Queensland Clinical Guidelines

Translating evidence into best clinical practice

Maternity and Neonatal **Clinical Guideline**

Early pregnancy loss

Queensland Government

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- Supporting consumer rights and informed decision making in partnership with healthcare practitioners, including the right to decline intervention or ongoing management
- Advising consumers of their choices in an environment that is culturally appropriate and which enables comfortable and confidential discussion. This includes the use of interpreter services where necessary
- Ensuring informed consent is obtained prior to delivering care
- Meeting all legislative requirements and professional standards
- Applying standard precautions, and additional precautions as necessary, when delivering care
- Documenting all care in accordance with mandatory and local requirements

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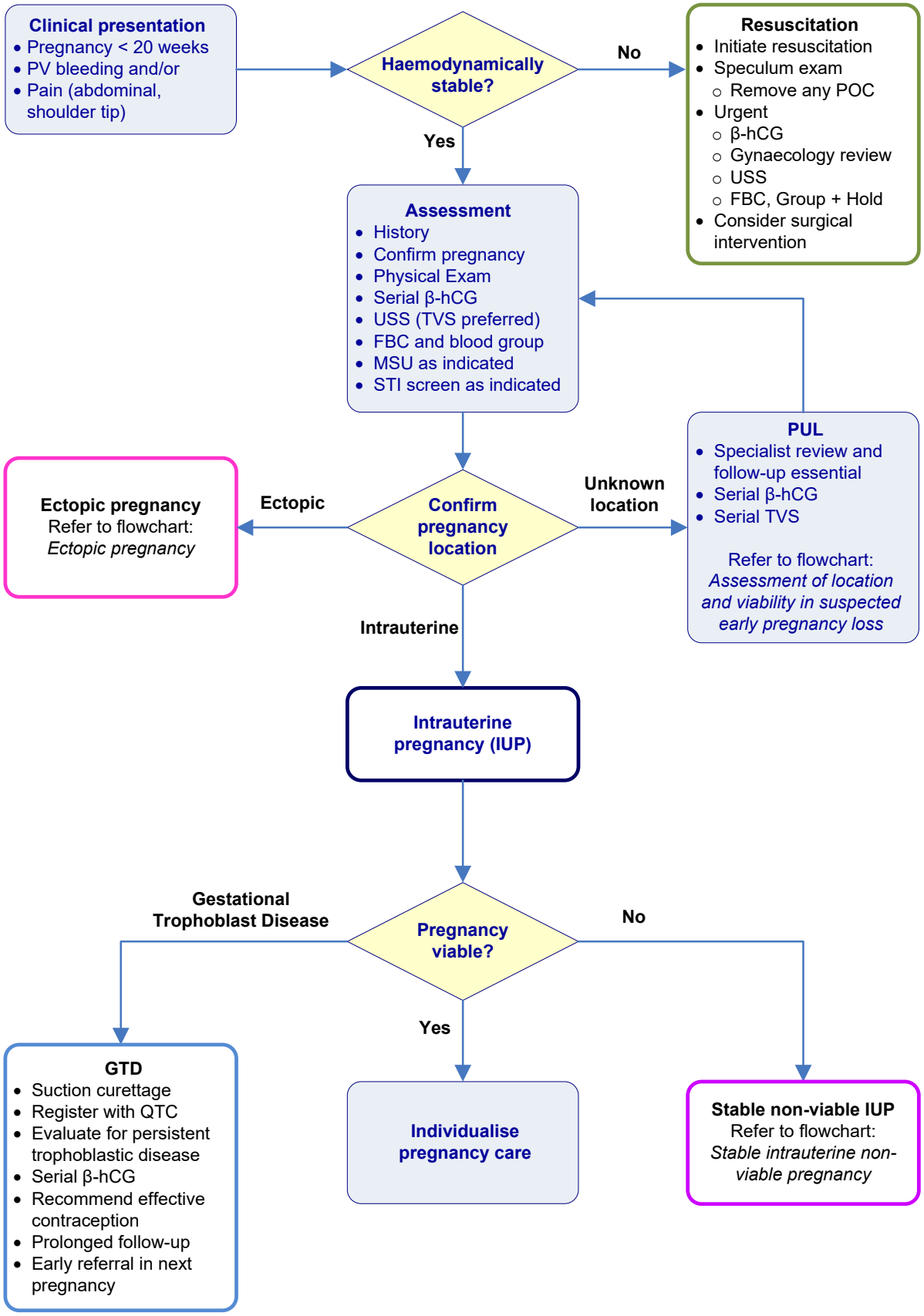
Flow Chart: Assessment of suspected early pregnancy loss

