The prevalence of congenital uterine anomalies in unselected and high-risk populations: a systematic review

Y.Y. Chan1,, K. Jayaprakasan2, J. Zamora3, J.G. Thornton2, N. Raine-Fenning2, and A. Coomarasamy4

1Department of Obstetrics and Gynaecology, Nottingham University Hospitals NHS Trust, Queen’s Medical Centre Campus, Derby Road, Nottingham NG7 2UH, UK 2Division of Human Development, School of Clinical Sciences, The University of Nottingham, Nottingham NG7 2UH, UK 3Clinical Biostatistics Unit, Ramón y Cajal Hospital, Madrid, Spain 4Academic Unit of Obstetrics and Gynaecology, Birmingham Women’s Hospital, Birmingham B15 2TG, UK

*Correspondence address. Tel: +44 115 823 0699; E-mail: yeeyin@gmail.com

Submitted on April 7, 2011; resubmitted on May 19, 2011; accepted on June 1, 2011

TABLE OF CONTENTS

- Introduction
- Methods
  - Search strategy
  - Selection criteria
  - Study selection
  - Data extraction
  - Statistical analysis
- Results
  - All uterine anomalies
  - Arcuate uteri
  - Canalization defects
  - Unification defects
- Discussion
  - Principal findings
  - Weaknesses of our review
  - Strengths of our review
  - Diagnostic tests
  - Women with preterm delivery
  - The unselected or general population
  - The infertile population
  - Women with miscarriage
  - Women with infertility and/or miscarriage
  - Distribution of congenital uterine anomalies
  - Implications for future research
- Conclusion

BACKGROUND: The prevalence of congenital uterine anomalies in high-risk women is unclear, as several different diagnostic approaches have been applied to different groups of patients. This review aims to evaluate the prevalence of such anomalies in unselected populations.
and in women with infertility, including those undergoing IVF treatment, women with a history of miscarriage, women with infertility and recurrent miscarriage combined, and women with a history of preterm delivery.

**METHODS:** Searches of MEDLINE, EMBASE, Web of Science and the Cochrane register were performed. Study selection and data extraction were conducted independently by two reviewers. Studies were grouped into those that used ‘optimal’ and ‘suboptimal’ tests for uterine anomalies. Meta-analyses were performed to establish the prevalence of uterine anomalies and their subtypes within the various populations.

**RESULTS:** We identified 94 observational studies comprising 89,861 women. The prevalence of uterine anomalies diagnosed by optimal tests was 5.5% [95% confidence interval (CI), 3.5–8.5] in the unselected population, 8.0% (95% CI, 5.3–12) in infertile women, 13.3% (95% CI, 8.9–20.0) in those with a history of miscarriage and 24.5% (95% CI, 18.3–32.8) in those with miscarriage and infertility. Arcuate uterus is most common in the unselected population (3.9%; 95% CI, 2.1–7.1), and its prevalence is not increased in high-risk groups. In contrast, septate uterus is the most common anomaly in high-risk populations.

**CONCLUSIONS:** Women with a history of miscarriage or miscarriage and infertility have higher prevalence of congenital uterine anomalies compared with the unselected population.

**Key words:** congenital uterine anomalies / prevalence / miscarriage / preterm / uterus

**Introduction**

Congenital uterine anomalies result from abnormal formation, fusion or resorption of the Müllerian ducts during fetal life (Moore et al., 2008). These anomalies have been associated with an increased rate of miscarriage, preterm delivery and other adverse fetal outcomes (Green and Harris, 1976; Rock and Schlaff, 1985; Acien, 1993; Raga et al., 1997; Grimbizis et al., 2001; Tomazevic et al., 2007).

However, such associations might be artefactual. The true population prevalence of congenital uterine anomalies is difficult to assess partly because there are no universally agreed standardized classification systems and partly because the best diagnostic techniques are invasive and, therefore, rarely applied to low-risk study populations. As a result, reported population prevalence rates have varied between 0.06% and 38% (Simon et al., 1991; Makino et al., 1992a, b; Clifford et al., 1994; Acien, 1996; Homer et al., 2000; Guimaraes Filho et al., 2006a, b). This wide variation is likely to be linked to the assessment of different patient populations and the use of different diagnostic techniques with variable, and yet to be determined, test accuracy as well as reliance on non-standardized classification systems. Previous reviews have not considered these factors when investigating the prevalence of uterine anomalies (Acien, 1997; Nahum, 1998; Grimbizis et al., 2001; Troiano and McCarthy, 2004).

Saravelos et al. (2008) carried out a critical review to determine the prevalence of congenital uterine anomalies. Their review has assessed the accuracy of different diagnostic procedures, but their search was limited to MEDLINE database and specifically limited to recurrent miscarriage, infertile and general population groups.

We conducted a systematic review of studies evaluating the prevalence of congenital uterine anomalies in the unselected population and in women with a history of infertility, including those undergoing IVF treatment, miscarriage, infertility and recurrent miscarriage combined, and preterm delivery and attempted to explore the inconsistencies present in the literature. This new systematic review is not only an update of the work by Saravelos et al. (2008) but also represents a different approach to the classification of optimal and suboptimal tests.

**Methods**

**Search strategy**

Articles were identified through the following electronic databases: MEDLINE (1950 to March 2011), EMBASE (1980 to March 2011), Web of Science (1990 to March 2011) and the Cochrane Central Register of Controlled Trials (The Cochrane Library until January 2011). A combination of Medical Subject Headings (MeSH) and text words were used to generate the list of citations (Table I). In addition, the reference lists of all relevant primary studies and review articles were manually searched to identify additional cited articles not captured by the electronic searches. Authors were contacted for additional details where required. The searches were conducted independently by two reviewers (Y.Y.C. and K.J.).

The search terms in Table I were designed specifically for MEDLINE. This search was modified for EMBASE, Web of Science and the Cochrane Library.

**Selection criteria**

Studies were selected if the incidence of any uterine anomaly was reported. Studies of all types of congenital uterine anomalies were included but limited to ‘Humans and Female’. Only cohort studies were included in the review. Studies were excluded when the population examined or the diagnostic methods used were not accurately defined. Only publications in English were considered in our selection.

