparous women and to quantify changes in sleep during pregnancy	Moderate risk of bias • Convenience sample "socioeconomically diverse" • Prospective	Sleep disturbances in pregnancy (Measured with validated questionnaires at baseline (mean 14 weeks) and third trimester (mean 30 weeks))	*Sleep disturbances at baseline (mean 13.8 weeks' gestation*): • Frequent snoring 11% • Excessive daytime sleepiness: 32.8% • Restless legs syndrome: 17.5% • Insomnia: 37.6% • Short sleep duration: 26.2% • Poor sleep quality: 39% *Sleep disturbances in third trimester (mean 30 weeks):* • Frequent snoring 16.4% • Excessive daytime

	• N=189/202 analysed (94%)				sleepiness: 38.1% • Restless legs syndrome: 31.2% • Insomnia: 54.3%% • Short sleep duration: 39.9% • Poor sleep quality: 53.5%
Fanslow 2008 [64] NZ	• Cross-sectional survey • Face-to-face interview • Random sample of women aged 18-64 living in Auckland or Waikato (selected by door-knocking at 6174 randomly selected addresses)	To describe pregnancy outcomes and explore the relationship between intimate partner violence and miscarriage or termination of pregnancy	Moderate risk of bias • Population sample • Retrospective data collection • Likely under-reporting: Findings are probably conservative estimates	Miscarriage or stillbirth (ever-not further defined)	Ever miscarried: 31% (urban); 35% (rural) Ever had stillbirth: 3%
Gadsby 1993 [6] UK* (in Einarson 2013 SR)	• Prospective study of primary care cohort • Recruited women presenting with pregnancy within 84 days of last menstrual period (LMP)(n=435) • 363 women included in this analysis • Excluded (72 women :with	To describe a more complete clinical picture of nausea and vomiting in pregnancy.	Low risk of bias • Participation rate 83% (411/435) (though not all included in this analysis) • Participants were representative of practice population • Used diary data from day 57 (median) since LMP • 2 weekly follow-up	Incidence of nausea and vomiting (self-assessed nausea or vomiting, not further defined) Characteristics of N&V (severity of symptoms assessed by duration: total number of hours and number of days from onset to resolution)	*Incidence of nausea and or vomiting in pregnancy:* • 80% had nausea or vomiting • 28% had nausea only • 52% had both nausea and vomiting *Characteristics of nausea and/or vomiting in pregnancy:* • Median onset 39 days (5-6 weeks) post LMP (range 8-79 days) • Peak symptoms in 9th

	miscarriage, (n=33), had termination (n=6), twins (n=5), treated for N&V (n=3), stillbirth (n=3) medical complications (n=4) ectopic (n=1), unco-operative (n=9), or lost to follow-up (n=8) • Large urban practice (n=14,500)				week (interquartile range 8-10) • Stopped (often abruptly) at mean 84 days (12 weeks) post LMP (range 44-213 days) • 91% of women had no symptoms after 16 weeks • 35% of women in paid employment (73/206) had time off work due to N&V: mean 62 hours; significantly correlated with severity of symptoms • Mean duration of symptoms: 56 hours (interquartile range 22-139); 41 days (interquartile range 28-56) • Nausea most commonly occurred between 6 am and midday, but could occur at any time of day.
Gartland 2010 [11] Australia	• Cross-sectional analysis of baseline data from a prospective cohort study • Included nulliparous women attending six antenatal care providers in	To investigate women's general health and well-being in early pregnancy and examine the relationship between maternal age and women's physical and mental health.	Moderate risk of bias • Low participation of eligible women: rate not calculable, but estimated at 28-30% • Symptomatic women probably less likely to participate, so findings may be an underestimate	Physical and mental health of women in early pregnancy compared with age standardised population norms General health measured with SF-36 questionnaire Symptoms measured on 4 point scale: never	Pregnant women reported significantly higher scores for general health (i.e. usual non-pregnant health compared to others) but significantly lower scores for previous 4 weeks for nearly all SF-36 domains. Greatest negative physical impact was for physical and vitality scales

	Melbourne. (n=1535 enrolled, 1507 included in analysis) • Mean gestation 15 weeks (range 6-24) • Population norms used for comparison		• Retrospective data collection on first trimester symptoms	rarely occasionally often	*Symptoms experienced "occasionally or often"*: 1. Exhaustion: 87% 2. Morning sickness: 64% 3. Back pain: 46% 4. Constipation 44% 5. Severe headache/migraine: 30% • 68% of women reported three or more health issues • 19% of women reported often experiencing three or more of the listed issues often Women aged 18–24 years reported more symptoms and worse physical and mental health status than older women, after adjustment for sociodemographic issues
Gavin 2005 [90] SR	• Systematic review • 4 databases searched to 2004, plus reference lists • Included cross-sectional, cohort, and case control studies that reported population-based prevalence or incidence of	To review evidence on the prevalence and incidence of perinatal depression and compare these rates with those of depression in women at non-childbearing times.	Moderate risk of bias • Studies quality rated • Study processes conducted in duplicate • Most studies were prospective • Some studies only interviewed pre-screened women • Some studies were not population-based: they were limited to	Major depression (diagnosed by structured clinical interview)	*Prevalence in pregnancy* • Up to 18.4% of pregnant women are depressed during their pregnancy (major or minor depression) • Up to 12.7% have an episode of major depression during pregnancy. • Prevalence in first trimester: 11% • Prevalence in second and

	perinatal depression (n=28) • Studies had to assess women for major depression, by clinical assessment or structured clinical interview.		subgroups of women at higher risk • Addressed heterogeneity by excluding outliers		third trimesters: 8% • All estimates have wide 95% CIs • Authors note that inconsistencies in data suggest a need for cautious interpretation of data I*ncidence* • Up to 14.5% of pregnant women have a new episode of major or minor depression during pregnancy
Gutke 2006 [46] Sweden	• Cross-sectional population-based survey • Analysis of baseline data of cohort study • Included all women who registered at two maternity care units and were at 12-18 weeks' gestation (n=313 analysed out of 322 eligible) • Women completed questionnaire, including details of any previous	To differentiate between pregnancy-related pelvic girdle pain (PPGP) and lumbar pain, and to study the prevalence of each syndrome and its consequences in terms of pain, functioning, and health.	Low risk of bias • 84% participation • Population based • Women questioned on current symptoms so no risk of recall bias	Pelvic girdle and lumbar pain (Pain measured with VAS scale, disability measured with Oswestry Disability Index)	*Prevalence of pain at weeks 12-18:* No lumbopelvic pain (NLPP): 38% Lumbo-pelvic pain: 62% *Among women with lumbo-pelvic pain*: • Pregnancy-related pelvic girdle pain (PPGP): 54% • Lumbar pain: 17% • Combined pain: 29% • No consequences caused by pain: 15% • 6% were moderately disabled by pain (Oswestry Disability Index >40%)

	back pain				
Heit 2005 [77] USA (included in Abdul Sultan 2013 SR)	• Retrospective population-based inception cohort study • Included all births in women diagnosed with VT within a US county 1966-95 (n=50, 080 births) • Excluded cases where pregnancy did not end in delivery or still birth • VT rate during pregnancy or postpartum compared with VT rate in non-pregnant women in the same population	To estimate the relative and absolute risk for deep venous thrombosis and pulmonary embolism during pregnancy and postpartum and to describe trends in incidence	Moderate risk of bias • Registry data • Followed up for 30 years • Sample 98% white	Venous thromboembolism (VT), deep vein thrombosis (DVT), pulmonary embolus (PE) (defined by diagnostic test such as imaging, or signs and symptoms plus prescription of a course of anticoagulants).	*VT rate in pregnancy:* 96 per 100,000 woman-years DVT rate: 85 per 100,000 PE rate: 11 per 100,000 Only 4 events occurred during first trimester. Incidence rates relatively constant for the last 20 weeks of pregnancy Risk of VT five times higher in post-partum period than in pregnancy (rates not reported here) The VT rate was highest in the youngest (15-19 years) and oldest (>35 years) women The VT rate in pregnant and postpartum women was four times higher than in non-pregnant women in the same population Authors comment that incidence of PE is declining – there were no events in last decade of study follow up – maybe due to earlier post op mobilisation
Hemminki 1999 [62] Finland	• Population-based cross-sectional survey	To investigate the occurrence of miscarriages over	Moderate risk of bias • Response rate 73% • Reliance on	Miscarriage per pregnancy and per woman (not further defined)	• 13.2% of pregnancies miscarried • 15% of women had at least