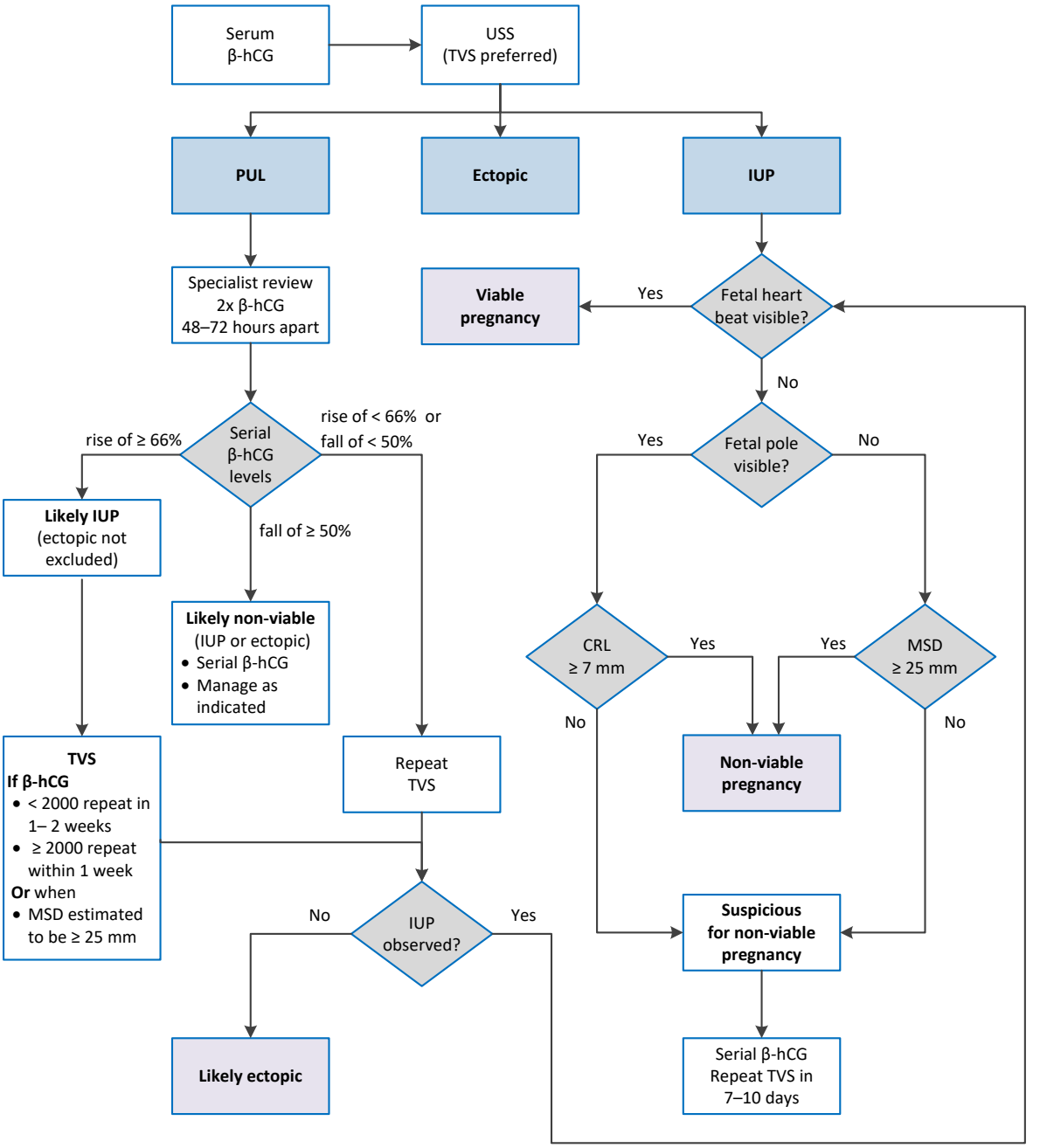


β-hCG: human chorionic gonadtrophin, **FBC:** full blood count, **GP:** General practitioner, **GTD:** gestational trophoblast disease, **IUP:** intrauterine pregnancy, **POC:** products of conception, **PUL**: pregnancy of unknown location, **PV:** per vaginam, **QTC:** Queensland Trophoblast Centre, **MSU**: midstream specimen of urine, **MCS**: microscopy, culture & sensitivity, **STI:** sexually transmitted infection, **TVS:** transvaginal scan, **USS:** ultrasound scan, **>:** greater than, **<:** less than

Queensland Clinical Guideline: Early pregnancy loss. Flowchart version: F17.29-2-V4-R22

Flowchart: Assessment of location and viability in suspected early pregnancy loss

Use clinical judgement and consider the woman's individual circumstances when recommending management



Non viable diagnostic criteria (TVS)

- MSD ≥ 25 mm and no fetus present
- Fetus with CRL ≥ 7 mm is visible, but no fetal heart movements demonstrated after observation of ≥ 30 seconds
- Absence of embryo with heartbeat ≥ 2 weeks after a scan that showed a gestational sac without a yolk sac
- Absence of embryo with heartbeat ≥ 11 days after a scan that showed a gestational sac with a yolk sac

TVS interval

- Estimate repeat TVS interval based on expected normal gestational sac growth rate of 1 mm/day