The classification system for uterine anomalies was adapted from the American Fertility Society guidelines (1988). The arcuate uterus is an anomaly where the uterine fundus displays a mild concave indentation or contour towards the uterine cavity (The American Fertility Society, 1988; Salim et al., 2003). Many authors consider the arcuate uterus a normal variant rather than a true anatomical or developmental anomaly (Heinonen et al., 1982; Buttram et al., 1988), but this can only be properly evaluated if the true prevalence of the anomaly can be defined and appropriate associations with relevant outcome measures assessed. Neither can be assessed in the absence of an accurate test to identify the anomaly and differentiate it from more complex uterine anomalies and the normal uterus. In view of this, studies that failed to identify or record any arcuate uterus were excluded from the subtype analysis as we were unable to determine if these studies excluded arcuate uterus or if they failed to identify them because of the inaccuracy of the diagnostic tests employed.
Study selection
Studies were selected in a two-stage process. First, the titles and abstracts from the electronic searches were examined independently by two reviewers (Y.Y.C. and K.J.) and full manuscripts of all citations that met the predefined selection criteria were then obtained. Secondly, examinations of the full manuscripts were carried out to make final inclusion or exclusion decisions. In cases of duplicates, the most recent or the most complete publication was used. Any disagreements about inclusion were resolved by consensus or arbitration by a third reviewer (N.R.-F.).

All selected papers were assessed for the following: study design; adequate sampling (random or consecutive rather than convenience sampling); adequate description of population characteristics; completeness of information in the data sets; and use of a validated diagnostic method.

Data collection and extraction
Data collection and extraction were performed by the two reviewers (Y.Y.C. and K.J.) independently. Data were extracted on patients’ characteristics, study quality, inclusion and exclusion criteria, diagnostic tools and anomaly occurrence rates.

In assessing the prevalence of congenital uterine anomalies, investigators have used different diagnostic methods, some of which may be more accurate or reliable than others. In view of this, we grouped the studies into two classes according to the diagnostic accuracy of the methods used based on evidence from other studies (Scarsbrook and Moore, 2003; Saravelos et al., 2008; Olpin and Heilbrun, 2009). Diagnostic methods that were accepted as ‘optimal diagnostic tests’ included three-dimensional transvaginal ultrasound, laparoscopy or laparotomy performed in conjunction with hysteroscopy or hysterosalpingography (HSG), magnetic resonance imaging (MRI) and saline sonohysterography. Suboptimal tests, which could identify and differentiate most but not all anomalies, included two-dimensional transvaginal ultrasound, hysteroscopy performed in isolation, HSG and clinical assessment at the time of Caesarean section. We devised this classification based on the ability of the test to demonstrate both the external contour of the uterus and the fundal aspect of the endometrial cavity.

Statistical analysis
Meta-analyses were performed to establish the prevalence of uterine anomalies, and their subtypes, in each group of women. For meta-analyses, log rates were pooled, weighting each study by the inverse of its variance, and the summary estimates were exponentiated. A random-effects model was used for analysis. Comparisons between the unselected population and the high-risk populations were carried out with the aid of meta-regression. Statistical analyses were performed using Stata 11.0 statistical software (Stata Corp, TX, USA).

Results
All uterine anomalies
The search yielded 6266 citations; of which, 1413 duplicates were excluded (Fig. 1). Another 4306 were excluded, as it was clear from the title and abstract that they did not fulfill the selection criteria. Full manuscripts were obtained for the remaining 547 articles from which, following scrutiny of each article, we identified 91 potentially relevant studies. Three additional studies, identified from manual searches, were also included resulting in 94 studies comprising 89 861 women (Supplementary data, Table SI).

Studies were grouped according to the characteristics of the different patient population, namely unselected or general population, infertility, miscarriage, infertility and recurrent miscarriage combined, and preterm delivery. However, no appropriate study investigating the prevalence of uterine anomalies in women with preterm deliveries was available.

Out of the 94 studies included, 59 were prospective, 26 retrospective and 9 did not define this aspect of study design. Seventy-nine studies had consecutive or random patient recruitment. Forty-one out of 94 (44%) studies used optimal diagnostic tests. Pooled prevalence rates for all uterine anomalies and various subgroups are shown in Table II.
Table II  The prevalence of uterine anomalies in different study populations stratified by the accuracy of the diagnostic test used to identify and define them.

| Population | Diagnostic test | Number of studies | Number of subjects | Prevalence of all anomalies % (95% CI) | Arcuate % (95% CI) | Canalization defects % (95% CI) | Unification defects | Others % (95% CI) |
|------------|----------------|------------------|-------------------|----------------------------------------|-------------------|--------------------------------|---------------------|-------------------|
|            |                |                  |                   |                                        |                   |                                |                     |                   |
| Unselected | Optimal        | 9                | 5163              | 5.5 (3.5–8.5)                         | 3.9 (2.1–7.1)     | 2.3 (1.8–2.9)                  | 0.4 (0.2–0.6)       | 0.1 (0.1–0.3)     |
|            | Suboptimal     | 13               | 52290             | 4.6 (2.3–9.1)                         | 2.2 (0.9–5.2)     | 0.2 (0.0–0.9)                  | 0.2 (0.0–0.7)       | 0.1 (0.1–0.5)     |
| Infertility| Optimal        | 19               | 10303             | 8.0 (5.3–12.0)                        | 1.8 (0.8–4.1)     | 3.0 (1.3–6.7)                  | 1.1 (0.6–2.0)*       | 0.5 (0.3–0.8)*    |
|            | Suboptimal     | 29               | 8643              | 6.1 (3.9–9.5)                         | 5.8 (3.4–10.1)    | 2.7 (1.5–4.8)*                 | 0.8 (0.5–1.4)       | 0.8 (0.5–1.2)     |
| Miscarriage| Optimal        | 6                | 2082              | 13.9 (8.9–20)*                        | 2.9 (0.9–9.6)     | 5.3 (3.7–16.8)*                | 2.1 (1.4–3.3)*       | 0.5 (0.3–1.1)*    |
|            | Suboptimal     | 21               | 3961              | 15.8 (11.9–20.9)*                     | 8.9 (6.4–12.4)*   | 4.3 (2.3–8.2)*                 | 2.8 (1.6–5.5)       | 0.6 (0.3–1.4)     |
| Mixed infertility and recurrent miscarriage | Optimal | 9 | 7053 | 24.5 (18.3–32.8)* | 6.6 (2.8–15.7) | 15.4 (12.5–19)* | 4.7 (2.9–7.6)* | 3.1 (2.4–7.6)* |
|            | Suboptimal     | 1                | 66                | 31.8 (20.7–48.8)                      | No study found    | None diagnosed                  | 4.5 (1.5–14.1)       | 27.3 (17.2–43.3)* |

No appropriate study investigating the prevalence of uterine anomalies in women with preterm deliveries was identified.

Optimal diagnostic tests: three-dimensional transvaginal ultrasound, laparoscopy or laparotomy with hysteroscopy or HSG, MRI, and saline sonohysterography.

