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Lynch syndrome for the gynaecologist

Lynch syndrome is an **autosomal dominant condition**

increased risk of **both endometrial and ovarian cancer.**

Gynaecological cancer is often **the first cancer diagnosis in women with Lynch syndrome.**

Colorectal cancer is the **most common** and **lethal cancer** seen in Lynch syndrome carriers.

Early diagnosis allows women to be enrolled in cancer surveillance programmes and enables cascade testing for their at-risk family members. There is a well-documented survival advantage for those with Lynch syndrome who are compliant with colonoscopic surveillance for bowel polyps. In addition, early identification of Lynch syndrome can enable the uptake of cancer risk-reducing strategies, including taking aspirin and lifestyle modification. The gynaecologist, therefore, has a crucial role in diagnosing Lynch syndrome and advising women of its implications

Germline sequencing is the definitive test for Lynch syndrome and must always be preceded by **informed consent taken by a trained individual.**

Up to **95%** of **Lynch syndrome carriers are unaware.**

Lynch syndrome may occur in up to people 1 in 278 making it **the most common inherited cause of cancer.**

Lynch syndrome arises from inherited mutations, in the genes encoding the proteins of the highly conserved DNA mismatch repair (MMR) system repair, known as pathogenic variants, affecting **MLH1, MSH2, MSH6 and PMS2, the MMR genes** responsible for ensuring fidelity during DNA replication.

Less commonly, inherited inactivation of the MMR system can arise from germline hypermethylation of the promoter region of MLH1

Table 1. The cumulative risk of endometrial and ovarian cancer in women with Lynch syndrome at 40 and 70 years of age, stratified by mutated gene

Gene	Endometrial cancer	
	Cumulative incidence at 40 years % (95% CI)	Cumulative incidence at 70 years % (95% CI)
<i>MLH1</i>	3.1 (0.4–5.8)	42.7 (33.1–52.3)
<i>MSH2</i>	1.5 (0.0–4.4)	56.7 (41.8–71.6)
<i>MSH6</i>	0	46.2 (27.3–65.0)
<i>PMS2</i>	0	26.4 (0.8–51.9)
Ovarian cancer		
	Cumulative incidence at 40 years % (95% CI)	Cumulative incidence at 70 years % (95% CI)
<i>MLH1</i>	2.6 (0.1–5.2)	10.1 (4.8–15.4)
<i>MSH2</i>	3.8 (0.0–8.0)	16.9 (5.7–28.0)
<i>MSH6</i>	4.2 (0.0–12.3)	13.1 (0.0–31.2)
<i>PMS2</i>	0	0

Abbreviations: CI = confidence interval

Cumulative lifetime risks of cancer in Lynch syndrome

Ovarian Up to 17%

Endometrial Up to 57%

Colorectal Up to 47%.

Table 2. An overview of cancer risk-reducing strategies for women with Lynch syndrome

Considerations	Hysterectomy (± bilateral salpingo-oophorectomy)	Aspirin	Lifestyle (smoking cessation, reduce weight, increase exercise, healthy diet)	Hormone-based therapy
<i>Target population</i>	Female LS carriers, family completed	All LS carriers, especially those with a raised BMI	All LS carriers	Females of reproductive age
<i>Timing</i>	For path_MLH1 and path_MSH2 at 35 years For path_MSH6 at 40 years For path_PMS2 at 50 years	From 18 years	Any age	From the age of menarche until natural age of menopause
<i>Mechanism of action</i>	Removes organs prone to cancer	Not fully understood	General cancer risk factor reduction	Reduced endometrial proliferation, anti-inflammatory effect
<i>Evidence</i>	Retrospective cohorts	Large international randomised controlled studies	Limited evidence in LS populations mostly drawn from non-LS population and small retrospective cohort data	Retrospective cohort data
<i>Contraindications</i>	Surgical and anaesthetic contraindications, wish for future fertility	Peptic ulcer disease, bleeding disorders/haemophilia, severe cardiac failure, active alcohol abuse	Those with pre-existing health conditions that would prohibit excessive physical exercise	History of estrogen-dependent or breast cancer, active arterial thromboembolic disease, undiagnosed vaginal bleeding, thrombophilia disorder, history of venous thromboembolism
<i>Harms</i>	Surgical harms such as infection, pain, visceral injury, death, etc. Also risks of early menopause (if BSO) such as vasomotor symptoms, increased risk of cardiovascular disease, osteoporosis	Dyspepsia, haemorrhage (usually minor as young population – trial data would support prescription unless any contraindications)	None	Dysuria, skin reactions, mood alterations
<i>Unknowns</i>	Whether two-stage surgical procedure to remove uterus after childbearing and ovaries after menopause improves outcomes	Optimal dosage	The effectiveness of such strategies in LS-specific cancer risk	Benefit of intrauterine systems in reducing endometrial cancer risk in LS carriers

Abbreviations: BMI = body mass index; BSO = bilateral salpingo-oophorectomy; EC = endometrial cancer; LS = Lynch syndrome; OC = ovarian cancer; path_ = pathogenic variant

Not all women with Lynch syndrome **wish to undergo riskreducing gynaecological surgery**; indeed, fertility-sparing options are required for those who wish to pursue motherhood.

Gynaecological surveillance aims to reassure women or **detect cancer at a precancerous or early stage** to improve morbidity and survival outcomes.

Table 3. Gynaecological surveillance methodologies currently used in women with Lynch syndrome

Type of cancer	Surveillance method	Benefit	Disadvantage	Estimated sensitivity (%)	Estimated specificity (%)
Endometrial cancer	Pelvic ultrasound	Cheap, widely accessible, acceptable to women, minimal complications, can assess ovaries	In premenopausal women, difficult to interpret; no tissue diagnosis; risk of incidental findings	15–100	55–100
	Endometrial biopsy	Outpatient procedure, tissue diagnosis, widely accessible	Painful, risk of infection/perforation, sampling error, need for repeat procedure	80–100	60–100
	Outpatient hysteroscopy ± directed biopsy	Outpatient procedure, tissue diagnosis, widely accessible, target biopsy	Small evidence base in LS, risk of infection/perforation, visceral injury, relatively expensive, can be prohibitively painful	90–100	90–100
Ovarian cancer	Pelvic ultrasound	Cheap, widely accessible, acceptable to women, minimal complications, can assess endometrium	Small evidence base in LS, high rate of incidental findings leading to unnecessary interventions	10–60	40–100
	Serum CA125	Cheap, widely accessible, acceptable to women, minimal complications, can be done in primary care	Small evidence base in LS, nonspecific and therefore can lead to unnecessary anxiety and intervention	20–58	80–98
	Combined (CA125 + pelvic ultrasound)	Cheap, widely accessible, acceptable to women, minimal complications, can assess endometrium, improved sensitivity compared with ultrasound alone	As above	70–89	80–99

NB: Sensitivity and specificity data for ovarian cancer is taken from wild type and other high-risk populations; the figures in women with Lynch syndrome are not known. CA125 = cancer antigen 125; LS = Lynch syndrome

The prevalence of Lynch syndrome in women with **endometrial** and **ovarian cancer** is around **3%** and **1–2%**, respectively.

There is an emerging consensus that all women with **endometrial cancer** should be screened for Lynch syndrome, **where resources permit**.