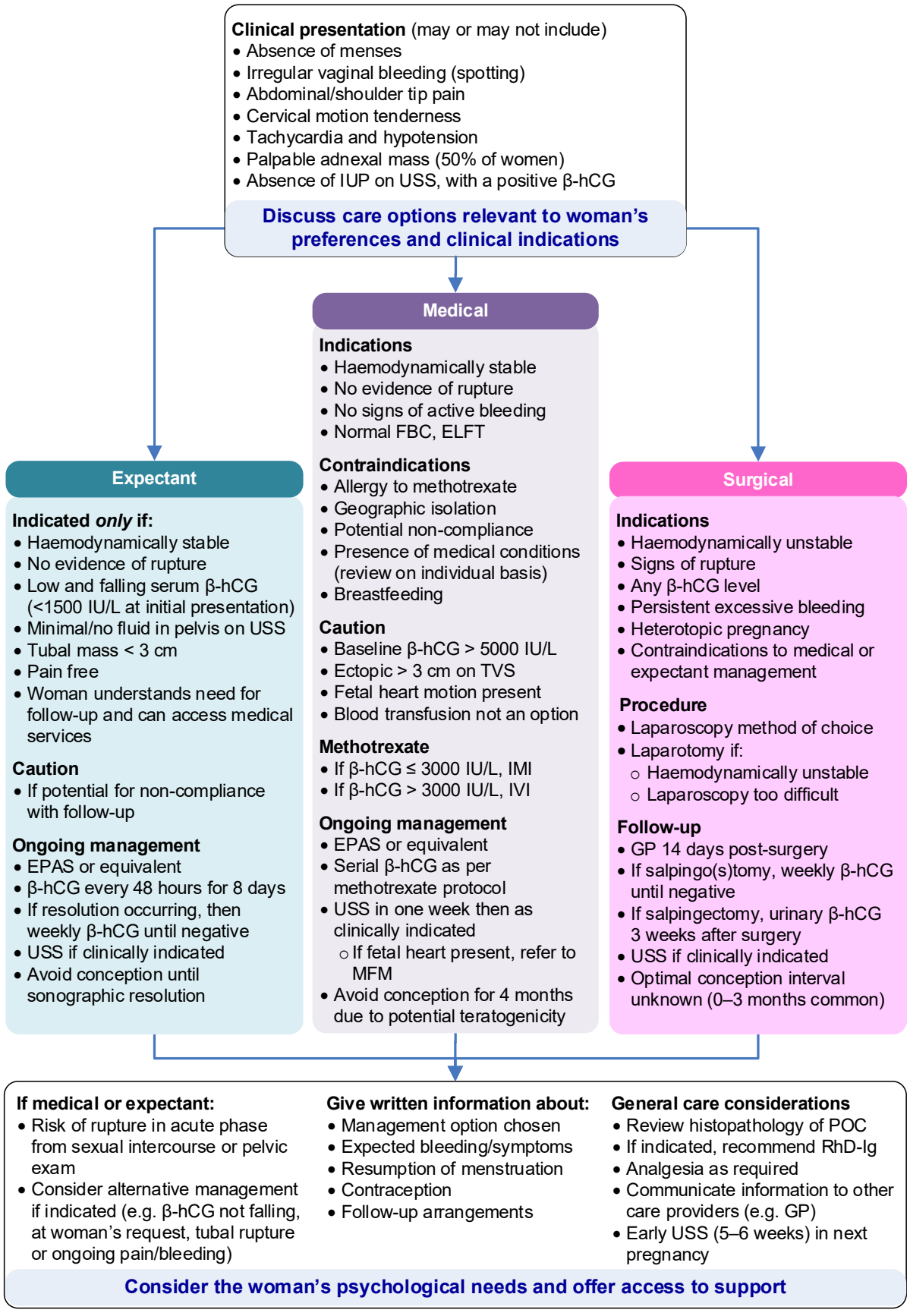
Worked example

- If MSD =12 mm, repeat TVS in 13 days or more (12 mm MSD + 13 mm growth over 13 days equals expected MSD of 25 mm)

β-hCG: human chorionic gonadtrophin (all β-hCG measurements in International units/L (IU/L)), **CRL:** crown rump length, **IUP:** intrauterine pregnancy, **MSD:** mean sac diameter, **PUL:** pregnancy of unknown location, **TVS:** transvaginal scan, **USS:** ultrasound scan, **>:** greater than, **<:** less than; **≥:** greater than or equal to; **≤:** less than or equal to

Queensland Clinical Guideline: Early pregnancy loss. Flowchart version: F17.29-4-V1-R22

Flow Chart: Ectopic pregnancy



β-hCG: human chorionic gonadtrophin, **ELFT:** electrolyte & liver function test, **EPAS:** Early Pregnancy Assessment Service, **FBC:** full blood count, **GP:** General Practitioner, **GTD:** gestational trophoblast disease, **IMI**: intramuscular injection, **IU/L**: international units per litre, **IUP:** intrauterine pregnancy, **IVI:** intravenous injection, **MFM:** maternal fetal medicine, **POC:** products of conception, **PUL**: pregnancy of unknown location, **PV:** per vaginam, **QTC:** Queensland Trophoblast Centre, **RhD-Ig:** RhD immunoglobulin, **TVS:** transvaginal scan, **USS:** ultrasound scan, **>:** greater than, **<:** less than; **≤:** less than or equal to