Infertility Optimal 19 10 303 8.0 (5.3–12.0) 1.8 (0.8–4.1) 3.0 (1.3–6.7) 1.1 (0.6–2.0)* 0.5 (0.3–0.8)* 0.3 (0.2–0.5)* 0.2 (0.1–0.4) 0.6 (0.3–1.4) 0.9 (0.1–12.6) 0.4 (0.2–0.9) 1.0 (0.4–2.4)

Studies with women undergoing IVF (three studies) were included in the infertile group.

* P < 0.05, differences are statistically significant when compared with an unselected population. Comparisons were made using meta-regression.

CI, confidence interval.

Unification defects include bicornuate, unicornuate and didelphys.

Overall, 0.1% (95% CI 0.1–0.3) of the unselected population had a uniconcave uterus, which are uncommon in the unselected population (4.7%, 95% CI 2.9–7.6, P = 0.001). The prevalence of congenital anomalies in women with infertility (22.2%, 95% CI 13–31) exceeded that in women with miscarriage (7.1%, 95% CI 4.5–11, P = 0.009), particularly if these coexist (7.8%, 95% CI 4.7–13, P = 0.001). The prevalence of all uterine anomalies in various high-risk populations diagnosed by optimal tests was consistent with those diagnosed by suboptimal tests.

Arcuate uterus are common in the unselected population affecting 3.9% (95% CI 2.1–7.1) of all women. Their prevalence, as diagnosed by optimal tests, is not increased in infertile women (1.8%; 95% CI 0.8–4.1) or in women with a history of miscarriage (2.9%; 95% CI 1.4–5.8). When compared with the unselected population, the prevalence of arcuate uterus was significantly higher in women with infertility (8.0%; 95% CI 5.3–12.0, P < 0.001) and miscarriage (5.3%; 95% CI 1.7–16.8, P < 0.001), particularly if these coexist (5.7%; 95% CI 3.0–9.5, P < 0.001), especially if this is combined with congenital anomalies (13.4%; 95% CI 8.5–20.0) in women with infertility. The prevalence of arcuate uterus (2.9%; 95% CI 1.4–5.8) did not significantly differ from that of women with a history of miscarriage (2.9%; 95% CI 1.4–5.8, P = 0.572). The prevalence of all uterine anomalies in various high-risk populations diagnosed by suboptimal tests was found to be consistent with those diagnosed by optimal tests.
miscarriage (0.5%; 95% CI, 0.3–1.1; \( P = 0.025 \)), miscarriage in association with infertility (3.1%; 95% CI, 2.4–4.7; \( P < 0.001 \)) and infertility (0.5%; 95% CI, 0.3–0.8, \( P = 0.01 \)) when compared with the unselected population. The prevalence of uterus didelphys was 0.3% (95% CI, 0.1–0.6) in the unselected population. This anomaly is no more prevalent in women with infertility (0.3%; 95% CI, 0.2–0.5), or in women with a history of miscarriage (0.6%; 95% CI, 0.3–1.4), but is significantly more common in infertile women with miscarriage (2.1%; 95% CI, 1.4–3.2, \( P < 0.001 \)).

Overall, the prevalence of unification defects in various populations diagnosed by suboptimal tests is consistent with those diagnosed by optimal tests.

**Discussion**

Our systematic review evaluated the prevalence of uterine abnormalities in the general ‘unselected’ population and in various high-risk groups stratified according to the diagnostic accuracy of the tests used to identify and define the anomaly. The review is not only an update of the work by Saravelos et al. (2008) but also represents a different perspective on the classification of optimal and suboptimal tests. In our review, optimal tests are investigations that are capable of accurately identifying and classifying congenital uterine anomalies accurately while suboptimal tests can identify and differentiate most but not all anomalies. In addition, the review by Saravelos et al. (2008) has not described the literature search and the study selection in detail. They have also limited their search to mainly MEDLINE database and some relevant articles are likely to be missed. Our comprehensive search and study selection using multiple databases have captured most, if not all relevant articles. Therefore, more papers were found for this review compared with Saravelos et al. (2008). We have also prospectively subclassified infertility by separating women who have infertility only and those who have combined infertility and miscarriage. It is important to subclassify infertility into these groups as they are likely to have clinically distinct problems, as described below.

**Principal findings**

In our review, we found that the prevalence of all congenital uterine anomalies diagnosed by optimal tests in the unselected population was 5.5%. This appears to be increased in women with a history of miscarriage and those who have combined infertility and miscarriage. Subgroup analyses showed that the specific anomalies, which are increased in these high-risk populations, are mainly canalization defects, namely subseptate or septate uteri, and unification defects.

**Weaknesses of our review**

Our review is limited by the retrospective nature of the analysis and heterogeneity of the patient population and diagnostic tests applied. We were unable to obtain all relevant clinical information for all of the women studied. We included all studies that met the selection criteria but did not exclude studies because of inadequate quality. We have found that several analyses showed statistically significant heterogeneity, which is most likely due to different patient populations, varied diagnostic tests and classification systems used.

There was clearly a lack of uniformity with the classification of uterine anomalies in the studies included. The most commonly used classification system is the one devised by the American Fertility Society in 1988, but this does not specify the diagnostic methods that should be used and the final diagnosis is based on the subjective impression of the clinician performing the test (Woelfer et al., 2001).

**Strengths of our review**

The strengths of our systematic review include its extensive electronic search using multiple databases and manual search approach. We attempted to address the problem of clinical heterogeneity by analysing different patient populations separately and by analysing the two groups of diagnostic tests used as suboptimal or optimal. We also consider our classification of which tests offer an optimal diagnosis and differentiation of uterine anomalies is more robust and relevant than the one used by Saravelos et al. (2008).

**Diagnostic tests**

In general, our review is in agreement with the findings by Saravelos et al. (2008). An important difference is, however, an overall lower prevalence of all anomalies in our review. This may reflect our different viewpoints on what constitutes an optimal diagnostic test for the identification and differentiation of uterine anomalies. We believe that two-dimensional transvaginal ultrasound, hysteroscopy and HSG are suboptimal in this respect, as they all have a tendency to misclassify uterine abnormalities owing to their poorer accuracy when used as diagnostic tests in isolation (Jurkovic et al., 1995; Wu et al., 1997; Braun et al., 2005; Andreotti et al., 2006; Guimaraes Filho et al., 2006a, b; Montz et al., 2007). This is particularly true of the more minor abnormalities, such as the arcuate and subseptate uteri, which may be missed or incorrectly classified. Most of these tests do not allow evaluation of the external contour of the uterus and are, therefore, unable to reliably differentiate a septate uterus from one that is subseptate or bicornuate. These suboptimal tests, however, are likely to perform better when major uterine anomalies are considered as these are more readily evident and theoretically, at least, easier to differentiate from one another with the exception of the more complex anomalies that involve the cervix and non-communicating corpora.