NICE recommends. Where resources are limited, testing can be restricted to those **who develop endometrial cancer under the age of 70 years**, or where other clinical features are suggestive of Lynch syndrome; for example, a strong family history of Lynch syndrome-associated cancers.

Ideally, women with Lynch syndrome should be seen at around the **age of 25 years** by an expert gynaecologist to learn about **the red flag symptoms of cancer**, discuss family planning and explore risk-reducing strategies.

Raising awareness about red flag symptoms empowers women to seek help appropriately.

The survival benefit achieved by risk-reducing surgery is **minimal** because Lynch syndrome-associated endometrial and ovarian cancers have a good prognosis. However, for many women with Lynch syndrome, avoiding a cancer diagnosis and the harms associated with its treatment is sufficient to choose risk-reducing surgery.

Preoperative counselling by both a clinical geneticist and gynaecologist is seen as best practice.

The laparoscopic approach is preferred because it leads to a shorter recovery time and improved short-term quality of life.

where possible, hysterectomy should be coordinated with other risk-reducing interventions, such as colonoscopy or colorectal surgery.

Hysterectomy and bilateral salpingo-oophorectomy at 40 years of age has been shown to be a cost-effective strategy.

The lifetime risk of gynaecological cancer is sufficiently high to **offer total hysterectomy** and **bilateral salpingo-oophorectomy for women with Lynch syndrome who have completed childbearing**

Risk-reducing strategies

Hysterectomy

The lifetime risk of gynaecological cancer is sufficiently high to **offer total hysterectomy +/- bilateral salpingo-oophorectomy for women with Lynch syndrome who have completed childbearing.**

The timing of such surgery is **gene-specific** .

Preoperative counselling by both a clinical geneticist and gynaecologist is seen as best practice.

The laparoscopic approach is preferred because it leads to a shorter recovery time .

Aspirin has been shown to **reduce the risk of cancer in Lynch syndrome.**

The oral contraceptive pill reduces the risk of sporadic ovarian and endometrial cancer, and the levonorgestrel-releasing intrauterine system reduces the risk of endometrial cancer in the general population, so it is thought these may also reduce cancer risk in Lynch syndrome.

While few studies have specifically explored the effect of lifestyle choices on cancer risk in Lynch syndrome, smoking cessation, maintaining a healthy body mass index and increased exercise are thought sensible

Gynaecological surveillance There is currently **no strong evidence to support gynaecological surveillance for the early detection of gynaecological cancer in Lynch syndrome.**

Tumour-based testing Germline testing

Tumour-based testing does not identify people with Lynch syndrome; it stratifies their risk for the condition. This is important because it is widely accepted that tumour-based tests can be done **without explicit consent**. They are used to identify individuals who should undergo definitive,

Immunohistochemistry tests for **loss of MMR protein expression** (MMR deficiency).

There is **a relative lack of specificity**, associated with somatic **loss of MMR expression**.

Microsatellites are repeated DNA motifs. If **microsatellite instability is high**, **Lynch syndrome is more likely**.

germline testing is the **only way** in which a Lynch syndrome diagnosis can be made.

It is expensive and can only be done in specialist centres.

These tumours are very immunogenic, eliciting a marked and unique immune response .

The main mechanism of immune evasion seen in MMR-deficient cancers is exploitation of **the PD-1/PD-L1 pathway**.

Novel strategies are being tested to harness the Lynch syndrome patient's own immune system to **prevent cancers** through **vaccination**.

Novel diagnostic methods, with the potential for complete automation, are in development.

Such technologies would **simplify and reduce the costs of Lynch syndrome screening and diagnostic pathways**.

SBA 1

With regard to Lynch syndrome, which of the following is false

- A) most carriers of the mutation associated with the syndrome know they have the condition.
- B) the first cancers associated with the syndrome are predominantly endometrial or ovarian cancers.
- C) when cancers occur, they have in them an unusually high immune infiltrate.

B) most carriers of the mutation associated with the syndrome know they have the condition.

SBA 2**Which of the following false**

- A . consent must be sought before definitive germline testing for Lynch syndrome by a trained professional.**
- B . immunohistochemical staining of tumours for the mismatch repair proteins or microsatellite instability analysis are recognised ways of screening cancers for characteristics suggestive of the syndrome.**
- C . the National Institute for Health and Care Excellence endorses universal screening of colorectal cancer patients for Lynch syndrome.**
- D . most gynaecological cancers found to have aberrant mismatch repair immunohistochemical staining will be in those with the syndrome.**
- E . the addition of MLH1 promotor hypermethylation testing in a Lynch syndrome diagnostic pathway improves specificity.**

E . the addition of MLH1 promotor hypermethylation testing in a Lynch syndrome diagnostic pathway improves specificity.

Less commonly, inherited inactivation of the MMR system can arise from germline hypermethylation of the promoter region of MLH1

SBA 3

Regarding gynaecological surveillance in women with Lynch syndrome, which of the following is false

- A . there is strong evidence to recommend its use.
- B. this should be offered to women around 25 years of age.
- C . counselling should include education on red flag symptoms of cancer and risk reducing surgery.

A . there is strong evidence to recommend its use.

Surveillance for gynaecological cancer in women with Lynch syndrome **remains controversial**; more robust data are needed to determine its effectiveness.

SBA 4

With regard to risk-reducing strategies for women with Lynch syndrome,

Which of the following is false

- A. hysterectomy is strongly recommended for all those with the syndrome.
- B. the timing of risk-reducing surgery depends on the syndrome gene.
- C. where possible, a laparoscopic approach is recommended.
- D. aspirin is not recommended as a means of reducing their overall cancer risk.

D. aspirin is not recommended as a means of reducing their overall cancer risk.

SBA 5

Regarding Lynch syndrome-associated gynaecological cancers,
Which of the following is false ?

- A . endometrial types that arise as a result of the syndrome have a poorer prognosis than sporadic types.
- B . checkpoint inhibition of the PD-1/PD-L1 pathway has been shown to be very effective in mismatch repair-deficient cancers.
- C. vaccination against these cancers is currently the focus of research.

A . endometrial types that arise as a result of the syndrome have a poorer prognosis than sporadic types.

Raised CA125

Raised CA125

CA125 may be elevated in many benign and malignant conditions.

a normal level of CA125 is considered to be **<35 IU/ml**.

Ovarian cancer is the **leading cause of death** from any gynaecological malignanc

Over 70% of women diagnosed will present with **late stage disease** (stage III or IV)

CA125 measurement during follow-up is not mandatory.

Serum CA125 levels are often **elevated in ovarian epithelial cancers** but

less commonly seen to be in **non-epithelial cancers of the ovary**.

