



Recurrent Pregnancy Loss: Beyond Euploid Embryo Transfer and Towards Equitable Early Pregnancy Care

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AT THE European Society of Human Reproduction and Embryology (ESHRE) Annual Meeting 2026, held in London, UK, Session 81, 'Unravelling Pregnancy Loss: Maternal Age, Inflammation, Uterine Environment, and Therapeutic Innovations', brought together experts to explore the complex biological, clinical, and healthcare factors contributing to pregnancy loss. The session examined recurrent pregnancy loss (RPL) from complementary perspectives, ranging from the role of embryo selection and reproductive technologies to national trends in pregnancy loss and inequalities in access to early pregnancy care.

Barbara Lawrenz, ART Fertility Clinics, Abu Dhabi and Al Ain, United Arab Emirates, presented evidence evaluating whether preimplantation genetic testing for aneuploidy (PGT-A) improves reproductive outcomes in women with unexplained RPL. Sindhu Sekar, University of Liverpool and Liverpool Women's NHS Foundation Trust, UK, subsequently presented a 20-year joinpoint analysis of miscarriage and ectopic pregnancy admissions in England, highlighting evolving patterns of hospital admissions alongside persistent socioeconomic inequalities that continue to shape women's access to specialist early pregnancy services.

RECURRENT PREGNANCY LOSS AND THE ROLE OF PGT-A

RPL remains a challenging condition, affecting approximately 1–2% of couples attempting to conceive. Although embryonic aneuploidy is recognised as a major cause of sporadic miscarriage, whether selecting euploid embryos through PGT-A improves outcomes in women with RPL remains uncertain.¹

Current ESHRE and American Society for Reproductive Medicine (ASRM) guidance does not recommend routine PGT-A for unexplained RPL, citing insufficient evidence that it improves live birth rates while acknowledging the associated financial costs and treatment burden.^{2,3}

Lawrenz emphasised that despite increasing use of PGT-A in clinical

practice, evidence supporting its benefit specifically in women with unexplained RPL remains limited.

Study Design

The investigators performed a retrospective cohort study including women with unexplained RPL who achieved pregnancy either following euploid embryo transfer after PGT-A or through spontaneous conception.

Patients with uterine abnormalities, endocrine disorders, antiphospholipid syndrome, thrombophilia, parental chromosomal abnormalities, or other

1–2%

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recognised causes of miscarriage were excluded. The analysis compared pregnancy outcomes between women undergoing IVF with PGT-A and frozen transfer of a euploid embryo and women who conceived spontaneously.

The primary outcome was the live birth rate. Secondary outcomes included miscarriage rate and cumulative live birth.

Baseline Characteristics

Women undergoing PGT-A were generally older than those conceiving spontaneously, with a median maternal age of 37 years compared with 33 years in the spontaneous conception group. The PGT-A cohort also demonstrated higher ovarian reserve markers, including anti-Müllerian hormone concentrations, and lower baseline follicle-stimulating hormone levels.

The median number of previous pregnancy losses was similar between groups.

Live Birth Rates Were Comparable

No statistically significant difference in live birth rates was observed between the two groups. Women who underwent euploid embryo transfer achieved live birth rates comparable to those who conceived naturally.

Similarly, miscarriage rates following confirmation of pregnancy were not significantly different between groups.

When cumulative live birth rates were assessed, no advantage of the PGT-A strategy was demonstrated.

Maternal Age Remained the Strongest Predictor

Consistent with previous evidence, maternal age remained an important determinant of reproductive outcome. Increasing age was associated with declining live birth rates, irrespective of whether pregnancy occurred following euploid embryo transfer or spontaneous conception.

“Maternal age remained an important determinant of reproductive outcome”

The findings suggest that while embryo aneuploidy contributes substantially to miscarriage risk, selecting euploid embryos alone does not overcome the multifactorial mechanisms underlying RPL.



Clinical Implications

Lawrenz concluded that current evidence does not support routine use of PGT-A solely for the indication of unexplained RPL. The findings are consistent with existing systematic review data demonstrating no improvement in live births despite euploid embryo selection.¹

The presentation highlighted that RPL is likely driven by multiple biological mechanisms beyond embryonic chromosomal status. Consequently, transferring a chromosomally normal embryo does not necessarily translate into improved reproductive outcomes.

The speaker emphasised that careful patient counselling remains essential, particularly given the emotional, physical, and financial burden associated with IVF and PGT-A treatment.

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Conclusion

The study adds to growing evidence suggesting that routine euploid frozen embryo transfer does not improve live birth rates in women with unexplained RPL. These findings support current ESHRE and ASRM recommendations, which advise against routine PGT-A for unexplained RPL outside carefully selected clinical scenarios.^{2,3} Further prospective studies are needed to identify whether specific patient subgroups may benefit from embryo selection strategies.