It is surprising, therefore, that our systematic review showed that prevalence of uterine anomalies in various populations is similar regardless of whether an optimal or suboptimal test was used. In contrast, Saravelos et al. (2008) reported significant differences in the prevalence of all uterine anomalies according to the purported accuracy of the diagnostic test. Their systematic review and meta-analysis considered hysteroscopy alone as an accurate test while MRI has unclear diagnostic accuracy. Hysteroscopy does not allow evaluation of the external contour of the uterus and, therefore, we considered hysteroscopy as a suboptimal test. In our opinion, MRI is an optimal test that allows a simultaneous assessment of the cavity and fundus of the uterus. MRI has been reported to have a high accuracy rate in diagnosing congenital uterine anomalies (Pellerito et al., 1992; Fischetti et al., 1995; Olpin and Heilbrun, 2009; Bermejo et al., 2010). MRI can also be used to extend the examination to the abdomen, which is potentially important because of the increased frequency of renal anomalies in patients with uterine anomalies (Gell et al., 1998; Li et al., 2000; Arnold et al., 2001).
Women with preterm delivery

Preterm labour has many aetiologies, but congenital anomalies have been suggested as one potential cause. Putative mechanisms include cervical incompetence (Airoldi et al., 2005), abnormal uterine contractions (Dabirashrafi et al., 1995) and reduced uterine volume (Reuter et al., 1989; Pellerto et al., 1992; Braun et al., 2005; Puscheck and Cohen, 2008). Unfortunately, despite these links, no appropriate studies investigating the prevalence of uterine anomalies in women with preterm delivery were identified in the search.

The unselected or general population

In our review, the prevalence of all congenital uterine anomalies diagnosed by optimal tests in the unselected population was 5.5%. This is higher than reported in many reviews, which suggested a rate of 0.17–4.3% (Simon et al., 1991; Raga et al., 1997; Nahum, 1998; Homer et al., 2000; Grimbizis et al., 2001) but lower than the recent systematic review by Saravelos et al. (2008), which suggested that 6.7% of all women have a uterine anomaly (Saravelos et al., 2008). These differences, as discussed above, are likely to reflect the different diagnostic tests used and varied clinical backgrounds in the different study populations.

The most common uterine anomaly diagnosed in the unselected population is the arcuate uterus (3.9%), followed by the canalization defects (2.3%) and then the bicornuate uterus (0.4%). This is not consistent with the findings from other studies or reviews, which have generally found canalization defects to be the most common (Nasri et al., 1990; Simon et al., 1991; Acien, 1997; Raga et al., 1997; Homer et al., 2000; Grimbizis et al., 2001). This discrepancy is again likely to reflect the lack of a uniform system for classification and possibly the misclassification of some arcuate uteri as normal or small subseptate uteri.

Assessing the prevalence of congenital uterine anomalies in the unselected population is difficult. Many anomalies remain asymptomatic and investigations are not warranted without specific indication. In our review, we have included patients undergoing sterilization (laparoscopically or hysteroscopically) and those being investigated for non-obstetric or fertility problems, such as pelvic pain, abnormal bleeding, ovarian cancer screening and suspected pelvic pathology. Our results should, therefore, reflect the prevalence of uterine anomalies in the fertile and general population combined, but the background and various presentations may affect the results. To the best of our knowledge, no studies have assessed a truly unselected population where subjects are recruited randomly from the general public as opposed to those undergoing medical assessment.

The infertile population

The effect of uterine anomalies on fertility is unclear, as are the pathophysiological processes underlying any potential detrimental effect. In our systematic review, the infertile population included women with both primary and secondary infertility. We found that women with infertility had a similar rate of uterine anomalies (8.0%), when compared with the unselected population, regardless of whether the diagnosis was made using optimal or suboptimal tests. This is in agreement with several other studies that have not shown an increased frequency of uterine anomalies in women known to have infertility (Acien, 1997; Grimbizis et al., 2001; Saravelos et al., 2008). In contrast, Taylor and Gomel (2008) suggested that congenital anomalies might negatively influence the complex processes of embryo implantation. Nahum (1998) reported a prevalence of 3.5% in women with infertility, which was 21 times more than the incidence of uterine anomalies in women with normal fertility but did not consider the reliability of the diagnostic tests used.

Canalization defect is the most common uterine anomaly in optimal tests in women with infertility (3.0%). This prevalence is comparable to the unselected population and in accordance with the findings of Homer et al. (2000) but lower than that suggested by Saravelos et al. (2008). Saravelos et al. (2008), as previously discussed, considered hysteroscopy as a reliable and accurate test to identify canalization defects. They have also included women with miscarriage as part of their infertile population whom we have considered as separate subgroup(s). Our review shows that bicornuate uteri are more prevalent, and certainly not uncommon, in women with infertility (1.1%) compared with the unselected population (0.4%). This finding is in agreement with Saravelos et al. (2008) and Raga et al. (1997) and suggests a possible association between the bicornuate uterus and implantation.

Women with miscarriage

The estimated prevalence of uterine anomalies diagnosed by optimal tests in the population of women with miscarriage is 13.3%, which is consistent with the literature (Raga et al., 1997; Grimbizis et al., 2001; Saravelos et al., 2008).

We appreciate that the different studies included used different inclusion criteria. We have included all studies that investigated women with miscarriage regardless of the pattern or number of miscarriages. However, most studies did not provide clear data as to whether miscarriage occurred during the first or second trimester, and the studies differ in the pattern of miscarriage, including consecutive and non-consecutive miscarriage, and in the number of previous miscarriages. It is important to note that most of the studies included in this current review investigated women with two or more miscarriages (Raga et al., 1997; Weiss et al., 2005; Guimaraes Filho et al., 2006, b; Dendrinos et al., 2008; Ghi et al., 2009; Bohllmann et al., 2010; Saravelos et al., 2010) and the results are not, therefore, necessarily directly applicable to women with a single previous miscarriage or those with a previous live birth (a factor that could not be assessed as it was not reported as a separate group by any author). The prevalence of congenital uterine anomalies in women with two or more miscarriages appears to be similar to those with three or more miscarriages, regardless of the diagnostic test used. This is supported by Weiss et al. (2005) and Saravelos et al. (2008) and suggests that women with a history of two miscarriages may warrant an investigation to exclude a congenital uterine anomaly.