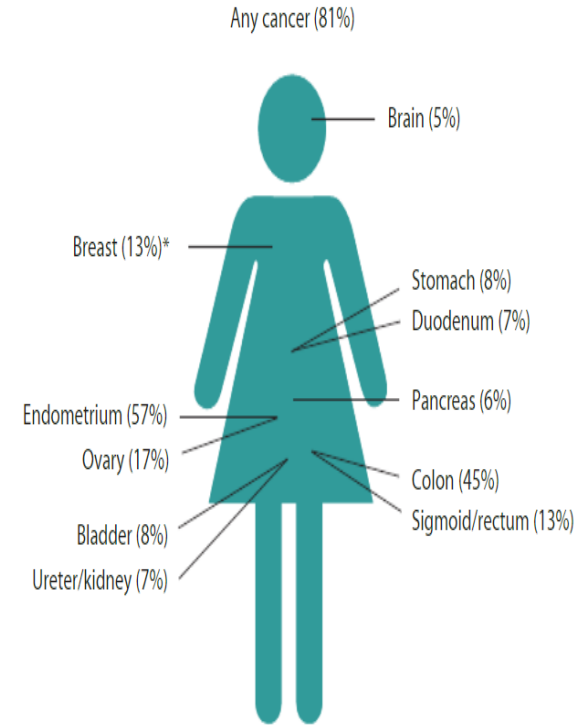


Figure 1. Percentage maximum risk of cancer in females at 75 years of age across different pathogenic gene variants. *In path_PMS2, the risk of breast cancer could be as high as 55%, but the data are of poor quality because of low incidence.

CA125 screening is used in the diagnosis of symptomatic patients.

no evidence to suggest that screening postmenopausal women with a one-off CA125 serum blood test will reduce patient mortality.

because 50% of women with stage I disease, and those with occult cancers identified at prophylactic surgery, have normal levels

of this tumour marker. (The sensitivity and specificity of CA125 assay is known to be poor.)

CA125 levels are elevated in only 75–90% of patients with advanced disease.

malignancy index (RMI) for patients presenting with ovarian cysts.

A level of over 250 IU/ml should trigger referral to a cancer centre for subsequent management.

Traditionally, assays for carbohydrate antigen 19-9 (CA19-9) and carcinoembryonic antigen (CEA) have been used in the screening criteria for gynaecological pelvic malignancies and may be beneficial for patients in whom no obvious cause of a raised CA125 level is found.

Serial monitoring of CA125 levels is advantageous in such patients.

because it has been observed that levels appear to rise progressively over time in patients with malignancy.

CA125 levels have been shown to be elevated in various benign conditions, including
benign ovarian cysts
tubo-ovarian abscess
Endometriosis
pelvic inflammatory disease
fibroids
ovarian hyperstimulation syndrome.

if women is that a serum CA125 level is crucial if any cystic lesion of **more than 1 cm** in diameter is identified on the ovary.

Levels of CA125 in **the ascitic fluid** **do correlate** with the **serum** levels, but are **much higher** than those seen in **the blood**.

This indicates that **the antigen originates** in the **ascitic fluid**, rather than in the tumour itself.

For **patients with symptoms of ovarian cancer**, current national guidance recommends **CA125 testing** as an initial investigation.¹ CA125 level is also required to calculate a risk

the diagnosis of ovarian cancer, a **CA125 test** is often used in conjunction with **transvaginal ultrasound** scanning (TVUSS).

there is little evidence that this approach can reduce mortality from ovarian cancer, partly because 50% of women with stage I disease, and those with occult cancers identified at prophylactic surgery, have normal levels of this tumour marker.

Box 1. Summary of NICE guidance for CA125 testing in primary care.¹

CA125 testing is advised for all women with red flag symptoms raising suspicion of ovarian cancer (especially if 50 years or older)

Symptoms include:

Bloating

Early satiety ± reduction in appetite

Pelvic ± abdominal pain

Increased urinary urgency or frequency

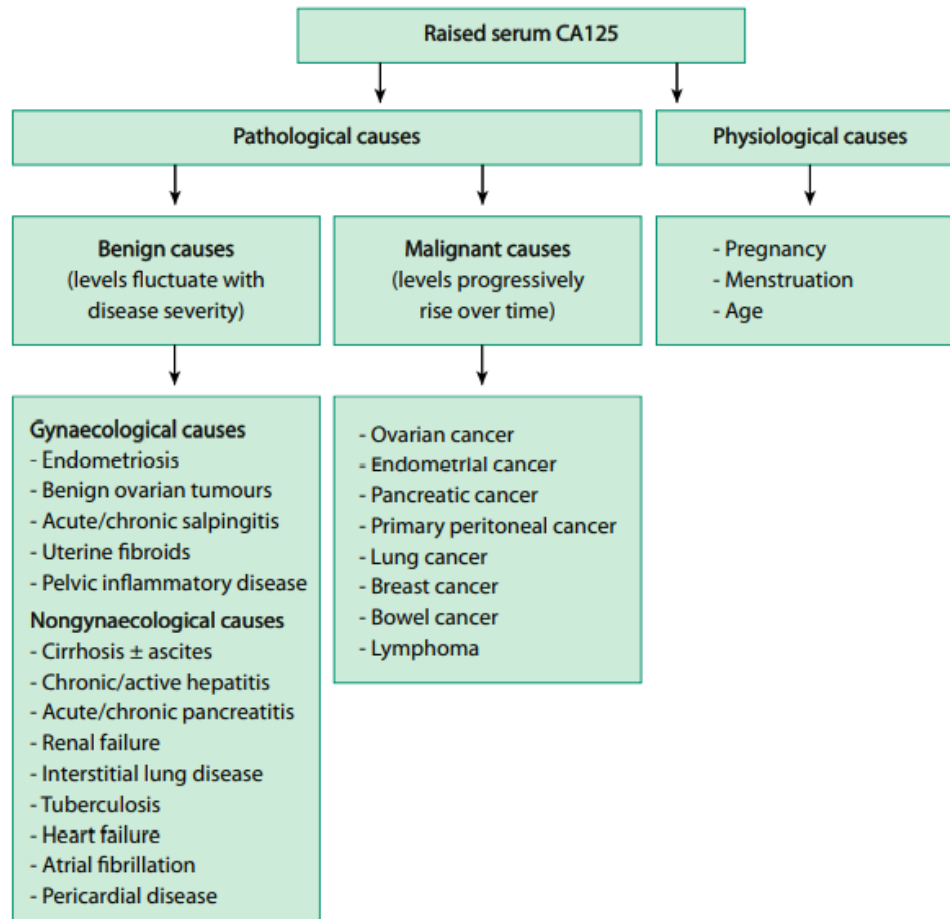
Other symptoms to consider:

Unexplained weight loss

Unexplained fatigue

Unexplained change in bowel habit

New onset symptoms of irritable bowel syndrome in women >50 years



2. Flow chart summarising the physiological and pathological causes of raised CA125.

SBA 6

Carbohydrate antigen 125 (CA125) is true

- A. elevated when the serum level is above 40 U/ml.
- B . expressed in tissues derived from embryonic coelomic tissue.
- C . a mandatory test in follow-up of patients with ovarian cancer.
- D . a reliable screening biomarker.

B . expressed in tissues derived from embryonic coelomic tissue.

SBA 7

Which of the following is false ?

- A. elevated in over 70% of women with advanced ovarian cancer.
- B. only elevated in ovarian epithelial cancers.
- C. normal in 50% of women with stage I ovarian cancer.

B. only elevated in ovarian epithelial cancers.

SBA 8

With regard to ovarian cancer, which of the following is true ?

- A. it is the leading cause of death from any gynaecological malignancy.**
- B. approximately 70% of women present in stage I–II.**
- C. a risk of malignancy index of over 300 only is a trigger for patient referral to a cancer centre.**

A. it is the leading cause of death from any gynaecological malignancy.

SBA 9

With regard to current guidance on the diagnosis of ovarian cancer, which of the following false

- A . pelvic ultrasound scan is considered the first line investigation for women presenting with symptoms of ovarian cancer.
- B . CA125 testing should be done in all postmenopausal women with a cystic lesion of 1 cm or more on the ovary.
- C. age-specific CA125 cut-offs are less accurate and increase false-positive results.