	• Random sample of Finnish women aged 18-44 on population register (n=3000 invited, 2189 participated)	the reproductive life span of women in a population-based study.	retrospective recall		one miscarriage • By the age of 40 to 44 years, 90% of the women had been pregnant, and for only half had all pregnancies ended in a birth. The sequence of a miscarriage or miscarriages coming first and a birth or births coming later was more common than vice versa.
Henry 2007 [87] Systematic review	Systematic review • 3 databases searched, plus references, to May 2007 • Included studies in English, of healthy pregnant women which included a nonpregnant control group (n=14) • Studies required to use an objective index of memory	To address how pregnancy affects memory	Moderate risk of bias • Unclear how primary studies recruited intervention and control groups • Quality of primary studies not reported • Smallish overall sample (14 studies, 412 pregnant women, 386 controls) • Groups appear fairly well matched demographically (age and years of education) • Funnel plot showed no evidence of publication bias • Significant and unexplained statistical heterogeneity for 3/7 outcomes	Measures of memory (Definition of implicit vs explicit memory*: "Whereas tests of explicit memory require deliberate recall of information from a specific learning episode, implicit memory refers to the unconscious accessing of previous experiences, in the absence of intentional recollection*".)	*Performance for pregnant vs non-pregnant women on measures of memory* . (Difference between groups, expressed as an effect size): *Short term memory*: -0.05 (SE 0.08) (3 studies, n=171) *Working memory*: -0.16 (SE 0.08) (4 studies, n=211) p<0.05 *Free recall*: -0.21 (SE 0.09) (8 studies, n=499) p<0.05 *Delayed free recall*: -0.22 (SE0.06) (4 studies, n=228) p<0.05 *Recognition* : 0.09 (SE 0.23) (2 studies, n=81) *Implicit memory*: -0.03 (SE 0.12) (5 studies, n=260) *Subjective memory:* -0.26 (SE 0.07) (7 studies, n=370) p<0.05

					As interpreted by study authors: • "The results indicate that pregnant women are significantly impaired on some, but not all, measures of memory, and, specifically, memory measures that place relatively high demands on executive cognitive control may be selectively disrupted." • "The magnitude of the deficits was invariably small, and thus the observed impairment may be regarded as relatively subtle" • "The same specific deficits associated with pregnancy are also observed postpartum"
Hossain 2007 [56] USA	• Prospective cohort study • Included women enrolling for prenatal care at two US centres. (n=2678) • Participants were	To evaluate association between self-reported early vaginal bleeding and preterm birth	Moderate risk of bias • 77% participation rate • Generalisability to other populations described as limited • Excluded 152 women lost to follow up (6%) • First trimester bleeding	Bleeding in pregnancy ongoing at 20 weeks (self-reported first or second trimester bleeding: Volume, duration and intensity of blood loss not measured)	• First trimester bleed: 23% • Second trimester bleed: 4% • Either trimester bleed: 25%

	well-educated, predominately non-Hispanic white women		apparently assessed retrospectively at up to 20 weeks' gestation		
Hutchison 2012 [5] NZ	• Cross-sectional postal survey • Included randomly selected third-trimester women booked to deliver at large Auckland maternity unit (National Women's Hospital) (650 sent out, 240 included) • Mostly NZ European women, median age 33 years median gestation 36 weeks.	To survey sleep problems in third trimester pregnant women and to compare sleep in the pre-pregnancy period with the third trimester	Moderate risk of bias • 38% participation (244/650) • Population based • Subject to recall bias with respect to pre-pregnancy values • Low inclusion rate of overweight or obese women	Sleep duration and quality; and fatigue during third trimester (Sleep quality measured with Pittsburgh Sleep Quality Index Fatigue measured with Epworth Sleepiness Scale)	*Sleep duration* • Mean number of hours of sleep pre-pregnancy: 8.1hrs (SD 1.1) • Mean hrs of sleep in previous week: 7.5hrs (SD 1.8) • 32% slept less than7 hours per night compared with 9% pre pregnancy • 16% slept less than 6 hours per night, compared with 2% pre-pregnancy *Sleep quality* • Rated as very/fairly good by 82% before pregnancy and by 29% in previous week • Rated as very/fairly bad by 4% before pregnancy and by 38% in previous week *Daytime fatigue:* • reported by 33% of women in pregnancy compared with 4% pre-pregnancy (EES >10) *Daytime sleepiness* • 41% of women reported often napping in daytime (compared to 5% pre-

					pregnancy) Main reason for trouble sleeping in pregnancy was discomfort (in 67% women)
Kaerlev 2004 [30] Denmark	• Register-based study • Included female employees aged 20-45 years from Danish hospital (n=4852) and survey of women in the cohort who had been pregnant during their employment (n=773)	To describe risk indicators of long-term sick leave during pregnancy among hospital employees	Moderate risk of bias • 85% response rate among pregnant women • Generalizability to other populations unclear • Registry data: potential for recording errors	Risk factors for long term sick leave among pregnant women	• 31% of women were on sick leave for at least 10% of their scheduled work time during their latest pregnancy • 22% absent at least 20% of the time. • Average sickness absence 6.1 days per month, = versus non-pregnant women 0.95 days per month. • Sick leave was more frequent in late than in early gestation. • Risk factors for long term sick leave were: part-time work, previous sickness absence not related to pregnancy, previous chronic back pain, much walking or standing, long working days, high work level, little practical support from supervisors and colleagues, low job control, much lifting, and night or shift work. • Sick leave was unrelated to

					family size, support from the family or number of working years.
Kane 2013 [78] UK	• Population-based cohort study using registry data (Scottish Morbidity Record) • Included all women discharged from Scottish maternity hospitals 1980-2005 • 1,475,301 maternity discharges analysed, comprising 95% of data (one health board excluded due to discrepancies in data)	To chart the incidence of pregnancy-related VT over the period 1980-2005 in Scotland, and discuss the results in relation to potential risk factors.	Moderate risk of bias • Population-based • Use of registry data, with potential for recording errors	Venous thrombosis (VT) (Defined using ICD-10 codes for deep vein thrombosis (DVT) and pulmonary thromboembolism (PTE))	*Antenatal VT* Overall incidence of 13.6 per 10,000 deliveries (95% CI 13-14.2) Antenatal DVTs rose over the period from 8.8 per 10,000 deliveries in 1980-85 to 12.2 in 2001-5 *PTE* Overall incidence of 2 per 10,000 deliveries (unclear what proportion were antenatal) (95% CI 1.7-2.2) PTE incidence rose over the period from 1.5 per 10,000 deliveries in 1986-90 to 3 in 2001-5 VTE risk factors included maternal age >35 years. Antenatal DVT risk highest in most deprived areas
Kovacs 2012 [47] Spain	• Population-based cross-sectional survey • Pregnancy >28 weeks • All women in participating centres (n=1158)	To determine the prevalence of low back pain (LBP), leg pain (LP), and pelvic girdle pain (PGP) in pregnant Spanish women and to identify the factors associated with a	Moderate risk of bias • 99% participation rate of eligible women • Retrospective data collection, though period of recall only 4 weeks	Lower back pain: pain between costal margins and inferior gluteal folds Pelvic girdle pain: pain in symphysis and/or between posterior iliac crest and gluteal fold, which may spread to posterolateral thigh.	Prevalence of back, leg and pelvic pain during past 4 weeks, at median of 35 weeks' gestation (range 31-38): • LBP: 71% • LP: 46% • PGP: 65%