The observed prevalence of arcuate uterus in the miscarriage population is similar to findings for the unselected population. The prevalence of canalization defects in this population is significantly higher than in the unselected population, which supports a contributory relationship between canalization anomalies and miscarriage. This finding is supported by previous studies (Acien, 1993; Woelfer et al., 2001; Shuiping et al., 2002).

The exact aetiology and pathophysiological processes of how canalization defects may lead to miscarriage remain uncertain. It has been
suggested that the endometrium overlying the septum is abnormal or at least suboptimal and this makes it a poor site for implantation (Candiani et al., 1983; Dabirashrafi et al., 1995; Fedele et al., 1996). Therefore, embryos that do implant on the septum are more likely to miscarry as a result of this, possibly because the septum has a disorderly and decreased blood supply, which is insufficient to support subsequent placentation and embryo growth (Candiani et al., 1983; Raga et al., 1997; Leible et al., 1998; Homer et al., 2000; Kupesic, 2001; Lin, 2004; Rackow and Arici, 2007). These hypotheses remain to be proven and there is evidence to contradict these theories (Pellerto et al., 1992; Dabirashrafi et al., 1995; Kupesic, 2001). Dabirashrafi et al. (1995) have found significantly more blood vessels in biopsy samples of the uterine septum, and Kupesic (2001) found that patients with vascularized septum had significantly higher prevalence of early pregnancy failure and late pregnancy complications than those with avascularized septa (Dabirashrafi et al., 1995; Kupesic, 2001). Other authors have suggested that miscarriage may result from higher or uncoordinated uterine contractions (Rock and Kupesic, 2001). Other authors have suggested that miscarriage may result from higher or uncoordinated uterine contractions (Rock and Kupesic, 2001). Other authors have suggested that miscarriage may result from higher or uncoordinated uterine contractions (Rock and Kupesic, 2001).

Women with infertility and/or miscarriage

This population of women was found to have significantly higher (24.5%) prevalence of uterine anomalies overall compared with the unselected population. In keeping with the other high-risk groups, the most commonly seen anomaly is the canalization defect, which is significantly more prevalent (15.4%) in this population than in the unselected population (2.3%). It is difficult to know if the higher prevalence is related to the presence of women with pure recurrent miscarriage or as a result of the inclusion of women who suffered from both infertility and recurrent miscarriage: it was not possible to separate these two populations to obtain prevalence information as these studies did not provide such individual data. Previous reviews have included these studies in their infertile or recurrent miscarriage populations (Nahum, 1998; Grimbizis et al., 2001; Saravelos et al., 2010) but, in our opinion, these women have two potentially clinically distinct problems and should not be included in these groups.

Distribution of congenital uterine anomalies

Based only on studies employing optimal tests, the most commonly diagnosed uterine anomaly in the unselected or general population is the arcuate uterus. The arcuate uterus is, however, no more prevalent in any of the high-risk groups studied than in the unselected population. Unification defects (bicorneate and unicorneate uteri and uterus didelphys) are generally more prevalent in all of the high-risk groups as are defects of canalization (septate or subseptate). It is important to note, however, that some canalization defects may have been diagnosed as arcuate uteri and vice versa, and equally some septate uteri, particularly those with a large septum extending to the cervix, may have been misdiagnosed as bicornuate uteri even with the use of optimal tests.

Implications for future research

Historically, and still today, many authors considered the combination of laparoscopy or laparotomy with hysteroscopy or HSG to be the gold standard for the diagnosis and differentiation of congenital uterine anomalies (Acien, 1997; Hamilton et al., 1998; Homer et al., 2000). The final diagnosis is, however, based on the subjective impression of the clinician performing the test, and in many cases, simultaneous views of the external contour of the uterus and upper cavity are not achieved. Because of these limitations and because the combined approach is also invasive and usually requires general anaesthesia, we feel that three-dimensional ultrasound, a highly accurate yet non-invasive test, has the potential to emerge as the reference standard for the identification and differentiation of congenital uterine anomalies. Reports have shown that three-dimensional ultrasound scan has high sensitivity and specificity, as high as 100% in diagnosing uterine anomalies (Carrington et al., 1990; Pellerito et al., 1992; Deutch and Abuhamad, 2008; Saravelos et al., 2008). In addition, they offer the ability to assess the abdomen simultaneously, which is potentially important owing to increased frequency of renal anomalies in patients with uterine anomalies (Gell et al., 1998; Li et al., 2000; Arnold et al., 2001). Three-dimensional ultrasound is preferred by some clinicians who use it as a standard to diagnose congenital uterine anomalies over MRI (Kupesic, 2005; Deutch and Abuhamad, 2008) as MRI is more time-consuming and expensive than ultrasound scanning. Salim et al. (2003) have proposed a modified classification for three-dimensional ultrasound, in which the diagnostic criteria used were more detailed than previously described and they included cut-offs levels for the fundal shape and distortion (Salim et al., 2003). These cut-offs were necessary to differentiate uterine anomalies with similar morphological features, such as subseptate and arcuate uteri. In the future, the Salim et al. (2003) classification should be used as a standard to describe uterine anomalies.

Besides that, there are many different tests available for the diagnosis and differentiation of uterine anomalies. A well-designed study of test accuracy is required to determine the best investigation for diagnosis of uterine anomaly.

The results and analyses of our review were hindered by the retrospective reporting, and heterogeneity of the patient population, diagnostic tests, and classification systems applied. In view of this, future studies should be performed prospectively. Studies should also critically consider the population being studied and diagnostic test used.

Some studies have reported associations between congenital uterine anomalies and poor reproductive outcomes (Acien, 1993; Zupe et al., 1996; Zlopasa et al., 2007). However, further large observational and prospective studies are essential to investigate the reproductive impact of different subtypes of congenital uterine anomalies. Studies are required to assess the management of women with uterine anomalies as treatments, such as hysteroscopic resection of the uterine septum, which have been suggested to improve the reproductive outcomes in these patients (Maneschi et al., 1993; Heinonen, 1997; Valli et al., 2004), are not without risk and involve irreversible damage to the endometrium which must be transected to access the myometrium. While some observational studies have reported an improved outcome following surgical intervention (Homer et al., 2000; Taylor and Gomel, 2008), there is a need to conduct randomized controlled trials to address the effectiveness and safety of such treatment.

Conclusion

In this review, we found that the prevalence of uterine anomalies diagnosed by optimal tests was 5.5% in an unselected population, 8% in
infertile women, 13.3% in those with miscarriage and highest at 24.5% in infertile women who also had a history of miscarriage. The higher rate of major congenital uterine anomalies in these high-risk groups, with the exception of isolated subfertility, suggests a causal role in poor reproductive outcome. The most commonly encountered anomaly varies according to the population studied with the arcuate uterus being more prevalent in an unselected group of women and the canalization defect being the most common anomaly in all of the high-risk groups. The high prevalence of canalization defects in high-risk populations should not be underestimated. The role of septic resection in these women deserves further investigation.