C. age-specific CA125 cut-offs are less accurate and increase false-positive results.

SBA 10

With regard to CA125 in ascitic fluid, which of the following is false ?

- A . levels correlate with those in the serum.
- B. it is produced by tumour cells.
- C . levels are higher than those in blood.

B. it is produced by tumour cells.

SBA 11

With regard to the use of CA125 in the screening of ovarian cancer,

Which of the following is false

- B) guidelines recommend it as part of initial investigation.
- C) a one-off serum blood test has been shown to reduce patient mortality.
- D) CA125 levels correlate positively with ascitic volume.

C) a one-off serum blood test has been shown to reduce patient mortality.



Does ovarian cystectomy pose a risk to ovarian reserve and fertility?

Functional ovarian cysts have been described as non pathological follicular cysts that failed to ovulate, a persistent corpus luteum cyst, or other unspecified ovarian cysts measuring more than 20 mm in diameter.

They are **the most common ovarian cysts** in adults and children and account for **46–53%** of all adnexal pathologies regress **spontaneously within one to three menstrual cycles**, so should **not require any interventions**.

With **the exception** of luteal cysts and persistent functional cysts, functional ovarian cysts.

Luteal cysts are observed in **10%** of natural menstrual cycles in **fertile women**.

luteal cysts occurred in **25%** of intrauterine insemination (IUI) cycles in women with **unexplained infertility**.

Dermoid cysts and their effects on fertility

A dermoid cyst is a benign type of germ cell tumour arising from totipotent ovarian cells.

They are the **most common pathological cysts in premenopausal women.**

They **are bilateral in 10–20% of cases** .

The recurrence rate following cystectomy is 3–4%.

the effects of dermoid cysts on ovarian function and fertility, and **none have shown a negative effect.**

the antimullerian hormone (AMH) **levels** in women with **unilateral** and **bilateral dermoid cysts** with those of controls and found **no significant difference.**

the ovarian cortex seemed to be stretched but not damaged by the dermoid cyst.

the ovarian cortical tissue surrounding benign cysts removed at cystectomy.

The cortical tissue surrounding dermoid cysts showed **normal morphological patterns** and a regular vascular network similar to that of the normal ovarian cortex.

One study showed a statistically significant **reduction in AMH following surgery for cysts over 5 cm** in diameter. Therefore, operating early, while the cyst is still small, **may prevent the need for a large cystectomy and thus lower the effect on the ovarian reserve.**

Endometriomas, or ovarian endometriotic cysts, are reported in **17–44%** of women with endometriosis and are a marker of more severe, deeper disease.

Furthermore, **28% of endometriomas are bilateral.**

With regard to effects on ovarian reserve, two prospective studies demonstrated **lower AMH levels** and **antral follicle counts (AFC)** in women with endometriomas **compared with age-matched controls.**

Endometriomas were also **thought to negatively affect** ovulation, one study showing lower ovulation rates in ovaries containing **endometriomas greater than 10 mm in diameter** compared with the healthy contralateral ovary.

more recently, Maggiore and colleagues conducted a larger prospective study all of whom had a unilateral endometrioma greater than 20mm in diameter, and performed ultrasound monitoring for ovulation over six cycles. **No difference was found in the ovulation rates between the affected ovary and healthy ovary**

Cystectomy for endometriomas prior to IVF treatment is not routinely recommended because it has not been shown to improve IVF outcomes.

A Cochrane review assessed the effectiveness of surgery versus no treatment for women with an endometrioma prior to undergoing assisted reproductive technology (ART).

Apart from **cyst excision**, several other surgical techniques exist, including drainage and bipolar coagulation or ablation using plasma or laser energy.

cystectomy to be superior to drainage and bipolar coagulation in terms of spontaneous pregnancy rates, **lower risk of recurrence** and pain symptoms among subfertile patients with endometriomas **greater than 3 cm in diameter**. Incision should be **away from the blood vessels in the hilum/mesovarium**.

Use of cold cut at the edge of the cyst opening may assist in identifying the cleavage plane.

Table 1. Clinical variables to be considered when deciding whether or not to perform surgery in women with endometriomas selected for IVF

Characteristics	Favours surgery	Favours expectant management
Previous interventions for endometriosis	None	≥1
Ovarian reserve ^a	Intact	Damaged
Pain symptoms	Present	Absent
Bilaterality	Monolateral disease	Bilateral disease
Sonographic feature of malignancy ^b	Present	Absent
Growth	Rapid growth	Stable

^aOvarian reserve is estimated based on serum markers or previous hyperstimulation cycles. ^bSonographic feature of malignancy refers to solid components, locularity, echogeniety, regularity of shape, wall, septa, location and presence of peritoneal fluid. Republished with permission.⁷⁹

Teratomas constitute **about half of all ovarian neoplasms in children** and **1%** of these are **malignant** immature teratomas.

Since **laparoscopic cystectomy has become the accepted practice for the management of mature cystic teratomas in adults**, the same approach should **apply to children and adolescents**.

With greater use of preoperative investigations, including pelvic imaging and tumour markers, along with a multidisciplinary team approach and conservative surgery, we should be able to better protect the future fertility of these young girls.

Malignant ovarian cysts are uncommon in children and adolescents.

Despite this, oophorectomy is **frequently performed in this age group**.

One study found that **75% of oophorectomies in children and adolescents** had been carried out for **benign** ovarian cysts.

Functional ovarian cysts account for about **45%** of all paediatric adnexal abnormalities and usually resolve spontaneously.

Ovarian torsion and its effect on fertility Ovarian torsion is a rare gynaecological emergency.

Approximately **3%** of all emergency gynaecological surgeries are for ovarian torsion.

Conservative management, which involves laparoscopic **unwinding of the twisted ovary**, is **the treatment of choice in prepubescent girls** and women of reproductive age, regardless of the colour of the ovary at the time of surgery.

When an ovary undergoes torsion and detorsion, it results in haemorrhage, congestion and apoptosis secondary to ischaemia, which can affect the ovarian reserve.

One retrospective study found that **detorsion of the ischaemic ovary** preserved ovarian function **in 91.3% of patients**; this was demonstrated by follicular development on ultrasound, normal ovary at subsequent laparotomy for other indications and successful fertilisation of oocytes retrieved from the ischaemic ovary following controlled ovarian stimulation.

compared with oophorectomy, **laparoscopic detorsion** has the potential **to preserve the ovarian reserve** and should remain the optimal treatment **in girls and premenopausal women**.

In cases where torsion has occurred in the presence of an ovarian cyst, an **elective cystectomy 2–3 weeks** later is advised to **allow time for the congestion and oedema to resolve**.

Several other studies have also demonstrated a **reduction in the ovarian reserve following cystectomy** for **endometriomas**.

There is also a **higher risk of oophorectomy when performing large cystectomies**.

Clinicians frequently advise patients to delay surgery until a cyst reaches a particular size, when there is a significant risk of ovarian torsion.

It may be **wiser to proceed with surgery when the cyst is small**; especially in those with **mucinous cystadenomas**, which have a propensity to **grow into large cysts**.