		higher risk			Main risk factors: • For LBP: any history of LBP. • For LP: lower academic level, younger age, depression, a lower number of hours of sleep per day, and a higher BMI • For PGP: higher score for depression, higher BMI, and more advanced stage of pregnancy "Currently working " was not associated with higher risk of LBP
Kristensen [31] 2007 Norway	• Population-based cohort study • Invited to participate in connection with routine ultrasound offered to all pregnant women in Norway at 17-18 weeks' gestation • Current study includes employed women in 1999-2005 cohort (n=28611) • Women completed questionnaires, at	The main objective was to examine whether job adjustment was associated with reduced absence	Moderate risk of bias • Population based • Overall response rate around 44% • Self-reported data	Absence from work Job adjustment (Job adjustment measured with the following questions: have your working conditions changed since you became pregnant, making it easier for you?'' and: ''if no, why have your working conditions remained unchanged?'', with the options ''not necessary'' and four alternatives. Responses were collapsed into three categories: ''not needed'', ''needed and obtained'' and ''needed, not obtained''.)	*Sick leave* 50.7% of participants took one or more days of six leave in weeks 13-28 (=14.9% of all person-days) 36.2% had more than 15 days of absence *Relationship between absence from work and job adjustment* Absence was strongly dependent on the pregnant woman's own perception of the need for job adjustment. Among those who needed job adjustment, absence levels were lower when this was obtained.

	approx weeks 17 and 30				
Kristiansson 1996 [9] Sweden*	• Prospective population-base cohort study • Included consecutive women attending antenatal clinics in two districts in Sweden (n=200 included, out of 222 eligible) • Repeated assessment of pain (questionnaires and examinations) throughout pregnancy	To describe the natural history of back pain occurring during pregnancy and immediately after delivery	Low risk of bias • Population based, prospective • 88.1% participation rate	Back pain (sacral, lumbosacral, lumbar and cervico-thoracic) Disability (outcomes measured with VAS scales)	*Incidence of back pain:* *Before week 12:* • Pain with onset before pregnancy: 21.5% • New onset pain: 19% • The mean score for the worst pain in the previous week was rated at 4/10 on a VAS scale *Week 36:* • Pain with onset before pregnancy: 16% • New onset pain: 47.3% • The mean score for the worst pain in the previous week was rated at 6.5/10 on a VAS scale There was a steady increase in pain up to week 18 Incidence increased sharply to week 22 then leveled off. Prevalence of new or ongoing pain at 24 weeks was 63.3% New-onset pain was usually sacral Pain usually short-term: long-term pain was rare. Pain intensity increased over

					pregnancy. Quartile with worst pain reported difficulty with normal activities, such as walking up or down stairs, leaning over a washstand, running, heavy physical work or lifting.
Kvisvik 2011 [52] Norway	• Prospective population-based study • Included all pregnant women in catchment area of two hospitals in Norway (n=3125 invited, 2126 participated, 1618 completed 2 questionnaires) • Excluded women with high-risk pregnancies or known complications • Questionnaires administered at booking, in late pregnancy and postnatally	To describe prospectively and in detail the overall course of all headaches collectively and also of migraine during pregnancy and the puerperium.	Moderate risk of bias • Population sample • Prospective follow-up • Participation rate 68% of those eligible • 52% of those eligible completed questionnaires 1 and 2	Prevalence of headaches and migraine during pregnancy (using International Headache Society criteria) Women with migraine kept headache diary.	*New onset of headache in pregnancy versus freedom from pre-pregnancy headache:* More women changed from having any headache before pregnancy to not having any headache during pregnancy (248/1,618=15%) than the other way around (101/1,618=6%) ($p< 0.001$). *Change in frequency of all headaches combined during pregnancy and puerperium:* There was no significant difference ($p=0.12$) in the frequency of all headaches combined during pregnancy (n=1,122 reported headache) compared to before pregnancy (n=1,269 reported headache) There was a gradual decrease during pregnancy in the frequency of headaches and migraine in general

					Characteristics of headaches during pregnancy and puerperium among migraineurs: The intensity and duration of headaches were significantly reduced in pregnancy among migraineurs
LaCroix 2000 Canada [39]* (in Einarson 2013 SR)	• Prospective study • Included all women seeking prenatal care at large teaching hospital • Enrolled at first prenatal visit • Excluded women with hyperemesis at presentation or who miscarried	To provide a detailed description of patterns of nausea and vomiting of pregnancy	Low risk of bias • Participation rate 195/200 (98%) • Completion rate 180/195 (92%) • Data collection started at mean of 8.2 weeks' gestation • 98% of participants were white: generalizability to other populations unknown	Incidence of nausea and vomiting Characteristics of N&V: Rated severity using descriptors from McGill Nausea Questionnaire (sets of words ranked in order of severity). Overall rating from *no nausea* to *excruciating*	*Incidence of nausea and vomiting in pregnancy:* 74% of women (66-80%) had nausea *Characteristics of nausea and vomiting in pregnancy:* Mean time of onset: 5.7 weeks Mean duration of symptoms 35 days (range 1-114) 38% of women had vomiting Vomiting occurred on average 10 times and over a mean of 5.6 days (range 1-49 days) Peak severity of nausea: 11th and 13th weeks Nausea ratings rarely extreme (i.e. horrible or excruciating). Ratings for severity of nausea and vomiting during pregnancy were comparable in severity to those reported in a study of moderately nausea-producing cancer chemotherapy

					50% of cases resolved by 14 weeks 90% of cases resolved by 22 weeks In women with 2nd and 3rd trimester nausea, the intensity remained constant For most women nausea lasted throughout the day
Lok 2010 [67] Hong Kong	• Prospective cohort study (n=190) • Conducted in tertiary referral hospital in Hong Kong • Included women who had had miscarriage (spontaneous pregnancy loss at up to 24 weeks) managed in study hospital • Control group were women seeking contraception advice in same age range, without pregnancy in past year (n=150)	To investigate psychological morbidity after miscarriage in a prospective manner over a 1-year longitudinal course.	Moderate risk of bias • Participation rate among miscarrying women: 75% (280/375) • 32% of sample did not complete measures at all time points. • Possible that study interview unintentionally had a therapeutic effect – though it was brief and focused on data collection • Characteristics of non-participators and non-completers did not appear to differ in any way that would obviously cause high risk of bias • Unclear whether sample was generalizable to NZ	• Psychological distress • Depressive symptomatology (used validated self-report tools: General Health Questionnaire (GHQ-12, cut-off score 4) and Beck Depression Inventory (BDI, cut off score 12). Measured at baseline, 3, 6 and 12 months post miscarriage	Among miscarrying women : • 55% scored high on GHQ-12 immediately after miscarriage • 25% scored high on GHQ-12 at 6 months • 11% scored high on GHQ-12 at one year • 27% scored high on BDI immediately after miscarriage • 19% scored high on BDI at 3 months • 9% scored high at one year GHQ-12 scores significantly higher in miscarrying women (compared to controls) at all time points, though differences lessened over time