CHANGING TRENDS IN PREGNANCY LOSS: PERSISTENT INEQUALITIES ACROSS ENGLAND

Sekar presented findings from a 20-year joinpoint analysis of miscarriage and ectopic pregnancy admissions in England, exploring how changes in clinical practice, healthcare

delivery, and population demographics have shaped patterns of pregnancy loss over the past 2 decades. Sekar opened the presentation by highlighting that miscarriage and ectopic pregnancy remain major public health challenges despite declining fetal and infant mortality rates. Around 23 million miscarriages occur worldwide each year, affecting approximately one in four pregnancies, while the impact extends far beyond the initial loss. Increasing evidence suggests that RPL is associated with long-term adverse maternal health outcomes, including venous thromboembolism and cardiovascular disease, yet pregnancy loss remains under-recognised and underfunded. Moreover, because many miscarriages occur before women access maternity services, the true burden remains underestimated in routine healthcare datasets.⁴

Twenty Years of National Data

To better understand long-term trends, the investigators analysed publicly available data from Hospital Episode Statistics (HES) and the Maternity Services Data Set (MSDS), examining hospital admissions for miscarriage and ectopic pregnancy in England between 2004–2024.

The researchers employed joinpoint regression analysis, a statistical method widely used in epidemiological surveillance to identify points at which significant changes in trends occur over time. Originally developed for cancer surveillance, the approach is now frequently used to inform healthcare policy and monitor changes in disease incidence and outcomes.^{5,6} The analysis also examined admission patterns according to maternal age and socioeconomic deprivation.

Changing Patterns of Miscarriage Admissions

Joinpoint analysis demonstrated a significant decline in miscarriage admissions between 2010–2018 (annual percentage change [APC]: –2.06%), followed by a non-significant increase between 2021–2024 (APC: +2.70%).



Sekar suggested that the reduction after 2010 likely reflected changes in service delivery rather than a true reduction in miscarriage incidence. During the early 2000s, Early Pregnancy Assessment Units (EPAU) became increasingly established across the UK, enabling more women to receive outpatient assessment and management. This shift was further supported by the National Institute for Health and Care Excellence (NICE) guidance recommending expectant, medical, and surgical management within specialist early pregnancy services where clinically appropriate.^{7,8}

The more recent increase in admissions appears multifactorial. While COVID-19 has been associated with miscarriage through several immunopathological mechanisms, Sekar cautioned that the resurgence cannot be explained by the pandemic alone. Increasing maternal age, rising obesity prevalence, environmental influences, and other established miscarriage risk factors are also likely to have contributed to the observed trends.⁹

Ectopic Pregnancy Admissions Followed a Similar Pattern

Hospital admissions for ectopic pregnancy also demonstrated significant changes over

time, with a marked increase between 2005–2012 (APC: +2.81%) and a further significant increase between 2021–2024 (APC: +4.28%).

The earlier increase coincided with evolving guidance on ectopic pregnancy management. Sekar highlighted that publication of the Royal College of Obstetricians and Gynaecologists Green-top Guideline promoted earlier diagnosis, laparoscopic management where appropriate, and the use of methotrexate in carefully selected women with suitable follow-up protocols.¹⁰

The presentation also highlighted the growing clinical challenge posed by pregnancies of unknown location. Improvements in pregnancy testing allow pregnancy to be detected before ultrasound can reliably visualise an intrauterine gestation, resulting in increasing numbers of women requiring serial assessment and follow-up. Alongside this, rising rates of obesity, pelvic inflammatory disease, sexually transmitted infections, endometriosis, assisted reproductive technologies, and previous Caesarean delivery may all be contributing to increasing ectopic pregnancy admissions.

Persistent Socioeconomic Inequalities

Perhaps the most striking finding was that improvements in clinical care have not translated into reductions in socioeconomic inequalities.

Women living in the most deprived areas experienced approximately 2.7-fold higher hospital admission rates for miscarriage and 2.4-fold higher admission rates for ectopic pregnancy than women living in the least deprived communities. Importantly, these disparities remained largely unchanged throughout the study period.

Sekar suggested that multiple interacting factors likely underpin these differences. Women living in deprived areas tend to be younger but also experience higher prevalence of recognised risk factors, including smoking, obesity, and sexually transmitted infections. Reduced access to timely maternity care may further compound these risks.

To explore this further, the investigators compared national deprivation maps with the geographical distribution of EPAUs across England. The analysis demonstrated an apparent mismatch between areas with the greatest socioeconomic deprivation and the availability of specialist early pregnancy services, suggesting that women at highest risk may face the greatest barriers to accessing appropriate care.

Implications for Policy and Future Research

The findings highlight several priorities for improving pregnancy loss care.

Sekar suggested that expanding EPAU capacity, strengthening workforce training,

and improving referral pathways could help reduce inequalities in access to specialist care. Targeted prevention strategies addressing modifiable risk factors, including smoking, obesity, and sexually transmitted infections, alongside greater use of digital platforms to deliver evidence-based reproductive health information, may further improve outcomes.

The presentation also identified several priorities for future research, including improving understanding of women's experiences of accessing EPAUs, evaluating long-term reproductive and mental health outcomes following pregnancy loss, integrating preconception care into early pregnancy services, and addressing the longstanding underinvestment in pregnancy loss research.

Conclusion

Concluding the presentation, Sekar emphasised that although pregnancy loss is common, its impact is profoundly personal. Behind every hospital admission is a woman, a family, and often unanswered questions about why the loss occurred and whether it could happen again.

While advances in specialist early pregnancy care have transformed management over the past 2 decades, the findings demonstrate that persistent inequalities remain. Reducing the burden of miscarriage and ectopic pregnancy will require not only continued improvements in clinical care, but also equitable access to specialist services, investment in prevention, and research focused on answering the questions that matter most to patients.



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