Bilateral cystectomy can also lead to a **greater decline in the ovarian reserve** than with **unilateral surgery**.

women having **surgery for bilateral endometriomas** have been shown to have an increased risk of developing **premature ovarian insufficiency**.

SBA 12

With regard to functional ovarian cysts, which of the following is incorrect?

- A) they are the most frequently occurring cysts in adults and children.
- B) luteal cysts are observed in 25% of natural menstrual cycles in fertile women.
- C) women with low ovarian reserve are at increased risk of developing them.
- D) luteal cysts result from unruptured follicles.
- E) they almost always regress spontaneously within one to three menstrual cycles.

B) luteal cysts are observed in 25% of natural menstrual cycles in fertile women.

SBA 13

With regard to dermoid cysts, which of the following is false

- A) they are bilateral in 30–40% of cases.
- B) they are associated with a reduction in ovarian reserve.
- C) All is false

C) All is false

SBA 14

With regard to endometriomas, which of the following is true

- A) women with endometriomas have lower ovarian reserve (as measured by antimullerian hormone and antral follicle counts) compared with age matched controls.
- B) cystectomy prior to in vitro fertilisation treatment has been shown to improve outcomes.
- C) recurrence rates are similar following either cystectomy or drainage and diathermy

A . women with endometriomas have lower ovarian reserve

(as measured by antimullerian hormone and antral follicle counts) compared with age matched controls.

SBA 15

With regard to benign ovarian cysts in children and adolescents, which of the following is true

A. malignant teratomas account for about 1% of all teratomas in children.

B. functional ovarian cysts account for about one-third of all paediatric adnexal masses.

A. malignant teratomas account for about 1% of all teratomas in children.

SBA 16

With regard to ovarian torsion, which of the following is false

- A. it accounts for approximately 3% of all emergency gynaecological surgery.
- B. laparoscopic detorsion appears to preserve ovarian function
- C. untwisting at the time of surgery should be followed by cystectomy if circulation returns.


C. untwisting at the time of surgery should be followed by cystectomy if circulation returns.

SBA 17

With regard to ovarian reserve assessments,
which of the following is incorrect?

- A) ovarian cystectomy has been associated with a reduction in the ovarian reserve.
- B) they are recommended before ovarian cystectomy in women who have severe endometriosis and bilateral endometrioma.
- C) In case of ovarian cystectomy the initial incision on the cyst should be made close to the mesovarium.
- D) In case of ovarian cystectomy gonadotrophin-releasing hormone agonist therapy is used for large endometriomas to reduce the thickness of the cyst wall.

C) In case of ovarian cystectomy the initial incision on the cyst should be made close to the mesovarium.



Very advanced maternal age

very advanced maternal age'

(vAMA) to refer to women who are **aged 45 years or more** at the time of delivery

Spontaneous conception in women of vAMA is **rare**, but **more common in parous women**.

Conception using autologous embryos is also rare;

the **live birth rate is 2.9%** in a cycle for **women aged 45 years**.

the live birth rate was so low, it was reported as being **0%**, for women aged **46 years** and older,

women of vAMA, focusing on women aged 48 years and over,

It showed that 78% of the women delivering had conceived using ART.

Of these, 51% had assisted conception performed outside the UK,
91% reported using egg donation and 21% had used donor sperm.

Of these women, 40% had one embryo transferred, 45% had two embryos transferred and 15% had three or more embryos transferred. Just under half of those who had multiple embryos transferred went on to have a multiple pregnancy.

.Pre-eclampsia complicates just **1.1%** of **natural conception** pregnancies and

12.6% of **oocyte donation** conceptions in women of vAMA.

Women of **vAMA** who become pregnant as a **consequence of ART** should, like all women, have a risk assessment at booking; they should be offered **low-dose aspirin (150 mg)** from **12 weeks of gestation until delivery**.

SGA. Miscarriage rates increase with increasing maternal age. In women of vAMA, the **overall risk of miscarriage is 53%**

Table 1. Summary of the risks from the current evidence for women of very advanced maternal age, comparing conception with assisted reproductive technologies (ART) and spontaneous conception

Condition	Pregnancy conceived by ART and oocyte donation (%)	Pregnancy conceived spontaneously (%)
Maternal pre-eclampsia	12.6	1.1
Delivery before 36 weeks of gestation	23.3	9.3
Risk of baby being born with low birth weight (<2500 g)	22.1	7.4

Table 3. A summary of maternal complications, risks and recommendations in women of very advanced maternal age (vAMA)

Maternal complication	Risk	Recommendation
Pre-existing medical complication	44% (of women aged 48 years or older)	Early referral to a high-risk antenatal clinic or maternal medicine clinic
Gestational diabetes mellitus	12.6–21.0% 35.1% (in twin pregnancies conceived by assisted reproductive technology)	Offer screening at 16–18 weeks of gestation in addition to screening at 26–28 weeks of gestation Women of vAMA are nine times more likely to require insulin
Hypertensive disease	6–32%	Pre-pregnancy counselling should be offered to all women with pre-existing hypertension, including a review of antihypertensive medications, an up-to-date echocardiogram, renal function tests and renal imaging Advise low-dose aspirin 150 mg from 12 weeks of gestation until delivery Regular blood pressure monitoring in the third trimester
Previous uterine surgery	26% (of women aged 48 years or older)	Early referral to a high-risk antenatal clinic
Placenta praevia	Three times more likely to have placenta praevia than younger women	Fetal anomaly ultrasound scan between 18 and 21 weeks of gestation Those involved in scanning should be aware of the increased risk of placenta praevia in women of vAMA
PPH	25% Women of vAMA are almost four times more likely to need blood products than younger women	Plans and precautions to minimise the risk of PPH should be discussed. Investigate and treat anaemia Discuss the role of prophylactic uterotonics in the management of the third stage of labour
Antenatal hospital admission	30%	Thromboprophylaxis is recommended for women of vAMA with additional risk factors Admission alone increases venous thromboembolism risk 12-fold
Admission to intensive care unit	33.5 times more likely to be admitted than younger women	Consider offering care in a place with appropriate intensive care support for both mother and neonate(s) High-risk women of vAMA to be seen in a high-risk anaesthetic clinic at 30–32 weeks of gestation On-call consultant anaesthetist should be made aware when a woman of vAMA is admitted to the unit

PPH = postpartum haemorrhage.

The risk of an ectopic pregnancy in women with vAMA is **three times** the overall risk of ectopic pregnancy in all women.

Clinicians should be aware there is some evidence that women aged 40 years and older with ectopic pregnancies are **twice** as likely to need **a blood transfusion** than younger women.

A VTE reassessment after miscarriage or ectopic pregnancy should be performed, following findings from the most recent confidential enquiry into maternal deaths in the UK.

women of vAMA have consistently recorded the highest multiple pregnancy rate, secondary to increasing availability of ART and the number of embryos transferred.

women of vAMA in the UK had a multiple pregnancy rate of **79.3/1000** compared with **15.4/1000** in all women.

Women of vAMA are **nine times** more likely to require insulin to treat GDM than younger women.

Pre-eclampsia, severe or early onset pre-eclampsia and eclampsia are more common in women of vAMA than in younger women.

Fitzpatrick et al.³ found that 6% of women aged 48 years and older developed **pre-eclampsia or eclampsia** compared with 2% of younger women.

Meyer²⁴ found that 32% of vAMA with multiple pregnancy conceived by ART developed **pre-eclampsia or eclampsia** compared with 6.2% of younger women who conceived a twin pregnancy by ART.