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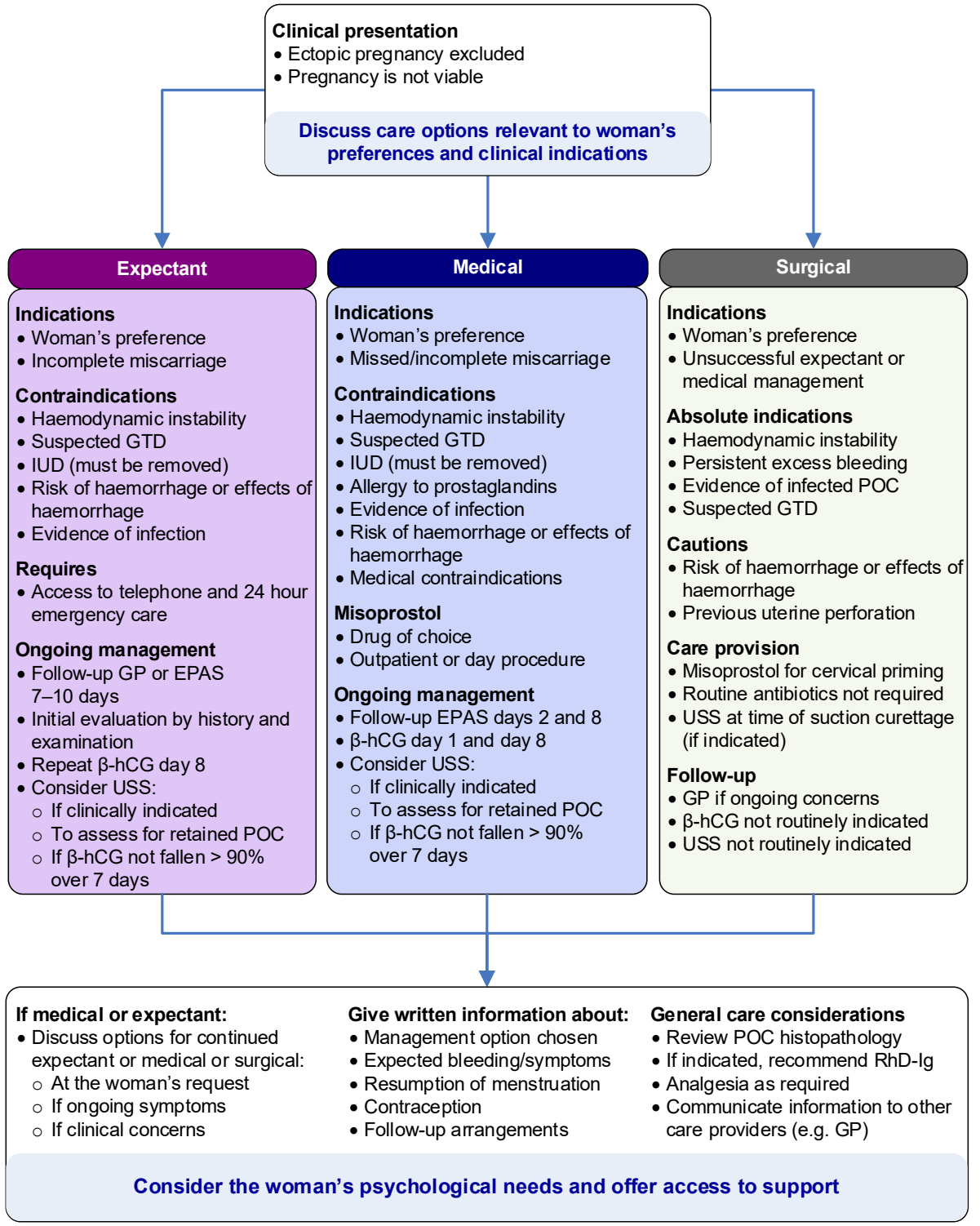
Flow Chart: Stable intrauterine non-viable pregnancy



β-hCG: human chorionic gonadtrophin, **EPAS:** early pregnancy assessment service, **FBC:** full blood count, **GP:** General Practitioner, **GTD:** gestational trophoblast disease, **IUD:** intrauterine device, **IUP:** Intrauterine pregnancy, **POC:** products of conception, **PUL**: pregnancy of unknown location, **PV:** per vaginam, **QTC:** Queensland Trophoblast Centre, **RhD-Ig:** RhD immunoglobulin, **TVS:** transvaginal scan, **USS:** ultrasound scan, **>:** greater than, **<:** less than

Queensland Clinical Guideline: Early pregnancy loss. Flowchart version: F17.29-1-V4-R22

Abbreviations

β-hCG	Beta human chorionic gonadotrophin
ELFT	Electrolytes, liver function test
EPAS	Early pregnancy assessment service
EPL	Early pregnancy loss
FBC	Full blood count
FMH	Fetomaternal haemorrhage
GP	General Practitioner
GTD	Gestational trophoblast disease
HM	Hydatidiform mole
IUP	Intrauterine pregnancy
LNMP	Last normal menstrual period
MSD	Mean sac diameter
POC	Products of conception
PUL	Pregnancy of unknown location
PV	Per vaginam
QTC	Queensland Trophoblast Centre
RhD	RhD blood type
RhD-Ig	RhD immunoglobulin
TAS	Transabdominal ultrasound
TVS	Transvaginal ultrasound
USS	Ultrasound

Definition of terms

Anembryonic pregnancy	A type of early pregnancy failure where a gestational sac develops, but the embryo does not form.
Complete miscarriage	Complete expulsion of products of conception (POC). Further management of miscarriage by medical or surgical intervention is not required.
Early Pregnancy Assessment Service	A hospital-based service which is able to assess and manage early pregnancy loss. Equivalent services may have different names or structures across Queensland.
Early pregnancy loss	For the purposes of this document, early pregnancy loss refers to a loss within the first 20 completed weeks of pregnancy.
Ectopic pregnancy	Pregnancy located outside of the uterus, usually in the fallopian tubes but may be in the cornu, cervix, caesarean section scar, ovary, or in other sites.
Expectant management	No specific intervention; awaiting spontaneous passage of POC.
Gestational Trophoblastic Disease	A spectrum of disease characterised by an autonomous overgrowth of fetal chorionic tissue or trophoblast. Includes molar pregnancy (complete or partial).
Heterotopic pregnancy	Multiple pregnancy with an intrauterine plus ectopic pregnancy (e.g. tubal, cervical, ovarian, abdominal).
Incomplete miscarriage	Incomplete expulsion of POC.
Inevitable miscarriage	Miscarriage or expulsion of products is imminent or in the process of happening.
Medical management	Use of drugs to aid the expulsion of POC.
Miscarriage	Pregnancy loss occurring before 20 completed weeks of gestation or less than 400 g birth weight.
Missed miscarriage	Ultrasound confirmed non-viable pregnancy with no bleeding.
Pregnancy of unknown location	Refers to cases where a pregnancy test is positive but the pregnancy cannot be visualized by ultrasound.[1]
Recurrent miscarriage	Three or more consecutive miscarriages. There is no specific term for non-consecutive pregnancy losses.
Threatened miscarriage	Any vaginal bleeding other than spotting before 20 weeks completed gestation with evidence of a progressive, viable pregnancy at ultrasound.