**Supplementary data**

Supplementary data are available at http://humupd.oxfordjournals.org/.

**Authors’ roles**

Y.Y.C. contributed to study conception and design, collection, analysis and interpretation of data, drafting the article and revising it critically for important intellectual content and final approval of the version to be published. K.J. contributed to study design, collection, analysis and interpretation of data, revising article critically for important intellectual content and final approval of the version to be published. J.Z. contributed to analysis and interpretation of data and final approval of the version to be published. J.G.T. contributed to study conception, revising article critically for important intellectual content and final approval of the version to be published. N.R.F. contributed to study conception, collection of data and revising article critically for important intellectual content and final approval of the version to be published. A.C. contributed to study conception and design, analysis and interpretation of data, revising article critically for important intellectual content and final approval of the version to be published.

**Funding**

The study was supported by The University of Nottingham.

**Conflict of interest**

The authors do not have any conflict of interest.

**References**

Acien P. Reproductive performance of women with uterine malformations. *Hum Reprod* 1993;8:122–126.

Acien P. Uterine anomalies and recurrent miscarriage. *Infertil Reprod Med Clin North Am* 1996;7:689–719.

Acien P. Incidence of Mullerian defects in fertile and infertile women. *Hum Reprod* 1997;12:1372–1376.

Airoldi J, Berghella V, Sehdev H, Ludmir J. Transvaginal ultrasonography of the cervix to predict preterm birth in women with uterine anomalies. *Obstet Gynecol* 2005;106:535–536.

Akar ME, Bayar D, Yildiz S, Ozcel M, Yilmaz Z. Reproductive outcome of women with unicornuate uterus. *Aust N Z J Obstet Gynecol* 2005;45:148–150.

Alatas C, Alksoy E, Akarsu C, Yakin K, Alksoy S, Hayran M. Evaluation of intrauterine abnormalities in infertile patients by sonohysterography. *Hum Reprod* 1997;12:487–490.

Alborzi S, Dehbash S, Khodaei R. Sonohysterosalpingographic screening for infertile patients. *Int J Gynaecol Obstet* 2002;82:57–62.

Andreatos RF, Fleischer AC, Mason LE Jr. Three-dimensional sonography of the endometrium and adjacent myometrium: preliminary observations. *J Ultrasound Med* 2006;25:1313–1319.

Arnold BW, Gilfeather M, Woodward PJ. Mullerian duct anomalies complicated by obstruction: evaluation with pelvic magnetic resonance imaging. *J Womens Imaging* 2001;3:146–152.

Ashton D, Amin HK, Richart RM, Neuwirth RS. The incidence of asymptomatic uterine anomalies in women undergoing transcervical tubal sterilization. *Obstet Gynecol* 1988;72:28–30.

Ayida G, Harris P, Kennedy S, Seif M, Barlow D, Chamberlain P. Hysterosalpingo-contrast sonography (HyCoSy) using Echovist-200 in the outpatient investigation of infertility patients. *Br J Radiol* 1996;69:910–913.

Ayida G, Kennedy S, Barlow D, Chamberlain P. A comparison of patient tolerance of hysterosalpingo-contrast sonography (HyCoSy) with Echovist-200 and X-ray hysterosalpingography for outpatient investigation of infertile women. *Ultrasound Obstet Gynecol* 1996;7:201–204.

Ayida G, Chamberlain P, Barlow D, Kennedy S. Uterine cavity assessment prior to in vitro fertilization: comparison of transvaginal scanning, saline contrast hysterosonography and hysteroscopy. *Ultrasound Obstet Gynecol* 1997;10:59–62.

Bermejo C, Martinez Ten P, Cantarero R, Diaz D, Perez Pedregosa J, Barron E, Labrador E, Ruiz Lopez L. Three-dimensional ultrasound in the diagnosis of Mullerian duct anomalies and concordance with magnetic resonance imaging. *Ultrasound Obstet Gynecol* 2010;35:593–601.

Blumenthal NJ, Hertzau Y, Ferreira MM, Mendelsohn DB, Goldberg S. Hysterosalpingography in the assessment of infertility in black patients. *S Afr Med J* 1994;65:854–856.

Bohllmann MK, Von Wolff M, Luedders DW, Beuter-Winkler P, Diedrich K, Hornemann A, Strowitzki T. Hysteroscopic findings in women with two and with more than two first-trimester miscarriages are not significantly different. *Reprod Biomed Online* 2010;21:230–236.

Brandner P, Neis KJ, Wagner S, Daub M. Uterine and fetal findings at hysteroscopy during spontaneous abortions before D&C. *J Am Assoc Gynecol Laparosc* 2001;8:552–557.

Braun P, Grau FV, Pons RM, Enguix DP. Is hysterosalpingography able to diagnose all uterine malformations correctly? A retrospective study. *Eur J Radiol* 2005;53:274–279.

Brown SE, Coddington CC, Schnoor J, Toner JP, Gibbons W, Oehninger S. Evaluation of outpatient hysteroscopy, saline infusion hysterosonography, and hysterosalpingography in infertile women: a prospective, randomized study. *Fertil Steril* 2000;74:1029–1034.

Brusco GF, Arena S, Angelini A. The role of diagnostic hysteroscopy in infertile women. *Minerva Ginecol* 2001;53:313–319.

Buttram VC Jr, Gibbons WE. Mullerian anomalies: a proposed classification. (An analysis of 144 cases). *Fertil Steril* 1979;32:40–46.

Buttram VC Jr, Gomez M, Siegler A, DeCherney A, Gibbons W, March C. The American Fertility Society classifications of adnexal adhesions, distal tubal occlusion, tubal occlusion secondary to tubal ligation, tubal pregnancies, Mullerian anomalies and intrauterine adhesions. *Fertil Steril* 1988;49:944–955.

Byrne J, Nussbaum-Blask A, Taylor WS, Rubin A, Hill M, O’Donnell R, Shulman S. Prevalence of Mullerian duct anomalies detected at ultrasound. *Am J Med Genet* 2000;94:9–12.

Candiani GB, Fedele L, Zamberletti D, De Virgiliis D, Caneelli S. Endometrial patterns in malformed uteri. *Acta Eur Fertil* 1983;14:311–318.

Carrascosa P, Baronio M, Vallejos J, Capuas C, Borghi M, Papier S, Suedo C, Carrascosa J. Diagnosis of uterine malformations. Performance of CT virtual hysterosalpingography. *Journal fur Reproduktionsmedizin und Endokrinologie* 2010;7:340.