Despite these figures, **most maternal outcomes are good** and there is some evidence that women of vAMA are not at greater risk of complications from hypertension solely based on their age.

When pre-existing maternal health is documented, **it seems that the main predictor of outcomes is maternal health and not maternal age.**

Pre-pregnancy counselling should be offered to all women with pre-existing hypertension, including a review of antihypertensive medications, an up-to-date echocardiogram, renal function tests and renal imaging.

Hypothyroidism is more common in women of vAMA.

Surveillance of thyroid function and treatment with levothyroxine is an effective management strategy.

Venous thromboembolism Evidence that maternal age affects rates of VTE is conflicting: Fitzpatrick et al.³ found that rates of thrombotic events were the same in women across all age groups; however, previous large studies have shown that women **over the age of 35 years have a 70% increase in VTE in the postpartum period.**

Current guidance in the UK simplifies risk and states that age greater than 35 years is a risk factor for VTE antenatally and postnatally. Women of vAMA who become pregnant as a consequence of ART should, like all women, have a risk assessment at booking; they should be offered low-dose aspirin (150 mg) from 12 weeks of gestation until delivery.

They should also be assessed for VTE, since women who have conceived with **ART are at increased risk, particularly in the first trimester.**

The most recent review of maternal deaths in the UK recommends clear pathways for women to access early prescriptions and support for thromboprophylaxis to ensure compliance.

Women of vAMA with **multiple pregnancy** have **increased rates of fetal and maternal complications** compared with women of vAMA with singleton pregnancies and younger women with multiple pregnancies.

Pregnancies in women of vAMA have increased risks of preexisting medical conditions, GDM, gestational hypertension, pre-eclampsia, abnormal placentation, ICU admission, caesarean delivery, postpartum haemorrhage (PPH), blood transfusion and prolonged admission to hospital.

They are less likely to smoke cigarettes.

44% of women aged 48 years or older had a reported pre-existing medical condition compared with 28% of younger women.

Women of vAMA are **three times more likely to have placenta praevia.**

All women should be advised to have a fetal anomaly ultrasound scan between **18 and 21 weeks** of gestation and those involved in scanning should be aware of the increased risk of placenta praevia in women of vAMA.

Women of vAMA are **three times more likely to have a placental abruption than younger women.**

It is difficult to predict and no effective prevention treatments are currently available.

Women of all ages are advised to report all vaginal bleeding to their antenatal care provider.

Placental abruption is a clinical diagnosis and there are no sensitive or reliable diagnostic tests available. Ultrasound has limited sensitivity in the identification of retroplacental haemorrhage.

Obesity Women aged 48 years or more are more likely to be overweight or obese than younger women.³ Pregnant women who are obese are at greater risk of pre-eclampsia,

Admission to hospital and intensive care Women of vAMA have a 30% risk of antenatal hospital admission and are **33.5 times more likely to be admitted to ICU than younger women.**

Postpartum haemorrhage PPH has been shown to be the most statistically significant complication affecting women of vAMA, whether they are primiparous or multiparous, having a singleton or multiple pregnancy, conceived spontaneously or by ART. **PPH affects one in four** women of vAMA.

Women with multiple pregnancies, pre-eclampsia and those receiving thromboprophylaxis are at particular risk. PPH affects one in four women of vAMA.

Women of vAMA are **almost four times more likely to need blood products following a PPH than younger women.**

3 Plans and precautions to minimise the risk of PPH should be discussed with the mother in the antenatal period, including the investigation and treatment of anaemia and the role of prophylactic uterotonics in the management of the third stage of labour.

Trisomy and congenital anomalies The risk of Down syndrome (trisomy 21) is directly related to maternal age if a pregnancy is conceived spontaneously. In donor embryos, it is related to the age of the donor.

The incidence of trisomy 21 at term is

- 1:1350 for a 25-year-old woman (or donor).
- 1:35 at the age of 45 years
- 1:25 at the age of 49 years.

Using **a cut-off of 1 in 150 at term** as a screen-positive result, **one in four women** of vAMA will screen positive.

A screen-positive result requires careful counselling. Invasive diagnostic testing

(amniocentesis or chorionic villous sampling) can be offered;

it gives accurate results but has a small risk of miscarriage.

an ectopic pregnancy in women with vAMA is **three times** vAMA are **three times more likely to have placenta praevia**.
three times more likely to have a **placental abruption** than younger women.
Pre-eclampsia 3 fold times

Four as likely to need **a blood transfusion** than younger women post partum.

Women of vAMA are **nine times** more likely to require insulin to treat **GDM** than younger women.

Admission to hospital and intensive care Women of vAMA have a 30% risk of antenatal hospital admission and are **33.5 times more likely to be admitted to ICU than younger women**.

SBA 18

Pregnancy following conception via assisted reproductive technologies in women of advanced maternal age, which of the following option is incorrect

- A) is significantly more likely to result in a live birth if a donor embryo rather than an autologous embryo is used.
- B) is associated with a two-fold increase in the risk of developing pre-eclampsia in comparison to a pregnancy following spontaneous conception.
- C) is an indication for aspirin (150 mg) from 12 weeks of gestation until delivery to decrease the risk of pre-eclampsia and small-for-gestational age.

B) is associated with a two-fold increase in the risk of developing pre-eclampsia in comparison to a pregnancy following spontaneous conception.

SBA 19

With regard to early pregnancy in women of very advanced maternal age,

Which of the following is incorrect?

- A. there is an overall 53% risk of miscarriage.
- B. the overall risk of ectopic pregnancy in those aged 44 years or more is twice that in younger women.
- C. there is evidence that women aged 40 years and above are twice as likely to need a blood transfusion during an admission for an ectopic pregnancy in comparison to younger women.

B. the overall risk of ectopic pregnancy in those aged 44 years or more is twice that in younger women.

3 TIMES

SBA 20

Women of very advanced maternal age are more likely than younger women to be,

A. multiparous.

B. overweight or obese.

C. All is true

C. All is
true

SBA 21

Which of the following is false

- A) Multiple pregnancy rates in women of very advanced maternal age, have been consistently higher than in any other age group due to multiple embryos being transferred during assisted reproductive technology.
- B) Women with advanced maternal age the most significant risk factor for developing pre-eclampsia is obesity.
- C) After ART , Aspirin 75 mg should be started from 12 weeks

C)After ART , Aspirin 75 mg should be started from 12 weeks

SBA 22

Which of the following is false

- A) Venous thromboembolism risk in women of very advanced maternal age, is increased mainly in the first trimester following assisted reproductive technology.
- B) advanced maternal age, There are three times more likely to have placenta praevia than younger women.
- C) Women of vAMA are three times more likely to have a placental abruption than younger women
- D) All true

D) All true

SBA 23

Which of the following is false

- A) Regarding postpartum haemorrhage, it complicates one in four pregnancies in women of very advanced maternal age.
- B) Regarding postpartum haemorrhage, women of very advanced maternal age are almost twice as likely to need blood products than younger women.
- C. Women of very advanced maternal age, are 33.5 times more likely to be admitted to intensive care than younger women.

B. women of very advanced maternal age are almost twice as likely to need blood products than younger women.

Women of vAMA are almost **four times** more likely to need blood products following a PPH than younger women.