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1 Introduction

Early pregnancy loss (EPL) is a relatively common event, occurring in approximately 20% of pregnancies.[2] Amongst women who have been pregnant, it is estimated that 25% will experience an EPL by the time they reach 39 years of age.[3] EPL can have negative consequences physically and psychologically. Potential physical complications include infection, haemorrhage, embolism, damage to uterus and associated structures, and anaesthetic complications. Psychological complications such as grief, depression and anxiety are common.

Whilst health care professionals and clinical care can do little to prevent a threatened pregnancy loss from progressing, high quality care can increase levels of satisfaction with care, minimise negative outcomes, and support women and their families to navigate their way through an emotional and highly stressful time.[4,5]

1.1 Clinical standards

Table 1. Clinical standards

Aspect	Consideration
Triage	• Triage women presenting with symptoms of EPL according to the Australasian Triage Score (ATS) ○ Ideally within the first 20 minutes noting that this is a very stressful and emotional time for the woman and her family • Assessment by an experienced clinician is required[6] • If haemodynamic instability, refer to Section 3 Haemodynamic instability
Care providers	• Women with suspected EPL may seek care through a variety of pathways and access points • A dedicated outpatient early pregnancy assessment service (EPAS) is recommended for all maternity services ○ Refer to Definition of terms and Appendix A: Early pregnancy assessment service • Refer or transfer women to the most appropriate service provider (e.g. higher level service, gynaecologist, obstetrician, general practitioner (GP) or EPAS
Communication between care providers	• Inclusive and timely communication between care providers (internal and external to a healthcare facility) will optimise the woman's experience of care • Develop local protocols and pathways to facilitate communication about the woman's care: ○ Between emergency, outpatient, and maternity departments (e.g. so future maternity bookings and reminders can be cancelled) • Provide timely written information to the woman's GP
Staff support	• Support staff caring for women with EPL to access education about grief and loss, counselling and recognition and assessment of psychological morbidity • Offer staff access to emotional support and debriefing as a routine part of service provision

Women's choice	• Women's treatment preference is a primary consideration when deciding management options[2]
	• Women are more motivated to follow their chosen treatment to completion when they have chosen it for themselves[7]
	• Provide an opportunity for women to:
	  ○ Make an informed choice regarding treatment options[8]
	  ○ Consider their choices
	• Delay decision making when safe to do so

Psycho-social support	• Provide care appropriate to the gestation and circumstances of each woman (including whether or not the pregnancy was wanted or planned) • Consider the impact of cultural/spiritual beliefs and preferences when offering care to the woman and her family (e.g. taking photos, creating memories) • Refer to Section 9 Psychological support

1.2 Principles of EPL care

Aspects of care common to all women experiencing EPL (regardless of pregnancy location or management option) are outlined in Table 2. Consider in conjunction with all care recommendations.

Table 2. General care principles for EPL

Aspect	Consideration

Histopathology	• Send products of conception (POC) obtained at the time of EPL or via surgical intervention for histopathology to confirm pregnancy and exclude ectopic pregnancy or unsuspected gestational trophoblastic disease (GTD)
	  ○ Transvaginal ultrasound (TVS) is not reliable in the detection of GTD
	• Discuss implications/requirements for histopathology with women who may miscarry at home according to their individual circumstances
	  ○ May be practically difficult and some may find it distressing
	  ○ If POC collection chosen, provide a labelled specimen container, pathology request form and instructions for delivery to pathology
	• If POC not collected, reassure that there are other options for follow-up

Return to normal menstrual cycle	• Resumption of normal menstrual cycle indicates resolution of EPL complications and completion of management[9]
	• Ongoing, irregular bleeding requires follow-up—consider:
	  ○ Beta human chorionic gonadotrophin (β-hCG) to exclude GTD
	  ○ Retained products or infection[9]

Ongoing and follow-up care	• There is limited evidence or consensus about optimal follow-up protocols
	• Establish local procedures and protocols:
	  ○ For follow-up care arrangements
	  ○ To ensure histopathology results are reviewed and actioned as required
	• Vary the recommendations for follow-up in this guideline as is clinically appropriate and indicated for individual women
	• If GTD, register with Queensland Trophoblast Centre (QTC)
	  ○ Refer to Section 8 Gestational trophoblastic disease

Advice to women after EPL	• Provide information (written and verbal) to all women with EPL about:
	  ○ When to seek emergency assistance
	  ▪ If experiencing strong pain unrelieved by paracetamol
	  ▪ Shoulder tip or diaphragmatic pain
	  ▪ Soaking of more than one pad within 60 minutes
	  ▪ Fainting
	  ▪ Elevated temperature
	  ○ Timing and nature of follow-up investigations and appointments, including contact details of relevant care providers
	  ○ Resumption of sexual activity
	  ○ Contraception
	  ○ Recommendations for conception interval (if any)
	  ○ Future pregnancy planning
	  ○ Resumption of menstruation/expected bleeding
	  ○ Accessing psychological support
	• Refer to Queensland Clinical Guidelines patient information:
	  ○ *Ectopic pregnancy*[10]
	  ○ *Bleeding and pain in early pregnancy*[11]
	  ○ *RhD negative in pregnancy*[12]

2 Assessment

Assessment and diagnosis is made through a combination of a physical examination, history, and clinical investigations. Initial assessment of haemodynamic stability is essential.