	• Excluded women with history of psychiatric illness, or if follow-up likely to be problematic .e.g. due to immigration factors • Ethnicity of participants not reported		population		BDI scores significantly higher in miscarrying women at 3 and 6 months (with differences lessening over time) ,but comparable at one year
Machonochie 2004 [63] UK	• Population-based cross-sectional survey • Random sample from UK electoral roll (n>60,000) • Targeted sample of women aged up to 55 who had ever been pregnant or attempted to achieve pregnancy (n=10, 828) • Selected women likely to be aged 55 or under, based on name (e.g. Elsie versus Kylie!) • Included in analysis 13,035 women, 30,661	To identify miscarriage rates among UK women who had ever been pregnant or ever attempted to achieve a pregnancy	Moderate risk of bias • Response rate 49% to initial questionnaire • 77% response from targeted sample (e.g. under 55 yrs) • Retrospective data collection • Risk of recall bias	Miscarriage: Spontaneous pregnancy loss <24 weeks gestation	Miscarriage rate: 11.5% of women, 12.7% of reported pregnancies.

	pregnancies				
Magann 2005 [53] Systematic review	• Systematic review • MEDLINE search to Nov 2004 • Includes studies of women with bleeding from unknown cause in second half of pregnancy (n=10 studies) • Excluded studies not reporting AEs	To determine the prevalence, complications and optimal management of pregnancies complicated by bleeding of unknown origin in the second half of pregnancy	Moderate risk of bias • Only one database searched • Only 4/10 studies gave sufficient information to permit calculation of second trimester bleeding, and time-frames of these studies varied • Characteristics of included studies not reported in detail: unclear which were population-based • Heterogeneity not formally quantified or addressed and no confidence intervals reported (however rates do not appear to vary widely)	Vaginal bleeding of unknown origin	*Incidence of bleeding of unknown origin in second half of pregnancy:* 2% Preterm delivery, stillbirth and fetal anomalies appeared to be increased in pregnancies with bleeding of unknown origin
Magann 2010 [36] Review	• Literature review • Searched 6 databases plus references • Included 9 studies which evaluated air travel and pregnancy outcomes	To review flight regulations and gestational complications associated with air travel in pregnant passengers, flight attendants, and aviators	High risk of bias • No clear inclusion criteria • Characteristics of included studies not reported in detail: unclear which were population-based • Heterogeneity in pooled data not assessed or reported – unclear	Outcomes include: spontaneous abortion thromboembolism pregnancy outcomes	*Outcomes in flight attendants vs controls:* *Spontaneous abortion or intrauterine fetal demise:* 393/2841 vs 168/1094, OR 0.88 95% CI 0.72 to 1.07 (3 studies pooled) *Preterm birth:* 67/514 vs 26/265, OR 1.37 95% CI 0.85 to 2.22 (3 studies pooled)

			whether pooling appropriate • Data applies to female flight attendants not pilots – applicability uncertain		*Thromboembolism:* Authors state "Even although both air travel and pregnancy each increase the risk for thromboembolism, the actual effect of air travel on the risk of thromboembolism in pregnancy is uncertain". *Authors conclude:* "The paucity of data on air travel and pregnancy outcomes makes it impossible to provide evidence-based answers from the limited information available. The studies that would either validate or refute the safety of air travel in pregnant passengers, flight attendants and aviators is (sic) inadequate and will remain so until additional studies have been undertaken".
Malmqvist 2012 [49] Norway	• X-sectional Survey • Population based • Included Norwegian-speaking women with singleton pregnancy of at	To investigate the cumulative prevalence of low back pain (LBP), pelvic pain (PP), and lumbopelvic pain during pregnancy,	Moderate risk of bias • Retrospective data collection (post delivery) • 58% participation of eligible women • Sample appeared	Pain and disability associated with pelvic and lower back pain in current and previous pregnancies (Pain measured as mild/mod/severe. Function measured with Oswestry	*Incidence of moderate or severe pain:* *At 5 months*: • 3.1% had lumbar pain • 13.2% had pelvic pain • 6.8% had combined pain A*t 9 months*:

	least 36 wks gestation presenting at a Norwegian hospital in a 4 month period (n=994 eligible, 569 completed questionnaire)	including features possibly associated with development of pregnancy-related PP, in an unselected population of women	representative of population	Disability Index (ODI) and by need for sick leave.)	• 9.8% had lumbar pain • 18.8% had pelvic pain • 16.7% had combined pain Overall, 57.4% had mod or severe lumbar and/or pelvic pain during pregnancy *Sick leave* Women with mod and severe LBPP had more sick leave during pregnancy (9-15 weeks) than women with less or no pain (5-6 weeks) *Received treatment for pelvic or lumbar pelvic pain during pregnancy* : 27.4% *Mean ODI score:* In women with no or mild pain: 4-14, indicating minimal disability In women with moderate or severe pain: 22-37, indicating moderate disability – this score on ODI suggests possible difficulty with sitting, lifting and standing, may be disabled from work.
McCarthy 2011[7] International, including NZ	• Prospective international cohort study • Included healthy	To investigate the association between HG and cognitive, behavioural and	Low risk of bias • Population sample • Prospective	Hyperemesis (defined as repeated vomiting in early pregnancy not due to other causes requiring any of	Incidence of hyperemesis: 4.8% Severe hyperemesis requiring hospitalisation: 2.1%

(SCOPE)*	nulliparous women with singleton pregnancy • Analysis of complete international cohort (n=3423) • Women with hyperemesis gravidarum (HG) compared with those without. • Outcomes measured at 15 and 20 weeks' gestation	emotional well-being and determine whether the severity of HG influenced any relationship observed. The study also aimed to clarify if HG is associated with adverse pregnancy outcomes.	• 99% complete follow-up • Potential recall bias for vomiting prior to 15 weeks	the following: inpatient admission, day stay with IV fluids, nasogastric feeding (at home or in hospital) or vomiting associated with loss of >5% of booking weight. Women with hospitalized HG were considered as having severe HG)	45% ceased vomiting before15 weeks 33% still vomiting at 15 weeks but had none thereafter 19% had ongoing vomiting from 15 to 20 weeks
McCormack 2008 [58] Australia	• Retrospective registry study: review of records on hospital database • Included women with singleton pregnancies delivering at the sole tertiary obstetric hospital in Western Australia 1998-2004 (n=28,014) • Excluded women with bleeding due to identifiable	To evaluate factor(s) associated with unexplained antepartum bleeding of unknown origin (ABUO) after 24 weeks of pregnancy and correlate unexplained haemorrhage with maternal and perinatal outcomes.	Moderate risk of bias • Retrospective data collection • Some women may have had multiple pregnancies included	Antepartum bleeding of unknown origin (Bleeding other than just spotting after 20 weeks of gestation, whose source could not be identified)	*Incidence of bleeding after 24 weeks' gestation*: 5% (1431/26583) ABUO was a simultaneously significant risk factor for term labour inductions, preterm delivery, NICU admission, hyperbilirubinaemia and reduced birthweight.