SBA 24

Regarding trisomy, which of the following is true

- A) the risk of having a child with trisomy 21 is 1:35 at the age of 45.
- B) if a cut off of 1 in 150 is used as a screen positive result, one in four women of very advanced maternal age will screen positive.
- C) All true

C) All true

1:1350 for a 25-year-old woman (or donor).

1:35 at the age of 45 years

1:25 at the age of 49 years.

Using **a cut-off of 1 in 150 at term** as a screen-positive result, **one in four women** of vAMA will screen positive.

Care in pregnancies subsequent to stillbirth or perinatal death



stillbirth ‘a baby delivered with no signs of life known to have died after 24 completed weeks of pregnancy.

98 percent of stillbirths occur in **low-** and **middle-income** countries (LMICs).

the estimated proportion of intrapartum stillbirths varies from approximately **10% in HICs** to **60% in South Asia** this is closely related to access to high-quality antenatal and intrapartum care.

Risk factors

low socioeconomic status

advanced maternal age

essential hypertension

pre-eclampsia

antepartum haemorrhage (APH)

fetal growth restriction (FGR)

A history of previous stillbirth is a recognised risk factor for stillbirth in a subsequent pregnancy.

in HICs, demonstrated a stillbirth rate in **2.5% of women with a previous history of stillbirth** compared with a rate of **0.4% when previous pregnancy resulted in a livebirth.**

study in the USA found that only **18% of stillbirths** occurred in women with risk factors identified at booking.

The authors concluded that **pregnancy history** was **the strongest risk factor for stillbirth**.

stillbirth recurrence was **more likely when a maternal or placental condition occurred in the second trimester of** the index pregnancy (**13–24 weeks of gestation**).

This study found recurrent **fetal** causes were **less common**.

There was a trend towards increased risk of recurrence in women with diabetes mellitus or hypertension .

adverse pregnancy outcome (defined as perinatal death, FGR, preterm birth at less than 34 weeks of gestation, hypoxic ischaemic encephalopathy or respiratory distress) is more frequent when stillbirth was related to placental vascular disorder (39.6%) than when stillbirth was related to a different cause

CoDAC (**Causes of Death and Associated Conditions**).

The proportion of stillbirths classified as 'unexplained' varies greatly depending on the classification system used.

Aberdeen and Wigglesworth have the highest proportion of unexplained stillbirths (44.3% and 50.2%, respectively), **while ReCoDe has the lowest proportion at approximately 15%.**

Importantly, the **inclusion of placental histology in the classification of stillbirth reduces the number of stillbirths classified as 'unexplained'.**

This may be because, in **11–65% of stillbirth cases**, placental lesions cause are associated with **fetal death.**

Other causes of stillbirth included placental problems (31.8%) and congenital anomalies (9.2%).

Intrapartum complications accounted for 1.8% of stillbirths.

Post mortem examination, **placental examination and cytogenetic analysis** are the **most valuable** investigations available **after a stillbirth.**

stillbirths in the found placental examination helped to determine the cause of death in 95%,

post mortem examination provided cause of death information in **72% of cases** and **cytogenetics** in **29% of cases.**

Histopathological examination of the placenta by a pathologist provides useful information in at least 50% of stillbirths and **reduces the reporting of 'unexplained' stillbirth** from 30% to 10%.

Placental lesions can be broadly categorised into **four groups**:

inflammatory, obstructive, disruptive and adaptive.

Obstructive (e.g. maternal and fetal vascular malperfusion)

adaptive lesions (villous dysmaturity) are most commonly seen in SGA stillbirths and FGR live births.

ascending infection is most common in the **mid-trimester, peaking at 22 weeks of gestation**.

maternal vascular malperfusion is most common in the early **third trimester**.

Inflammatory lesions, such as chronic histiocytic intervillitis (CHI) and villitis of unknown aetiology (VUE), are associated with stillbirth. Although these are comparatively infrequent (incidence of CHI is 0.06% of pregnancies; VUE incidence is 5.1%), they are important findings because they are thought to be recurrent – particularly CHI, which has a recurrence rate of 80% in subsequent pregnancy and needs specific drug therapy.

Interpretation of histopathological findings should be carefully related to clinical history since lesions can also be#

women who have had a stillbirth are more likely to stop smoking than women whose prior pregnancy ended in a livebirth.

If a woman stops smoking **before 16 weeks of gestation**, risk is the same as that for nonsmokers; therefore, early intervention reduces the risk of adverse outcome.

Where indicated, drug therapy to reduce recurrent placental complications (e.g. aspirin) should be commenced in the first trimester.



There are few dedicated clinical services ('**Rainbow Clinics**') that care for women in a subsequent pregnancy after stillbirth or neonatal death.

Models of multidisciplinary continuity of care combined with regular antenatal surveillance are associated with improved clinical outcomes, particularly a reduction in preterm birth and improved patient experience.

women with a history of stillbirth should have ultrasound measurement of fetal biometry.

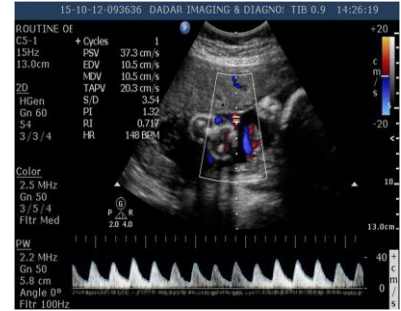
Care in pregnancies after stillbirth

a subsequent pregnancy following stillbirth or neonatal death and that most parents did not receive adequate emotional and psychological support.

Sixty-seven percent of parents received additional antenatal visits and **70% received additional ultrasound scans**; however, only **10% had access to a bereavement counsellor**

Thus, care in the subsequent pregnancy not only

needs to focus on the increased risk of adverse pregnancy outcome, but also on the **emotional and psychosocial effects on parents that persist into the subsequent pregnancy.**



In particular, parents are at increased risk of **intense anxiety, depression, fear**, complex emotional responses and refrain from forming bonds with the unborn baby as a coping mechanism.

Providing this **level of emotional care requires specially trained staff**, bereavement counsellors and time, which can rarely be adequately provided in a busy 'routine' antenatal clinic.

There is **no 'ideal' inter-pregnancy interval** to **reduce adverse outcome in a subsequent pregnancy**; in particular, the risk of stillbirth/SGA/pre-eclampsia in HICs is not altered by short or long inter-pregnancy intervals.

Many families embark on a pregnancy within 12 months of the stillbirth; indeed, **66% of parents** who participated in a large international survey reported **conceiving their subsequent pregnancy within 1 year of the stillbirth**

The most commonly used intervention to reduce recurrent stillbirth from placental causes is aspirin:

150 mg once at night, ideally commenced **before 16 weeks** of gestation and continued **until at least 36 weeks**.

higher doses of aspirin (e.g. 150 mg rather than 75 mg) are more effective at preventing FGR and pre-eclampsia.

Although there are no data specifically on women whose previous pregnancy **ended in stillbirth**, this is thought to **be beneficial for women whose stillbirth was associated with placental disease**.

There is currently no high-grade evidence to support the use of **low-molecular-weight heparin** (LMWH) with the primary aim to prevent fetal complications in women with a history of stillbirth.

However, **it should be used in women at high risk of maternal venous-thromboembolism**.

Presently, it should be reserved for women with antiphospholipid antibody syndrome or CHI. chronic histiocytic intervillitis.