Table 3. Confirmation of pregnancy and assessment

Aspect	Consideration

History	• Menstrual history and last normal menstrual period (LNMP)
	• Date of positive pregnancy test
	• Previous pregnancies and outcomes, particularly miscarriages
	• Other significant gynaecological history
	• If assisted conception, identify method of conception
	• Relevant ultrasound scan (USS) and quantitative β-hCG
	• Symptoms of early pregnancy
	• Presence of associated symptoms:
	  ○ Vaginal bleeding (timing, extent and severity)
	  ○ Pain (lower abdominal cramping or backache)
	  ○ Postural syncope
	  ○ Vomiting
	  ○ Shoulder tip/diaphragmatic pain
	• Passage of POC

Confirm pregnancy	• Perform an urgent serum quantitative β-hCG (pregnancy test) on all women of reproductive age presenting with a history of recent or current abdominal pain, pelvic pain, shoulder tip pain and/or per vaginam (PV) bleeding, syncope or signs of shock (irrespective of LNMP, contraception, history of sterilisation or reported sexual inactivity) ○ If delay in reporting a serum test is expected, use urine β-hCG as clinically indicated • A negative serum β-hCG essentially excludes ectopic (except in the unusual circumstance of a chronic ectopic where β-hCG has been positive in the recent past)

Physical exam	• Baseline observations (temperature, heart rate, respiratory rate, blood pressure)
	• Abdominal examination
	  ○ Tenderness (rigidity and guarding)
	  ○ Distension
	• PV blood loss (check loss on pad)
	• Vaginal examination (individualised as clinically indicated):
	  ○ Speculum examination:
	  ▪ Source and amount of bleeding
	  ▪ Evidence of POC in the cervical os (if present, remove and submit for histology)
	  ○ Bi-manual examination:
	  ▪ Cervical motion tenderness
	  ▪ State of internal cervical os
	  ▪ Assess for adnexal masses (ectopic pregnancy or other masses)
	• Size of uterus relative to menstrual dates

Ultrasound scan	• Perform an USS as soon as possible and urgently if clinically indicated • Document whether TVS or transabdominal (TAS) on the USS report to aid interpretation • Refer to Appendix B: Sonographic anatomy, landmarks and documentation
Other investigations	• Full blood count (FBC), blood group, antibody screen • Midstream specimen of urine for microscopy, culture and sensitivity as clinically indicated • Screen for sexually transmitted infections as clinically indicated (e.g. for women in high risk groups, relevant history)

2.1 Viability and location of pregnancy

Table 4. Determining viability and location of pregnancy

Aspect	Consideration
Ultrasound scan	• TVS by an experienced sonographer is the gold standard in the first trimester • If TVS unavailable, TAS may be used, recognising that it is not as accurate as TVS for diagnosis of early pregnancy complications
β-hCG	• Serum β-hCG first becomes positive at 9 days post conception o β-hCG greater than 5 IU/L confirms pregnancy • A single β-hCG value does not differentiate between a viable and nonviable pregnancy[13] • For a potentially viable intrauterine pregnancy (IUP) up to 6–7 weeks gestation o Mean doubling time for β-hCG is 1.4–2.1 days o 85% show serial β-hCG rise of at least 66% every 48 hours[14] o 15% show serial β-hCG rise between 53–66% every 48 hours[14] o The slowest recorded rise over 48 hours is 53%[15]
Correlating β-hCG and TVS	• USS and serial β-hCG enable the location and potential viability of an early pregnancy to be ascertained • Quantitative serum β-hCG levels used in conjunction with serial TVS are often the only way to distinguish between an early non-viable pregnancy and ectopic pregnancy in gestations less than 6–7 weeks
Discriminatory zone	• The discriminatory zone is the serum β-hCG level above which a gestational sac should be visible on TVS or TAS if an IUP is present[15] • An IUP is usually visible on TVS when mean sac diameter (MSD) is greater than or equal to 3 mm, however one single β-hCG value may not be discriminatory and serial β-hCG is advised in stable circumstances • One study reported, where no IUP and no abnormal TVS findings and[16]: o β-hCG 2000–3000 IU/L a 2% chance of subsequent viable IUP o β-hCG greater than 3000 IU/L a 0.5% chance of subsequent viable IUP • Cautions: o No proven discriminatory zone for β-hCG for multiple gestations o In the presence of fibroids, USS may be less reliable
Complete miscarriage	• IUP can only be confirmed conclusively after identification of a yolk sac[13] • If no prior report or evidence of an IUP, a diagnosis of complete miscarriage cannot be made based on TVS findings of an 'empty uterus' • A diagnosis of complete miscarriage requires follow-up with serum quantitative β-hCG until negative and TVS if clinically indicated, to exclude undiagnosed ectopic
Pregnancy of unknown location (PUL)	• It may not be possible to confirm if a pregnancy is intrauterine or extra-uterine at first visit o Specialist review and close follow-up is essential o Serial β-hCG and TVS may be required
Serum progesterone	• If PUL, a single progesterone level may assist in identifying women with a low risk of having an ectopic pregnancy or persistent PUL[17] • In one study[17] an initial serum progesterone of less than or equal to 2 nanomol/L correctly classified: o 206 of 210 PUL as low risk for ectopic (negative predictive value 98%) o 134 of 138 ectopic pregnancies as not low risk for ectopic (sensitivity 97%)

2.2 Interpretation of β-hCG and TVS in a clinically stable woman

Table 5. β-hCG and TVS correlation in a clinically stable woman

β-hCG	TVS	Recommendation
Greater than 2000 IU/L	No IUP, complex adnexal mass and/or free fluid	• High probability of ectopic pregnancy • Refer to Section 4
	No IUP, no abnormal findings	• Consider serum progesterone level • Repeat β-hCG from 48–72 hours • Repeat TVS as clinically indicated
β-hCG levels less than 2000 IU/L		• Repeat β-hCG from 48–72 hours • If β-hCG rising over one week, then TVS (or earlier if clinically indicated)
β-hCG levels declining or sub-optimally rising		• No IUP on TVS, indicates a non-viable pregnancy (intrauterine or ectopic) • Follow-up to ensure adequate resolution of either diagnosis