	causes (n=638)				
McCowan 2009 [25], Dekker 2012 International, including NZ (SCOPE)*	• Prospective international cohort study • Included healthy nulliparous women with singleton pregnancy 2004-8 • Analysis of Australian and New-Zealand cohorts (McCowan 2009; n=2535) • Analysis of complete international cohort (Dekker 2012; n=3234) • Participants interviewed at 14-16 and 19-21 weeks, and had US scan at 19-21 weeks.	To compare pregnancy outcomes between women who stopped smoking in early pregnancy and those who either did not smoke in pregnancy or continued to smoke (McCowan 2009) To identify risk factors for spontaneous preterm birth (<37 weeks gestation (Dekker 2012)	Low risk of bias • Population sample – • Prospective study, • 99% complete follow-up Findings may not be applicable to high-risk nulliparous women or to populations of mixed parity.	Spontaneous preterm birth (defined as spontaneous preterm labour or preterm premature rupture of the membranes resulting in preterm birth at less than 37 weeks' gestation.)	Spontaneous preterm birth rate in NZ/Oz cohort: In stopped smokers and non-smokers: 4% In smokers: 10% Spontaneous preterm birth rate in complete international cohort: 4.9%
Ministry of Health (MOH) 2010 [35] NZ	• Sourced from National Minimum Dataset (NMDS): coded clinical data supplied to MOH by public health providers	To present information on women delivering in hospital, their newborns and the maternity services provided to them by	Moderate risk of bias • Registry data: risk of coding error unknown • Findings only apply to women referred to hospital: does not include miscarriages	1. Miscarriage (Pregnancies that end spontaneously before 20 weeks' gestation. Excludes induced terminations of pregnancy)	*Rates of hospital miscarriage in 2006:* Women aged under 20: 8% Women aged 20-40: approx 3-8% Women aged 40 or more: 15.3%

		New Zealand hospitals in 2006	occurring at home or elsewhere	2. Other indications for antenatal hospital admission and for same-day antenatal admission	Pacific women: 6.6% Maori women: 6% Asian women: 5.3% European women: 5.1% *Most common indications for hospital admission (as a proportion of total antenatal admissions) and length of stay in 2006:* Other maternal diseases complicating pregnancy: 25%; 2.1 days Excessive vomiting: 17.3%; 2.4 days Antepartum haemorrhage not otherwise classified: 9.4%; 1.9 days Genitourinary infection: 7.4%; 2 days Gestational hypertension without proteinuria: 6.4%; 2.1 days Gestational hypertension with proteinuria: 4.3%; 2.6 days Haemorrhage in early pregnancy: 3.3%; 1.3 days *Selected indications for same-day admission (as a proportion of total same-day antenatal admissions) in 2006*: Other maternal diseases complicating pregnancy: 28% Excessive vomiting: 6.5% Antepartum haemorrhage not

					otherwise classified: 5.7% Genitourinary infection: 4.2% Gestational hypertension without proteinuria: 5.1% Gestational hypertension with proteinuria: 2.5% Haemorrhage in early pregnancy: 6.9%
Ministry of Health (MOH) 2010a [34] NZ	• Sourced from National Minimum Dataset (NMDS): coded clinical data supplied to MOH by public health providers	To present information on women delivering in hospital, their newborns and the maternity services provided to them by New Zealand hospitals in 2007	Moderate risk of bias • Registry data: risk of coding error unknown • Findings only apply to women referred to hospital: does not include miscarriages occurring at home or elsewhere	Miscarriage (Pregnancies that end spontaneously before 20 weeks' gestation. Excludes induced terminations of pregnancy) Indications for antenatal hospital admission and for same-day antenatal admission	*Rates of hospital miscarriage in 2007*: Women aged under 20: 5.9% Women aged 20-40: approx 3-8% Women aged 40 or more: 11.3% Pacific women: 5.8% Maori women: 5.5% Asian women: 4.9% European women: 4.8% *Most common indications for hospital admission (as a proportion of total antenatal admissions) and length of stay in 2007:* Other maternal diseases complicating pregnancy: 24%; 2.1 days Excessive vomiting: 17.1%; 2.2 days Antepartum haemorrhage not otherwise classified: 10%; 1.8 days Genitourinary infection: 8.1%; 2 days

					Gestational hypertension without proteinuria: 5.9%; 1.9 days Gestational hypertension with proteinuria: 4.4%; 2.8 days Haemorrhage in early pregnancy: 2.9%; 1.4 days *Selected indications for same-day admission (as a proportion of total same-day antenatal admissions) in 2006*: Other maternal diseases complicating pregnancy: 27% Excessive vomiting: 6.7% Antepartum haemorrhage not otherwise classified: 4.9% Genitourinary infection: 3.8% Gestational hypertension without proteinuria: 4.7% Gestational hypertension with proteinuria: 2.8% Haemorrhage in early pregnancy: 6.7%
Ministry of Health (MOH) 2012 [86]	• Report of registry data • Uses hospital data from the National Minimum Dataset (NMDS) and information on community events contained in lead maternity carer (LMC) claim	To summarise the maternal and newborn information stored in the National Maternity Collection	Moderate risk of bias • Registry data: risk of coding error unknown	Preterm birth (babies born at under 37 completed weeks' of gestation).	• In 2010, 7.4% of liveborn babies were born pre-term • Māori babies were the most likely to be born pre-term (8.1%) and Pacific and Asian babies were the least likely to be born pre-term (6.5%). • The highest rate of pre-

	forms. • Includes data on completed pregnancies in 2010 (n=64,433 women, 64,936 live babies)				term births was seen in babies from a quintile 4 or quintile 5 area (7.8% and 7.5%, respectively). Babies from quintile 1 areas were the least likely to be born pre-term (7.0%).
Mogren 2005 [51] Sweden	• Population-based cross sectional survey • Included all women giving birth (i.e. live birth or still birth at >23 weeks' gestation) at two Swedish hospitals (n=1114 eligible) • Data collected post delivery	To investigate prevalence and risk factors for low back pain and pelvic pain (LBPP) during pregnancy.	Moderate risk of bias • Retrospective data collection • Questionnaire validated • Participation rate 83% (891/1114)	LBPP was defined as "recurrent or continuous pain for more than 1 week from the lumbar spine or pelvis" during actual pregnancy, defined with the help of patient-drawn markings of localisation of pain on a schematic drawing in the questionnaire	*Prevalence of antenatal LBPP*: 72% *Among women with LBPP:* • 60% had both back and pelvic pain • 12% had anterior pelvic pain only • 28% had posterior pain only *Characteristics of LBPP:* • Mean gestational age at start of LBPP was 22 weeks (range 1-39) • On a VAS 1-10 scale, mean value of highest pain score of LBPP during pregnancy: 5.8 (SD 2.2) • Mean value of highest pain score during delivery: 5.4 (SD 3.8) • Body mass index is a significant determinant for LBPP during pregnancy.
Mota 2008 [29] USA	• Cross-sectional survey • Utilises population data	To examine health-related quality of life (HRQOL) and the prevalence of mental	Moderate risk of bias • Retrospective analysis of survey data • Potential coding errors	Past-year mood, anxiety and substance use disorders (assessed by the Alcohol Use	*Prevalence of disorders in currently pregnant vs nonpregnant women [excluding postpartum women];*

