**TOPIC 12 · PREGNANCY LOSS & RECURRENT PREGNANCY LOSS**

What we know about common causes, evaluation, prognosis, treatment options and trying again.

## Why 8 core sources?

Eight is the ideal number here. The topic needs to cover both a single early miscarriage and recurrent pregnancy loss without treating them as the same condition. The selected sources include the newest ASRM and ESHRE guidelines, ACOG guidance on early pregnancy loss, prospective prognosis data, lifestyle evidence and three treatment areas that often generate exaggerated expectations: progesterone, PGT-A and anticoagulation.

## The evidence in context

Pregnancy loss is common, and most isolated early miscarriages are related to sporadic chromosomal abnormalities, particularly with increasing maternal age. Recurrent pregnancy loss is a distinct clinical condition, and major scientific societies now support evaluation after two losses. Investigation should be targeted: genetic factors, uterine anatomy, antiphospholipid syndrome, endocrine conditions and other factors are assessed according to history. Even after repeated losses, many women ultimately achieve live birth. Crucially, no treatment is a universal solution: progesterone, PGT-A, heparin/aspirin and other interventions have specific indications, differing levels of evidence and do not apply to everyone.

## 1. ASRM Practice Committee (2026)

**Recurrent pregnancy loss: a committee opinion**

Original source

**What it studied** → The newest American Society for Reproductive Medicine guidance on the definition, evaluation and management of recurrent pregnancy loss (RPL). ASRM now defines RPL as the spontaneous loss of two or more pregnancies, including biochemical pregnancies.

**What it found** → ASRM emphasises that most isolated miscarriages are sporadic and often genetic, with a strong influence of maternal age. RPL requires a dedicated systematic evaluation that may address genetic, anatomical, endocrine, immune and other factors. In a substantial proportion, no single clear cause is identified.

**What it means in practice** → RPL should not be dismissed as repeated 'bad luck', nor treated as a single diagnosis. After two losses, targeted evaluation and an individualised discussion of prognosis and treatment options are appropriate.

**Limitations** → A committee opinion synthesising a large and heterogeneous evidence base. For several proposed treatments, certainty of evidence remains limited or conflicting.

## 2. ESHRE Guideline Development Group (2023)

**ESHRE Guideline: Recurrent Pregnancy Loss - Update 2022**

Original source

**What it studied** → A European evidence-based guideline on recurrent pregnancy loss covering definition, diagnosis, prognosis, investigation and treatment.

**What it found** → ESHRE defines RPL as the loss of two or more pregnancies and emphasises evidence-based targeted investigation rather than broad testing without clear clinical utility. It also recognises substantial psychological burden and the importance of patient-centred care.

**What it means in practice** → The purpose of evaluation is not to 'find something at any cost', but to identify factors that genuinely alter prognosis or management and to avoid unnecessary, expensive or unproven interventions.

**Limitations** → Some recommendations rely on low- or very-low-certainty evidence because large, high-quality RCTs are still lacking in several areas of RPL.

## 3. ACOG (2018)

### Early Pregnancy Loss - Practice Bulletin No. 200

Original source

**What it studied** → An ACOG guideline on the diagnosis and management of early pregnancy loss, emphasising diagnostic certainty and expectant, medical and surgical management options.

**What it found** → Early pregnancy loss is common and many cases are related to embryonic chromosomal abnormalities. ACOG stresses that diagnosis should be confirmed before intervention and that several safe management options exist depending on clinical circumstances and patient preference.

**What it means in practice** → A single miscarriage does not by itself mean there is a chronic fertility problem. Good care after loss includes accurate diagnosis, management choices and clear information - not premature conclusions or blame.

**Limitations** → This guideline focuses mainly on early pregnancy loss and its management rather than the full recurrent-pregnancy-loss spectrum.

## 4. Nielsen et al. (2024)

### Evaluating risk factors in recurrent pregnancy loss: a prospective cohort study and its impact on live birth outcomes

Original source

**What it studied** → A large prospective cohort from a specialist Danish RPL unit assessing the prevalence of different clinical risk factors and their relationship with live birth in subsequent pregnancy.

**What it found** → RPL proved to be heterogeneous: different risk factors coexisted in different women and influenced prognosis in different ways. Despite a history of loss, a substantial proportion achieved live birth in a subsequent pregnancy.

**What it means in practice** → A history of RPL does not mean another miscarriage is inevitable. Individual prognosis should incorporate age, number and pattern of previous losses, investigation findings and the wider clinical picture.