2.3 Diagnosis of non-viable intrauterine pregnancy

Table 6. Diagnosis of non-viable IUP

Aspect	Consideration

Context	• Previously accepted criteria for excluding a viable pregnancy has been shown not to be stringent enough to avoid interventions that inadvertently damage pregnancies that might have had normal outcomes[16]
	• Diagnosis of non-viable IUP requires:
	  ○ Experienced clinicians
	  ○ High quality TVS equipment and experienced operator[18]

Findings suspicious but not diagnostic[16]	• MSD 16–24 mm and no embryo • Crown rump length (CRL) less than 7 mm and no heartbeat • Absence of embryo with heartbeat 7–13 days after USS that showed a gestational sac without a yolk sac • Absence of embryo with heartbeat, 7–10 days after USS that showed a gestational sac with a yolk sac • Absence of embryo 6 weeks or more after LNMP • Empty amnion (amnion seen adjacent to yolk sac with no visible embryo) • Enlarged yolk sac (greater than 7 mm) • Small gestational sac in relation to the size of the embryo (less than 5 mm difference between MSD and CRL)
TVS diagnostic criteria[18]	• MSD is greater than or equal to 25 mm and no fetus present • Fetus with CRL greater than or equal to 7 mm is visible, but no fetal heart movements demonstrated after observation of at least 30 seconds • Absence of embryo with heartbeat 2 weeks or more after USS that showed a gestational sac without a yolk sac • Absence of embryo with heartbeat 11 days or more after USS that showed a gestational sac with a yolk sac
Repeat TVS interval	• Diagnosis cannot be made until the MSD is (or has failed to reach) 25 mm therefore the interval between initial and subsequent USS is dependent on the MSD at initial presentation • Estimate TVS interval based on expected normal gestational sac growth rate of 1 mm/day ○ Example: If MSD = 12 mm, repeat TVS in 13 days or more (12 mm MSD+13 mm growth over 13 days = expected MSD of 25 mm) • Avoids repeated inconclusive TVS

3 Haemodynamic instability

Haemodynamically unstable women, presenting with vaginal bleeding and or pain (abdominal, diaphragmatic or shoulder tip pain) and who are believed to be pregnant, require urgent intervention. Presume ruptured ectopic pregnancy or incomplete miscarriage with cervical shock or massive haemorrhage.

Table 7. Haemodynamically unstable

Aspect	Consideration
Resuscitate	• Resuscitate as required following standard medical emergency procedures • Ensure sufficient IV access (e.g. two x 16 gauge IV cannulae) • Perform urgent speculum examination and remove POC from cervix and or vagina—this may stop vaginal bleeding and restore blood pressure • Insert indwelling catheter to empty bladder • Obtain urgent gynaecological review and USS concurrently with resuscitation • If ectopic pregnancy confirmed or unable to be excluded, continue resuscitation en route to theatre • Urgent FBC and group and hold
Control bleeding	• If vaginal bleeding persists and ectopic has been excluded, consider pharmacological therapy • Refer to Queensland Clinical Guideline: *Postpartum haemorrhage*[19] for first and second line drug regimens and considerations including: o Ergometrine maleate 250 micrograms IV or IM o Misoprostol 800–1000 micrograms per rectum o Critical bleeding massive transfusion protocol
Surgical intervention	• Unstable haemodynamics is a clinical indication for: o Surgical evacuation of the uterus for incomplete EPL ▪ Suction curettage is preferable to sharp curettage as the latter is associated with increased morbidity[20] o Laparoscopy and/or laparotomy for removal of ectopic pregnancy o In the second trimester, consider hysterotomy or laparotomy as is indicated

4 Ectopic pregnancy

Table 8. Ectopic pregnancy

Aspect	Consideration
Context	• Occurs in 1.5–2% of pregnancies[21] • Commonly (95%) occur in the fallopian tube[22,23] • Absence of IUP on USS with a positive serum β-hCG level raises suspicion of an ectopic pregnancy • Failure to promptly diagnose and manage an ectopic pregnancy can be life threatening[23] ○ In Australia 2008–2012, five of the 105 maternal deaths were due to ectopic pregnancy[24]

Clinical presentation[23]	• Absence of menses
	• Irregular vaginal bleeding (spotting)—but not in all cases
	• Abdominal pain, tenderness and palpable adnexal mass in 50% of women
	• Cervical motion tenderness
	• Absence of IUP on TVS with positive serum β-hCG
	• Suspect a ruptured ectopic if:
	  ○ Shoulder tip or diaphragmatic pain (10–20% of ruptured ectopics)
	  ○ Tachycardia/hypotension from profound intraperitoneal haemorrhage

Options for treatment	• There is limited high level evidence comparing expectant, medical and surgical options with regard to primary treatment success, recurrent ectopic, tubal patency and future IUP rates[25-27] • Choice of surgical, medical and expectant care[26] depends on the clinical situation and woman's preference[23] • Offer information to women about the risks and benefits of options for treatment relevant to the clinical circumstances • Falling or stationary β-hCG does not exclude the risk of rupture following medical or expectant management
Non fallopian tube ectopic	• For interstitial (corneal), caesarean scar, cervical, heterotopic, ovarian and abdominal ectopic pregnancies[22], surgical or medical management may be appropriate depending on individual circumstances ○ Methotrexate may be given IV or IM or by injection directly into the sac • Individualise management and seek expert advice as required