Carrington BM, Hricak H, Nurruddin RN, Secaf E, Laros RK Jr, Hill EC. Mullerian duct anomalies: MR imaging evaluation. *Radiology* 1990;176:715–720.

Chenia F, Hofmeyr GJ, Moolla S, Oratis P. Sonographic hydrotubation using agitated saline: a new technique for improving fallopian tube visualization. *Br J Radiol* 1997;70:833–836.

Clifford K, Rai R, Watson H, Regan L. An informative protocol for the investigation of recurrent miscarriage: preliminary experience of 500 consecutive cases. *Hum Reprod* 1994;9:1328–1332.
Cohen MA, Sauer MV, Keltz M, Lindheim SR. Utilizing routine sonohysterography to detect intruterine pathology before initiating hormone replacement therapy. Menopause 1999;6:68–70.

Cumming DC, Taylor PJ. Combined laparoscopy and hysteroscopy in the investigation of the ovulatory infertile female. Fertil Steril 1980;33:475–478.

Darbashtrafl H, Mohammad K, Moghadami-Tabrizi N. Ovarian malposition in women with uterine anomalies. Obstet Gynecol 1994;83:293–294.

Darbashtrafl H, Bahadoni M, Mohammad K, Alavi M, Moghadami-Tabrizi N, Zandinejad K, Ghafari V. Septate uterus: new idea on the histologic features of the septum in this abnormal uterus. Am J Obstet Gynecol 1995;172:105–107.

Deendrinos S, Grigorou O, Sakkas EG, Makrakis E, Creatsas G. Hysteroscopy in the evaluation of habitual abortions. Eur J Contracept Reprod Health Care 2008;13:198–200.

Deutsch TD, Abuhamad AZ. The role of 3-dimensional ultrasonography and magnetic resonance imaging in the diagnosis of Mullerian duct anomalies: a review of the literature. J Ultrasound Med 2008;27:413–423.

Dicker D, Goldman JA, Ashkenazi J, Feldberg D, Dekel A. The value of hysteroscopy in elderly women prior to in vitro fertilization-embryo transfer (IVF-ET): a comparative study. J In Vitro Fertil Embryo Transf 1990;7:267–270.

Diejomach MFE, Al-Azemi M, Jirous J, Bandar A, Egbase P, Al-Sweih N. Accuracy of three-dimensional ultrasound in the evaluation of Mullerian duct anomalies. North Am J Obstet Gynecol Clin North Am 1995;22:473–489.

Dedele L, Bianchi S, Hysteroscopic metroplasty for septate uterus. Obstet Gynecol Clin North Am 2000;27:81–101.

Dedele L, Bianchi S, Di Nola G, Franchi D, Candiani GB. Endometriosis and nonobstructive Mullerian anomalies. Obstet Gynecol 1992;79:515–517.

Dedele L, Bianchi S, Marchini M, Franchi D, Tozzi L, Dorta M. Ultrastructural aspects of endometrium in infertile women with septate uterus. Fertil Steril 1996;65:750–752.

Fischetti SG, Politi G, Lomeo E, Garozzo G. Magnetic resonance in the evaluation of habitual abortions. Hum Reprod 1998;13:2463–2473.

Fisher ND, Hargrave DF, Marchese SG, Muracca-Clements M, Garver KL. Etiology of recurrent pregnancy losses and outcome of subsequent pregnancies. Obstet Gynecol 1983;62:574–581.

Hartman A, Hartman M, Hartman J, Tur-Kaspa I. 3D ultrasound vs sonohysterography for the diagnosis of uterine anomalies: a prospective blinded study of 1000 consecutive women. Fertil Steril 2004;82:565.

Heinonen PK. Reproductive performance of women with uterine anomalies after abdominal or hysteroscopic metropotomy or no surgical treatment. J Am Assoc Gynecol Laparosc 1997;4:311–317.

Heinonen PK, Saanikoski S, Pystynen P. Reproductive performance of women with uterine anomalies. An evaluation of 182 cases. Acta Obstet Gynecol Scand 1982;61:157–162.

Hinchliff MD, Mills AA. 1000 office-based hysteroscopies prior to in vitro fertilization: feasibility and findings. JSLS 2004;8:103–107.

Homer HA, Li TC, Cooke ID. The septate uterus: a review of management and reproductive outcome. Fertil Steril 2000;73:1–14.

Japar de Sa Rosa e Silva AC, Rosa e Silva JC, Candido Dos Reis FJ, Nogueira AA, Ferriani RA. Routine office hysteroscopy in the investigation of infertile couples before assisted reproduction. J Reprod Med 2005;50:501–506.

Jayaprakasan K, Chan YY, Sur S, Deb S, Clewes JS, Raine-Fenning NJ. The prevalence of uterine anomalies and their impact upon early pregnancy in women conceived following assisted reproduction treatment. Ultrasound Obstet Gynecol 2011;37:727–732.

Jurkovic D, Geipel A, Gruboeck K, Jauniaux E, Naitucci M, Campbell S. Three-dimensional ultrasound for the assessment of uterine anatomy and detection of congenital anomalies: a comparison with hysterosalpingography and two-dimensional sonography [see comment]. Ultrasound Obstet Gynecol 1995;5:233–237.

Jurkovic D. Gruboeck K, Tailor A, Nicolaides KH. Ultrasound screening for congenital uterine anomalies. Br J Obstet Gynaecol 1997;104:1220–1321.

Kupesic S. Clinical implications of sonographic detection of uterine anomalies for reproductive outcome. Ultrasound Obstet Gynecol 2001;18:387–400.

Kupesic S. Three-dimensional ultrasound in reproductive medicine. Ultrasound Rev Obstet Gynecol 2005;5:304–315.

Kupesic S, Plavsic BM. 2D and 3D hysterosalpingo-contrast-sonography in the assessment of uterine cavity and tubal patency. Eur J Ob Gynecol Reprod Biol 2007;133:64–69.

Kupesic S, Kunjaj A, Skenderovic S, Beljsa D. Screening for uterine abnormalities by three-dimensional ultrasound improves perinatal outcome. J Perinat Med 2002;30:9–17.

Lafer-Narin S, Ragavendra N, Parmenter EK, Grant EG. False-normal appearance of the endometrium on conventional transvaginal sonography: comparison with saline hysterosonography. Am J Roentgenol 2002;178:129–133.