	from National Epidemiologic survey 2001-2 • Included women aged 18-44, either currently pregnant (n=451) or not (n=10,544) • Data collected by face-to-face interview	disorders in pregnant and past-year pregnant women compared to non-pregnant women	• Population based	Disorder and Associated Disabilities Interview Schedule-DSM-IV version)	• Pregnant women were less likely than non-pregnant women to have depression (7.3% vs 11.4%), alcohol abuse or dependence (2.8% vs 8.3%), or any mental disorder (19.2% vs 29.3%) • Multiple linear regression analyses demonstrated that pregnant and non-pregnant women had higher mental component scores than past-year pregnant women. • There was no difference between pregnant and non-pregnant women in the prevalence of dysthymia, manic episodes, phobias, or drug abuse/dependence
North 2011 [94] International, including NZ (SCOPE)*	• Prospective international cohort study • Included a New-Zealand cohort • Included healthy nulliparous women with singleton pregnancy (n=3572) at five centres 2004-8	To develop a predictive model for preeclampsia based on clinical risk factors for nulliparous women and to identify a subgroup at increased risk for whom specialist referral might be indicated	Low risk of bias • Prospective • Large multicentre sample • 76% participation rate (3780/4961) • Data on pregnancy outcome available for 99% of sample	Any pre-eclampsia Pre-term pre-eclampsia (Pre-eclampsia was defined as systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg, or both, on at least two occasions four hours apart after 20 weeks' gestation with either proteinuria or any multisystem complication of pre-eclampsia (e.g. acute renal insufficiency).	• *Prevalence of preterm pre-eclampsia in healthy nulliparous women:* 1.3% • *Prevalence of any preeclampsia: 5.3%* • *Pre-eclampsia developed at a mean of 36.9 (SD 3.3) weeks' gestation* Clinical risk factors at 14-16 weeks' gestation were age, mean arterial blood pressure,

	• Participants interviewed at 14-16 and 19-21 weeks, and had US scan at 19-21 weeks.			Pre-term pre-eclampsia was defined as pre-eclampsia resulting in delivery before 37 weeks' gestation)	body mass index (BMI), family history of pre-eclampsia, family history of coronary heart disease, maternal birth weight, and vaginal bleeding for at least five days. Factors associated with reduced risk were a previous single miscarriage with the same partner, taking at least 12 months to conceive, high intake of fruit, cigarette smoking, and alcohol use in the first trimester.
Parazzini 2013 [75] Italy	• Retrospective cohort study • Utilised 1996-2010 data from Lombardy Region Database • Included women aged 15-50 (n=1,777,011 pregnancies and 17,028 cases of ectopic pregnancy) • Abstract only available (full text currently embargoed)	To supply data on time trends for the incidence of ectopic pregnancies in Southern European populations	Moderate risk of bias • Retrospective analysis of registry data • Potential for data entry or coding errors	Ectopic pregnancy	*Age-adjusted ectopic pregnancy rates:* • 1996: 4.4 per 10,000 women • 2010: 5.8 per 10,000 women *Rate per pregnancy:* • 1996: 9.4 per 1000 pregnancies • 2010: 9.8 per 1000 pregnancies The authors comment that rates of ectopic pregnancy seem to be increasing
Persson 2006; Daniellson 2012 [32, 33]	• Swedish National Public Health Reports	To monitor and analyse the development of health in various	Moderate risk of bias • Retrospective data • Potential for data coding	Pregnancy morbidity (and other health indicators)	• A third of women are treated in hospital at some point during pregnancy

Sweden	• Based on Swedish National Health Registers	groups of the population. By doing this the public health reports form a basis for evaluation and improvements of health policies	errors		• Absence from work due to illness is very common among women in the final stages of pregnancy. • Backaches are the most frequent cause • Other health problems such as difficulty sleeping, urinary incontinence and gastrointestinal complaints are also common..
Piccardi 2013 Italy [88]	• Case report • Case is a female air force pilot who underwent a 2-D Mental Rotation Task in the second trimester of pregnancy, post-partum and one year after delivery • Outcomes compared with two non-pregnant groups of women, with and without flying experience	To investigate the ability of a female ItAF pilot to mentally rotate a stimulus (in terms of both accuracy and speed) during pregnancy and 1 yr after delivery.	Very high risk of bias • Single case • No pre-pregnancy measures for comparison: • Conclusions are based on assumption: " *We cannot infer how the subject would have performed on the MRT before pregnancy, but we can assume that her performance would have been similar to that of other female pilots"* • Poor reporting - authors emphasize differences between groups even where they were not statistically significant	Mental rotation ability (Each subject had to indicate which figure out of five alternatives corresponded with the target figure rotated up to 180°. The task included 20 subsequent stimuli and the score ranged from 0 (no correct answer) to 20 (all correct))	• The subject performed the task within one SD below the mean for female pilots, without significant difference between pregnancy, post-partum or one year after delivery (though her performance was improved at one year post-delivery) • Performance during pregnancy was significantly better than non-pilots but worse than pilots. At one year post delivery, performance was not significantly different from the pilot group. • During pregnancy, the subject's response time was significantly slower than with pilots and significantly faster than non-pilots.

					• One year after delivery, her performance was still better than the non-pilot group and was almost the same as the pilot group. *Authors comment:* In this case, visuospatial ability requiring effortful processing underwent variations during pregnancy and postpartum. Further studies are needed in order to confirm our observations in a wider population.
Ray 1999 [76] Canada	• Systematic review • Includes 12 studies of DVT in pregnancy or puerperium • Searched MEDLINE 1966-1998; also searched reference lists	To answer two questions about DVT during pregnancy and the puerperium: 1) In which leg is there a higher incidence of disease? 2) When is DVT likely to present during pregnancy or the puerperium?	Moderate risk of bias • Only searched one database • Unclear whether age of studies (1969-97) may reduce applicability • 80% of DVTs diagnosed using "objective testing" (e.g. imaging). Sensitivity analysis conducted excluding studies only using clinical diagnosis	Characteristics of vein thrombosis (DVT) in pregnancy: which leg and when it occurred (As diagnosed in primary studies)	*Of DVTs occurring in pregnancy:* • 22% occurred in the first trimester (95% CI 17.4 to 27.3) • 34% occurred in the second trimester (95% CI 28.1 to 39.8) • 48% occurred in the third trimester (95% CI 39.2 to 56.2) Findings were similar when studies using clinical examination alone were excluded DVT most commonly occurred in the left leg. Risk in the puerperium was higher than antepartum

Robinson 2006 [50] Norway	• Population-based survey, • Included all women in 2 municipalities in Norway who responded to postal questionnaire and who had a prior delivery (n=1187)	To estimate the prevalence of PGP according to pain location. An additional aim was to study the impact on function, the use of crutches, and waking up at night, according to location of pain	Moderate risk of bias • Approx 73% response rate to initial questionnaire • Retrospective data collection • Possible recall bias due to long time since delivery	Pelvic girdle pain: prevalence and functional effects	*Prevalence of pelvic girdle pain (PGP) in last pregnancy:* 46% *Use of crutches to manage PGP*: 7% of pregnant women; 16% of women with PGP *Waking up at night with PGP*: 15% of all pregnant women; 33% of women with PGP *Sick leave:* 67% of all postpartum women sick-listed during pregnancy, of these 41% were sick-listed due to PGP *Authors' note:* The observation that 7% of all pregnant women used crutches because of self-reported PGP demonstrates that this condition causes severe functional disability for many pregnant women. In this group, false classification of PGP is unlikely since women with gynecological, urological, and lumbar pain are not likely to use crutches
Russell 2013 [91] Systematic review	• Systematic review • Searched 4 databases and references to August 2012 • Included English-	To provide an estimate of OCD prevalence in pregnant and postpartum women	Moderate risk of bias • Searched 4 databases • Review processes conducted in duplicate • Primary studies rated for quality	Prevalence of OCD (diagnosed using structured clinical interview)	*Prevalence of OCD in pregnancy:* 1.64% (95% CI 1.23% to 2.20%): High heterogeneity (I^2 81%)