CHI is a rare placental lesion associated with poor obstetric outcome and has a high risk of recurrence in subsequent pregnancies (80%).

the number of live births increased in the treatment group from 32% to 67% with quadruple therapy of aspirin, LMWH, prednisolone and hydroxychloroquine and resulted in better pregnancy outcomes than aspirin alone.

Timing of birth Increasing evidence suggests the optimal time for delivery for the general obstetric population is **at 39 weeks of gestation** because after this point the risk of neonatal death does not fall, but the risk of stillbirth increases.

(IOL) 'at term' would **reduce perinatal mortality by 70%**.

additional emotional care is required in many women who have previously suffered stillbirth and **induced delivery from 38 weeks of gestation may be indicated.**

Table 4. Placental lesions associated with stillbirth⁴²⁻⁴⁴

Category	Placental lesions	Associated with	Subsequent pregnancy
Maternal vascular malperfusion	<p>Placental hypoplasia Placental weight <10th centile ± thin cord <10th centile</p> <p>Infarction Crowding and congestion of villi, migration of neutrophils into intervillous space, compressed or obliterated intervillous space, increased fibrin deposition, pyknosis and karyorrhexis of trophoblast, ghost villi</p> <p>Acute, subacute or chronic</p> <p>Retroplacental haemorrhage Blood accumulation on maternal surface, compression of overlying parenchyma</p> <p>Distal villous hypoplasia Paucity of villi in relation to surrounding stem villi, villi thin and elongated, increased syncytial knots</p> <p>Focal or diffuse</p> <p>Accelerated villous maturation Small or short hypermature villi for gestation, increased syncytial knots, increased intervillous fibrin</p> <p>Mild, moderate or severe</p>	<p>Fetal growth restriction</p> <p>Pre-eclampsia</p> <p>Preterm and term stillbirth</p> <p>Spontaneous preterm birth</p>	<p>Assess maternal cardiovascular status</p> <p>Glucose tolerance test</p> <p>Thrombophilia screen</p> <p>Renal function</p> <p>Low dose aspirin</p> <p>Preconception weight loss</p> <p>10-25% recurrence risk</p>
Fetal vascular malperfusion	<p>Thrombosis Arterial or venous</p> <p>Acute, subacute or chronic</p> <p>Fibrin deposits, endothelial oedema, iron deposits in basement membrane, thrombi attached to vessel wall, fibrosis in proximal villi, calcification</p> <p>Avascular villi Loss villous capillaries, fibrosis of villous stroma, small, intermediate or large foci</p> <p>Villous stromal-vascular karyorrhexis Rupture of fetal vessels in primary villi with haemorrhage and inflammatory cells</p> <p>Stem vessel obliteration Oedema in fetal vessel wall, obliteration vessel lumen</p> <p>Intramural fibrin deposition</p>	<p>Fetal growth restriction</p> <p>Preterm and term stillbirth</p>	<p>Thrombophilia screen</p> <p>Glucose tolerance test</p>
Delayed villous maturation	<p>Reduced vasculosyncytial membranes</p> <p>Continuous cytotrophoblast layer</p> <p>Centrally placed capillaries</p> <p>Focal or diffuse</p>	<p>Term stillbirth</p>	<p>Glucose tolerance test</p> <p>Preconception weight loss</p> <p>Unknown recurrence risk</p>
Ascending uterine infection	<p>Maternal stage 1: acute subchorionitis or chorionitis</p> <p>Maternal stage 2: acute chorioamnionitis</p> <p>Maternal stage 3: necrotising chorioamnionitis</p> <p>Fetal stage 1: chorionic vasculitis or umbilical phlebitis</p> <p>Fetal stage 2: involvement of umbilical vessels</p> <p>Fetal stage 3: necrotising funisitis</p>	<p>Spontaneous preterm birth</p> <p>Adverse neonatal outcome</p>	<p>If spontaneous preterm birth with chorioamnionitis, 10-25% recurrence risk</p>
Immune inflammatory lesions	<p>Villitis of unknown aetiology Low or high grade</p> <p>Lymphohistiocytic ± occasional plasma cells</p> <p>Chronic villitis Fibrous villi, obliterated fetal vessel, perivillous fibrin</p> <p>Intervillositis Acute: neutrophils in villi/intervillous space, fibrin</p>	<p>Fetal growth restriction</p> <p>Miscarriage</p> <p>Preterm stillbirth</p>	<p>Maternal autoimmune testing</p> <p>Preconception weight loss</p> <p>Low dose aspirin</p> <p>± LMWH</p> <p>± Immunosuppressive therapy</p> <p>Villitis of unknown aetiology, 25-50% recurrence risk</p>

Table 4. (Continued)

Category	Placental lesions	Associated with	Subsequent pregnancy
	Chronic: small placenta, diffuse intervillous invasion of lymphocytes, macrophages and eosinophils, villous necrosis, perivillous fibrin Histiocytic: small placenta, diffuse intervillous invasion of histiocytes		Chronic histiocytic intervillitis, 75–90% recurrence risk

LMWH = low-molecular-weight heparin

SBA 25

In relation to investigation of a stillbirth, which of the following is false ?

- A) histopathological examination of the placenta by a pathologist provides useful information in at least 50% of cases
- B) cytogenetic analysis is the most useful investigation to identify a cause of stillbirth.
- C) histopathological examination of the placenta by a perinatal pathologist reduces the reporting of 'unexplained' stillbirth.

C) histopathological examination of the placenta by a perinatal pathologist reduces the reporting of 'unexplained' stillbirth.

SBA26

When a mother has a history of stillbirth in the previous pregnancy,

Which of the following option is incorrect ?

- A) the likelihood of preterm birth is reduced in a subsequent pregnancy.
- B) the likelihood of placental abruption is increased in a subsequent pregnancy.
- C) the recurrence risk is highest when cause of the index stillbirth was of placental origin.

A) the likelihood of preterm birth is reduced in a subsequent pregnancy.

SBA 27

When caring for patients in a subsequent pregnancy after stillbirth,

Which of the following options is incorrect ?

- A) women and their families are at increased risk of intense anxiety, depression, and complex emotional responses that persist into the subsequent pregnancy.
- B) most families embark on a subsequent pregnancy within 12 months of the stillbirth.
- C) women who have a history of stillbirth are less likely to stop smoking than women who have had a live birth.
- D) aspirin commenced before 16 weeks' gestation has been shown to significantly reduce the risk of stillbirth in high-risk women.
- E) guidelines exist to standardise the care provided across the UK to women who have experienced a stillbirth.

C) women who have a history of stillbirth are less likely to stop smoking than women who have had a live birth.

SBA 28

The risk of stillbirth recurrence in a subsequent pregnancy can be reduced,

Which of the following option is incorrect ?

- A) with the use of serial ultrasound scan measurements of fetal biometry and uterine and umbilical artery Doppler waveforms.
- B) With regard to establishing the cause of stillbirth, using the relevant condition at death (ReCoDe) system is associated with the lowest unexplained rate.
- C) a mother has a history of stillbirth in the previous pregnancy, the likelihood of complications is significantly influenced by the time interval between the two pregnancies.

C) a mother has a history of stillbirth in the previous pregnancy, the likelihood of complications is significantly influenced by the time interval between the two pregnancies.

You will fail only when you stop trying



16/08/2021