Lazzarin N, Vaquer E, Exacoustos C, Romanini E, Amadio A, Arduini D. Midluteal phase Doppler assessment of uterine artery blood flow in nonpregnant women having a history of recurrent spontaneous abortions: correlation to different etiologies. Fertil Steril 2007;87:1383–1387.

Leible S, Munoiz H, Walton R, Sabaj V, Cumsille F, Sepulveda W. Uterine artery blood flow velocity waveforms in pregnant women with mullerian duct anomaly: a biologic model for uteroplacental insufficiency. Am J Ob Gynecol Reprod Biol 1998;178:1048–1053.

Li S, Qayyum A, Coakley FV, Hricak H. Association of renal agenesis and mullerian anomalies with congenital uterine anomalies in women conceived in vitro fertilization: feasibility and findings. JSLS 2004;8:103–107.

Lin PC. Reproductive outcomes in women with uterine anomalies. J Womens Health (Larchmt) 2004;13:33–39.

Lindheim SR, Sauer MV. Upper genital tract screening with sonohysterography in patients receiving donated oocytes. Int J Ob Gynecol Obstet 1998;60:47–50.

Makino T, Hara T, Oka C, Toyoshima K, Sugi T, Iwashia K, Umeuchi M, Izuka R. Survey of 1120 Japanese women with a history of recurrent spontaneous abortion. Eur J Ob Gynecol Reprod Biol 1992a;44:123–130.

Makino T, Umeuchi M, Nakada K, Nozawa S, Izuka R. Incidence of congenital uterine anomalies in repeated reproductive wastage and prognosis for pregnancy after metropotomy. Int J Fertil 1992b;37:167–170.

Malek KA, Hassan M, Soliman A, El-sawah H, Azab AO. A prospective comparative study to assess the accuracy of MRI versus HSG in tubouterine causes of female infertility. Middle East Fertil Soc J 2005;10:250–257.
Malik E, Berg C, Szerzlik K, Stoz F, Rossmanith WG. Reproductive outcome of 32 patients with primary or secondary infertility and uterine pathology. Arch Gynecol Obstet 2000;264:24–26.

Maneschi F, Marana R, Muzii L, Mancuso S. Reproductive performance in women with bicornuate uterus. Acta Eur Fertil 1993;24:117–120.

Maneschi F, Zupi E, Marconi D, Valli E, Romanini C, Mancuso S. Hysteroscopically detected asymmetrical mullerian anomalies. Prevalence and reproductive implications. J Reprod Med 1995;40:684–688.

Montaz MM, Ebrashy AN, Marzouk AA. Three-dimensional ultrasonography in the evaluation of the uterine cavity. Middle East Fertil Soc J 2007;12:41–46.

Moore KL, Persaud TVN, Torchia MG. Rock JA, Schlaff WD. The obstetric consequences of uterovaginal anomalies. Clin Radiol 2003;58:747–754.

Seifert D, Maccario S, Visetin L, DiGregorio A. Hysteroscopy in an IVF-ER program. Clinical experience with 360 infertile patients. Acta Obstet Gynecol Scand 1987;66:135–137.

Sharma FN, Lee G, Gutmann JN, Lavy G. The role of office hysteroscopy in vitro fertilization. Fertil Steril 1992;58:1237–1239.

Shokeir T, Abdelshafeed M. Sonohysterography as a first-line evaluation for uterine abnormalities in women with recurrent failed in vitro fertilization-embryo transfer. Fertil Steril 2009;91:1321–1322.

Shuqink M, Xuming B, Jinghe L. Pregnancy and its outcome in women with malformed uterus. Chin Med Sci J 2002;17:242–245.

Sun Y, Fang L, Su Y, Guo Y. Uterine cavity shape and the best site for embryo transfer. Fertil Steril 2001;75:788–790.

Taylor PJ, Lewinthal D, Leader A, Pattinson HA. A comparison of Dextran 70 with SHG (SHG) for intrauterine abnormalities in infertility compared to two dimensional hysterosalpingography. Hum Reprod 2009;24:886–911.

Valli E, Vaquero E, Lazzarin N, Romanini C. Tale PJ, Lewinthal D, Leader A, Pattinson HA. A comparison of Dextran 70 with SHG (SHG) for intrauterine abnormalities in infertility compared to two dimensional hysterosalpingography. Hum Reprod 2009;24:886–911.

Sun Y, Fang L, Su Y, Guo Y. Uterine cavity shape and the best site for embryo transfer. Fertil Steril 2001;75:788–790.

Taylor PJ, Lewinthal D, Leader A, Pattinson HA. A comparison of Dextran 70 with SHG (SHG) for intrauterine abnormalities in infertility compared to two dimensional hysterosalpingography. Hum Reprod 2009;24:886–911.
van Iddekinge B, Hofmeyr GJ. Recurrent spontaneous abortion—aetiological factors and subsequent reproductive performance in 76 couples. *S Afr Med J* 1991; **80**:223–226.

Ventolini G, Zhang M, Gruber J. Hysteroscopy in the evaluation of patients with recurrent pregnancy loss: a cohort study in a primary care population. *Surg Endosc* 2004; **18**:1782–1784.

Weiss A, Shalev E, Romano S. Hysteroscopy may be justified after two miscarriages. *Hum Reprod* 2005; **20**:2628–2631.

Woelfer B, Salim R, Banerjee S, Elson J, Regan L, Jurkovic D. Reproductive outcomes in women with congenital uterine anomalies detected by three-dimensional ultrasound screening. *Obstet Gynecol* 2001; **98**:1099–1103.

Zanetti E, Ferrari LR, Rossi G. Classification and radiographic features of uterine malformations: hysterosalpingographic study. *Br J Radiol* 1978; **51**:161–170.

Zlopasa G, Skrablin S, Kalafatic D, Banovic V, Lesin J. Uterine anomalies and pregnancy outcome following resectoscope metroplasty. *Int J Gynaecol Obstet* 2007; **98**:129–133.

Zupi E, Solima E, Marconi D, Valli E, Romanini C. Uterine anomalies prevalence and reproductive outcome in women undergoing diagnostic hysteroscopy. *Gynaecol Endosc* 1996; **5**:147–150.

Wu MH, Hsu CC, Huang KE. Detection of congenital mullerian duct anomalies using three-dimensional ultrasound. *J Clin Ultrasound* 1997; **25**:487–492.

Zanetti E, Ferrari LR, Rossi G. Classification and radiographic features of uterine malformations: hysterosalpingographic study. *Br J Radiol* 1978; **51**:161–170.

Zlopasa G, Skrablin S, Kalafatic D, Banovic V, Lesin J. Uterine anomalies and pregnancy outcome following resectoscope metroplasty. *Int J Gynaecol Obstet* 2007; **98**:129–133.