	language studies reporting incidence of obsessive compulsive disorder (OCD) in pregnancy (n=12 studies) • Also included control led studies (matched for region and time-frame) estimating 12-month prevalence in general female population		• Studies required to use structured diagnostic interviews • Unclear whether primary studies population-based • Huge variation in OCD rates across studies • Authors excluded study with highest prevalence, as an outlier – no rationale given		Comparisons with studies with non-pregnant controls suggested an increase in pregnancy relative to general population: RR 1.45 (95% CI 1.07 to 1.96)
Sangsawang 2013 [12] Systematic review	• Systematic review • Includes 18 prevalence studies (and 8 treatment studies) • Searched Pubmed to 2012	To provide details of the pathophysiology leading to SUI in pregnant women and SUI prevalence and treatment during pregnancy	Moderate risk of bias • Only searched one database • Inclusion criteria for prevalence studies unclear • Differences in study method and design, definitions of UI, evaluation questionnaire, and stage of pregnancy	Prevalence of urinary incontinence in pregnancy	• Prevalence of types of urinary incontinence in pregnancy: • Stress urinary incontinence: mean 41% (range 18.6–60 %) • Urinary incontinence with urgency: range 2% to 35% • Mixed urinary incontinence: range 3.8% to 13.1% • Incontinence increased with gestational age, with rates of 13-19% reported in the first trimester, 19.1% in the second trimester, increasing to

					about 30% at 28-30 weeks and 35% at 36-38 weeks' gestation • Wide disparity in estimates: tended to be higher in USA and lower in China • In most European and Australian studies, between 30% and 45% of women reported urinary incontinence at some stage during pregnancy, with higher rates in multiparous women
Saxon 1996 [17] USA	• Retrospective cohort study • Chart review of all women with ectopic pregnancy diagnosed and treated at three McGill University teaching hospitals over a ten year period (1984-94) (n=693 cases) • Data taken from hospital records	To examine the association between rupture of tubal ectopic pregnancy and demographic risk factors and to evaluate tests that might aid in predicting tubal rupture.	Moderate risk of bias • Retrospective analysis of registry data • Potential for coding error • Not population-based	Characteristics of ruptured and unruptured ectopic pregnancy	*Gestational age at diagnosis;* • Unruptured ectopic pregnancy: 6.9 weeks (SD 1.9) • Ruptured ectopic pregnancy: 7.2 weeks (SD 2.2) *Most common risk factors:* • Previous ectopic pregnancy • Previous pelvic inflammatory disease • Previous IUD use • Previous infertility treatment • Previous tubal ligation • Previous tubal surgery 43% of cases had at least one

					of these risk factors.
Sipila 1992 [54] Finland*	• Prospective population-based cohort study • Included all women with pregnancies ongoing at 25 weeks in a Finnish administrative province (11 hospitals, 8718 pregnancies)	To evaluate perinatal outcomes in pregnancies complicated by vaginal bleeding	Low risk of bias • Population sample • Includes 99% of births in the region • First trimester bleeding assessed retrospectively at 24 weeks • Excludes miscarriages before 24 weeks	Bleeding in pregnancies ongoing at 25 weeks (Defined as light (i.e. not requiring hospital admission) or heavy (i.e. requiring admission) Unclear whether included spotting)	• First trimester bleed: 7% • Heavy first trimester bleed: 1.5% (22% of women with first trimester bleeding) • Second trimester bleed: 2% • Heavy second trimester bleed: <1% (39% of women with second trimester bleeding) • Either trimester bleed: 9% • Occurrence of bleeding not influenced by whether work was sedentary or (physically or mentally) strenuous
Smith 2000 [40] Australia* (in Wood 2013 SR)	• Cross-sectional survey • Included baseline data from women participating in an RCT of treatment for nausea (n=593) • Women with a confirmed pregnancy, presenting at less than 14 weeks pregnant, with symptoms of nausea and/or	To describe the impact of nausea and vomiting on women in early pregnancy (SF-36)	Moderate risk of bias • Volunteer sample • Retrospective data collection, but relatively short period of recall • Non-commercial funding • Unclear to what extent participants were representative of women with N&V in pregnancy	Impact of nausea and vomiting in early pregnancy	Among women with nausea and vomiting in early pregnancy: • 90% had symptoms by 6 weeks • 96% found symptoms mildly to moderately distressing • 44% had vomiting in previous 12 hours • SF-36 scores were lower on all dimensions than in healthy non-pregnant controls, especially for energy and physical functioning – comparable

	vomiting were eligible to join the trial. • Mean gestational age was 8.5 weeks (range 4.4 to 14) • Values for non-pregnant controls derived from population norms				to published data for chronic illness. • 99% had reduced ability to carry out day to day activities. • Over half of women employed took time off • 4% resigned • 28% made changes to work schedule (coming in late or leaving earlier) • 65% thought they were less attentive at work.
Smits 2012 International, including NZ (SCOPE) [15]*	• International population-based prospective cohort study • Includes NZ cohort • Included healthy nulliparous women recruited at 14-16 weeks' pregnancy (n=3431) • 76% participation rate (3780/4961) • 95% of women who agreed to participate were enrolled 3572/3780 (208 later declined or were ineligible)	Evaluate association between patterns of bleeding and risk of pre-eclampsia	Low risk of bias • Population sample – set in countries with universal free antenatal care • 76% of potentially eligible women agreed to participate (3780/4961) • 95% of women who agreed to participate were enrolled 3572/3780 • 3431 analysed • Prospective study, • First trimester bleeding assessed retrospectively at 14-16 weeks • Rigorous follow-up: Data were available for>99% of variables of	Bleeding in pregnancy ongoing at 20 weeks (Spotting: a few spots of blood after toilet or on pants; Light bleeding: heavier than spotting but lighter than an average period; 'Like a period': bleeding requiring pads that need to be changed one to five times per day; Heavy bleeding with clots: soaking pads every couple of hours with or without passing of clots	• 23% had vaginal bleeding in first 20 weeks' gestation. • 19% had bleeding in first trimester only • 5% had bleeding in second trimester *Among bleeders:* • 72% bled in first trimester only • 73% had only one bleeding episode • 69% had spotting only • 21% had light bleeding only • Peak of bleeding was in 6th week of pregnancy • About 10% of women with bleeding had moderate to heavy bleeding, with no

	• 3431 analysed (141 excluded, mainly because did not attend second study visit)		interest • Findings may not be applicable to high-risk nulliparous women or to populations of mixed parity.		trend across gestational age • Most women who bled did so during the first trimester only (about three-quarters), had only one bleeding episode (about three quarters), and for about two-thirds of the women the maximal intensity was spotting. About half the women (54%) had bleeding episodes lasting no more than one day. *Bleeding and pre-eclampsia:* • There was no strong association between "any bleeding" and pre-eclampsia. • Risk of pre-eclampsia was increased by episodes of bleeding of 5 or more consecutive days (OR 2.15, 95% CI 1.01 to 4.57) and by multiple episodes (OR 2.33, 95 CI 1.16 to 4.67), compared to shorter/single episodes of bleeding.
Stone 1995 [80] NZ*	• Prospective population-based cohort study • Included women booking for	To measure the blood pressures throughout pregnancy, labour and delivery of over	Low risk of bias • Participation rate 3818/4109 (93%) • 2.7% attrition rate	• Gestational hypertension (diastolic BP >90 at least twice or >110 once) • Preeclampsia (gestational hypertension with oedema	*Incidence of antepartum gestational hypertension:* 10.8% *Incidence of antepartum preeclampsia*: 3.2%