**Limitations** → A specialist tertiary-centre cohort with possible referral bias. Observed associations do not prove that every risk factor is causal.

## 5. Ng et al. (2021)

**Systematic review and meta-analysis of female lifestyle factors and risk of recurrent pregnancy loss**

Original source

**What it studied** → A systematic review and meta-analysis of modifiable lifestyle factors in women with recurrent pregnancy loss, including BMI, smoking, alcohol and caffeine.

**What it found** → Obesity and some other lifestyle factors were associated with higher RPL or subsequent-loss risk, but evidence for many factors was limited or inconsistent.

**What it means in practice** → General health and reduction of clear risks matter, but it is not appropriate to attribute a miscarriage to one food, one coffee, one stressful day or one isolated behaviour.

**Limitations** → Predominantly observational evidence, potential confounding and limited data for several exposures. Associations do not prove that changing one factor will prevent the next miscarriage.

## 6. Haas et al. / Cochrane (2025)

**Progestogen for preventing miscarriage in women with recurrent miscarriage of unclear etiology**

Original source

**What it studied** → An updated Cochrane assessment of progestogens for preventing miscarriage in women with recurrent miscarriage, with live birth as a major outcome.

**What it found** → For women with recurrent miscarriage of unclear aetiology, progestogens probably make little or no difference to live birth compared with placebo, based on moderate-certainty evidence for this outcome.

**What it means in practice** → Progesterone should not be presented as a universal treatment for every woman with RPL. Its use depends on the specific clinical scenario, symptoms and current guidance.

**Limitations** → Different progestogens, routes of administration and clinical scenarios were included. Conclusions for unexplained RPL do not automatically apply to threatened miscarriage or particular subgroups.

## 7. Mumusoglu et al. (2025)

**Preimplantation genetic testing for aneuploidy in unexplained recurrent pregnancy loss: a systematic review and meta-analysis**

Original source

**What it studied** → A systematic review/meta-analysis of IVF with PGT-A in women with unexplained RPL, assessing pregnancy loss and reproductive outcomes.

**What it found** → The analysis reported lower clinical pregnancy loss and higher live-birth rates per transfer and per patient with PGT-A. However, the authors judged the evidence to be low quality and called for well-designed RCTs against expectant management.

**What it means in practice** → PGT-A may be an option in selected cases, but it is not an established universal solution for unexplained RPL. Its value should be discussed in relation to

age, time, cost, IVF burden and personal priorities.

**Limitations** → Mainly low-quality non-randomised evidence, selection bias and per-transfer comparisons that may favour a PGT-A strategy. Superiority over natural conception/expectant management has not been proven in an RCT.

## 8. Hamulyák et al. / Cochrane (2020)

**Aspirin or heparin or both for improving pregnancy outcomes in women with persistent antiphospholipid antibodies and recurrent pregnancy loss**

Original source

**What it studied** → A Cochrane systematic review of aspirin, heparin or their combination in women with persistent antiphospholipid antibodies and recurrent pregnancy loss.

**What it found** → Heparin combined with low-dose aspirin may increase live birth in women meeting relevant antiphospholipid-syndrome criteria, although certainty is not high for all comparisons.

**What it means in practice** → This is an important example of targeted treatment: when a specific evidence-based factor such as APS is identified, a specific treatment may exist. It does not justify empirical anticoagulation for every case of unexplained RPL.

**Limitations** → A small evidence base, differing heparin regimens and uncertainty for several outcomes. Findings apply to women with antiphospholipid antibodies/APS, not unexplained RPL without them.

## Library conclusion

The website should communicate two messages at once. First, a miscarriage is often a sporadic biological event and is not evidence that a woman did something wrong. Second, repeated losses warrant organised, evidence-based evaluation and individualised care. Prognosis is not identical to past history: even in unexplained RPL, the chance of a future live birth can remain meaningful. No complementary or psychological intervention should be presented as a proven method of preventing miscarriage.

## Template for future maintenance

Maintain separate evidence categories for sporadic early pregnancy loss, RPL definition/evaluation, prognosis, genetic/chromosomal factors, APS/thrombosis, uterine/endocrine factors, progesterone, PGT-A and lifestyle. For each new study, identify whether the outcome is miscarriage rate, ongoing pregnancy or live birth and whether the population is unexplained RPL or a defined subgroup. For every source: Full citation + link → What it studied → What it found → What it means in practice → Limitations → Date last reviewed.