	antenatal care and delivering in the Wellington regions in an 8 month period in 1989 (n=3818) • BP recorded at 6 week intervals throughout pregnancy • Women with chronic hypertension excluded from analysis	3,500 women living in Wellington in the anticipation that the population would be representative of New Zealand	• Represents about 10% of NZ deliveries • Sample not representative of NZ population, but deemed applicable to urban NZ populations with significant numbers of Maori and Pacific women	and proteinuria) • Oedema	*Incidence of any pre-eclampsia*: 3.3% *Incidence of eclampsia*: 0.05% *Incidence of ankle oedema*: 11.9% • After 25 weeks there was a significant rise in both systolic and diastolic BP in all gestation intervals • Predictive factors for hypertensive disorders were obesity and Pacific ethnicity • Rates were higher than in other parts of the world, even among non-obese women
Viktrup 1992 [14] Denmark (in Sangsawang SR)	• Prospective population-based cohort study • Included consecutive primiparae at a Danish hospital (n=305)	To examine the individual impact of pregnancy and delivery on continence	Moderate risk of bias • Population based • Women interviewed 3-5 days postpartum – possible recall bias • Participation rate of eligible women not reported	Urinary symptoms in pregnancy (and postpartum)	*Any stress incontinence in pregnancy*: 32% *Daily stress incontinence*: 6% *Incontinence causing a hygienic or social problem*: 1% Authors comment that using the criteria of the International Continence Society (*Incontinence causing a hygienic or social problem*), the frequency of "true" stress incontinence is low and the psychosocial impact of the symptoms is modest.
Vleeming 2008 [42] Systematic	• European guidelines for the diagnosis and	The primary objective of this guideline is to provide a set of	Moderate risk of bias • Rigorous search	Point prevalence of pelvic girdle pain in pregnancy (unclear which time-point is of	*Albert 2006* Point prevalence of pelvic girdle pain at week 33 = 20.1%

review	treatment of pelvic girdle pain • For determining incidence of pregnancy-related pain, included prospective studies of pelvic pain in which diagnosis confirmed by a pain history and, preferably by a clinical examination. (n=4)	recommendations that can support future national and international guidelines on PGP	• Selected studies all prospective and population based • Review reports point prevalence rather than prevalence throughout pregnancy • Authors' conclusions appear to be well-supported by only one of the four selected studies.	interest) For the purpose of this review, overall prevalence rates extracted from primary studies (where reported)	*Ostgaard 1990* • Point prevalence of low back pain and sacroiliac pain at week 30 about 32% • Sacro iliac pain alone at week 30: 19% • Point prevalence at 12 weeks: 22% • 9-month prevalence of either pain=49%, of whom 22% had ongoing back pain when they became pregnant • Authors noted "Physically heavy work, lifting, twisting, forward bending, poor work satisfaction, postwork fatigue, inability to take rest breaks and constrained working postures were vocational factors associated with increased complaints of back pain during pregnancy" *Larsen 1999* • Incidence of pelvic pain in pregnancy (sic) : 14% [Vleeming states point prevalence of 16%] *Berg 1988*

					Incidence of low back pain in pregnancy = 49%, severe in 9% of cases. 9% of women gave up work due to low back pain. Vleeming et al did not report cumulative incidence, and concluded that point prevalence of pregnant women suffering from PGP is about 20%.
Weiss 2004 [66] USA	• Retrospective analysis of baseline data from a prospective multicentre cohort study (n=16,506 records with complete data) • Study included women having antenatal care, whom they enrolled at 10-14 weeks' gestation • Data on bleeding in previous 4 weeks collected on study enrolment • Study also included follow-up of obstetric outcomes	To determine whether patients with first-trimester threatened abortion are at increased risk for poor pregnancy outcome	Moderate risk of bias • Participation rate in primary study not stated • Current study only includes participants with full follow up data– exclusion rate unclear • Recall bias risk minimized by conducting all interviews at <14 weeks' gestation and within 4 weeks of bleeding episode • Medical records reviewed for a random 10% of participants	• Threatened abortion (bleeding classified as none, light (spotting) or heavy (similar to menses)] • Pregnancy loss before 24 weeks (in pregnancies ongoing at 14 weeks)	*Incidence of first trimester bleeding (within 4 weeks of trial enrolment):* • 14% had any bleeding • 13% had light bleeding • 1% had heavy bleeding Incidence of pregnancy loss between 14 and 24 weeks*:* *0.5%* Risk of fetal loss was proportional to amount of vaginal bleeding. Compared with the control group (no bleeding), women with light and heavy vaginal bleeding were significantly more likely to have a spontaneous loss before 24 weeks of gestation (OR 2.5 and 4.2 respectively). Authors' comment:

					"Women with symptoms of a threatened abortion after 10 weeks of gestation are extremely likely to reach viability. The likelihood of maintaining a viable pregnancy in women with threatened abortion was 98% through 24 weeks of gestation".
Wood 2013 [38] Australia SR	• Lit search included eight databases 1999-2011 • Included studies (n=38) of the impact of nausea and vomiting in pregnancy (NVP) • Excluded studies of hyperemesis • Excluded non-English-language studies • Studies combined in narrative synthesis	To provide a review of the literature to explore the impact of NVP on women's quality of life, particularly their ability to maintain social and professional commitments.	Moderate risk of bias • No details about included studies (e.g. study design) • No statistical estimates or measures of variation • Narrative summary: broad scope and wide range of outcome measures create potential for selective/subjective reporting • Heterogeneity: studies reported outcomes using a wide range of tools	Impact of nausea and vomiting in pregnancy (NVP) (measured as in primary studies)	*Impact on quality of life (5 studies)* Studies using a range of measures "identified detrimental and far-reaching effects on quality of life" *Impact on lifestyle, household duties and other day to day activities (3 studies*) "Studies consistently reported that women with NBP.. cannot maintain usual living and social habits *Impact on paid working ability (12 studies & reviews) Selected findings:* • In a US cohort study women with N&V (n=174) took a mean of 14 days leave due to NVP, with variations in this rate dependent on severity of NVP. NVP restricted women's' activity at work (Attard 2002) • An Australian study of 593

					volunteers with N&V in early pregnancy described its impact on employment (see entry above for Smith 2000) • In a prospective Swedish survey (n=4041) pregnant women who took sick leave due to NVP took on average 13 days of leave, comprising 28% of all sick leave taken up to week 28 (Kallen 2003). • A Canadian cross-sectional observational study of pregnancy women with NVP (n=139) found that it diminished work productivity, with increased severity of symptoms exacerbating the decline.
Yang 2004 [57] USA	• Prospective cohort study • Included pregnant women at 24-29 weeks gestation (n=2829, 2820 had complete data and included in analysis) • Participants recruited from university medical centre and county	To evaluate association between self-reported vaginal bleeding and preterm birth	Moderate risk of bias • Described as moderately high-risk sample • First trimester bleeding assessed retrospectively at 24-31 weeks • Authors acknowledge that "bleeding episode" was poorly defined so some characteristics may have been misclassified	Bleeding in pregnancy ongoing at 24-29 weeks (self-reported: (Light spotting; Heavy bleeding (required a pad or soaked underwear)) Pre-term birth	*Bleeding*: 24.4% *Among women with bleeding*: • 77.2% had initial event in first trimester (19% of total sample) • 70% had a single episode' • 79.4% had light spotting • 78.5% had less than 5 days' bleeding in total • Most commonly, women had one episode of light spotting for 1-2 days

	health department: described as a moderately high-risk population				• Women with initial bleeding in second trimester had less total blood loss than women with initial bleeding in first semester