4.1 Risk factors for ectopic pregnancy

One third of women diagnosed with an ectopic pregnancy will have no risk factors[2]

Table 9. Risk factors associated with ectopic pregnancy

Risk factor[22]	(Adjusted*) OR	95% CI
Previous tubal surgery	4.0*	2.6 to 6.1
Previous ectopic pregnancy	8.3	6.0 to 11.5
Infertility (risk increases with length of)	2.1–2.7*	–
Previous genital infection confirmed	3.4*	2.4 to 5.0
Previous miscarriage	3.0*	> 2
Current smoker (risk increases with amount/day)	1.7–3.9*	–
Smoking (past or ever)	1.5*	1.1 to 2.2
Intrauterine device use more than 2 years	2.9*	1.4 to 2.3
Age 40 or older (compared to 25–29 years)	2.9*	1.4 to 6.1
Sterilisation[ǂ]	9.3	4.9 to 18.0
Documented tubal pathology	3.7*	1.2 to 4.8

*adjusted for: previous pelvic infection, smoking, recruitment area, level of education and age
ǂ compared with pregnant controls only

4.2 Expectant management of ectopic pregnancy

Expectant management is an option for selected women. Clear criteria for selection have not been well defined.[26]

Table 10. Expectant management of ectopic pregnancy

Aspect	Consideration
Context	• Among selected cases (early gestation, with β-hCG values below 1000 IU/L and decreasing) up to 70% reported to resolve spontaneously without therapy[21] • Inform women of the possibility of tubal rupture despite decreasing β-hCG
Indicated only if:	• Haemodynamically stable • Low and falling β-hCG (less than 1500 IU/L at initial presentation)[28] • Tubal mass less than 3 cm • No pain • Nil to minimal evidence of blood in the pelvis on USS • No geographical isolation
Cautions	• Consider individual circumstances • Not suitable for women who are potentially non-compliant or not motivated to long term recovery
Ongoing management	• Follow up via EPAS • β-hCG: o Every 48 hours for 8 days (to confirm levels falling) o If satisfactory resolution occurring, may commence weekly levels until negative • USS not routinely recommended—consider if: o β-hCG not consistently falling o Clinically indicated • Offer surgical or medical management: o At the woman's request o If there is ongoing or increasing pain or bleeding o β-hCG is not consistently falling o Tubal rupture with haemoperitoneum occurs
Advice for women	• Refer to Section 1.2 for information/advice requirements • Advise: o Pelvic examination and sexual intercourse carry risk of rupture in acute phase of resolution o Avoid future pregnancy until sonographic resolution of mass, noting that sonographic resolution of mass takes longer than biochemical resolution of β-hCG • Early USS in next pregnancy (5–6 weeks gestation)

4.3 Medical management of ectopic pregnancy

Methotrexate is the drug of choice although regimens vary.[29,30] If no local protocols exist, refer to Appendix C: Methotrexate regimens for ectopic pregnancy.

Table 11. Medical management of ectopic pregnancy

Aspect	Consideration
Context	• Methotrexate is a folic acid antagonist which prevents the growth of rapidly dividing cells by interfering with DNA synthesis[31]
Indications	• Unruptured ectopic pregnancy; haemodynamically stable and no signs of active bleeding[26,29,32] • Unusual sites (e.g. cervical ectopic, interstitial, caesarean scar) • Low initial serum β-hCG[26] ○ Best results achieved if β-hCG less than 5000 IU/L[22] but may be used at any β-hCG level in the unruptured ectopic[30] • FBC, electrolytes and liver function tests (ELFT) are within normal range
Contra-indication[29]	• Haemodynamically unstable • Allergy to methotrexate • Evidence of significant haemoperitoneum on TVS • Renal disease/insufficiency (methotrexate cleared via the renal system) • Abnormal FBC, ELFT • Acute liver disease, aplastic anaemia, thrombocytopenia • Immunodeficiency • Active pulmonary disease • Active peptic ulcer disease • Coexistent viable IUP (heterotopic pregnancy) • Breastfeeding • Potential for non-compliance with prolonged follow-up (35–109 days) • Geographic isolation
Cautions[29]	• Baseline serum β-hCG greater than 5000 IU/L • Ectopic pregnancy greater than 3–4 cm diameter on TVS • Presence of fetal heart motion on TVS • When blood transfusion is not acceptable to the woman • If body mass index (BMI) greater than or equal to 40 kg/m^2, and IMI dosage is capped at 2 m^2 BSA, an additional dose is more likely to be required to achieve complete resolution[33]
Ongoing management	• Follow up with EPAS • β-hCG as per methotrexate protocol • Repeat USS in one week and thereafter as clinically indicated (e.g. β-hCG not consistently falling, ectopic site other than fallopian tube) ○ If fetal heart present on USS, refer urgently to MFM for follow-up—direct injection of potassium chloride may be indicated

Advice for women	• Refer to Section 1.2 for information/advice requirements
	• Provide information about usual cytotoxic precautions post treatment with methotrexate
	• Avoid:
	  ○ Sun exposure (to limit skin inflammation)
	  ○ Foods and vitamins containing folate/folic acid
	• Advise:
	  ○ Pelvic examination and sexual intercourse carry risk of rupture in acute phase of resolution
	  ○ Common side effects of methotrexate include: nausea, tiredness, altered bowel habits and mouth ulcers which usually settle without treatment within a few days
	• Advise to delay next pregnancy for four months post administration of methotrexate due to potential teratogenicity of methotrexate[34,35]
	  ○ Ensure sonographic resolution of mass prior to future pregnancy, noting that sonographic resolution of mass takes longer than biochemical resolution of β-hCG[36]
	• Early USS in next pregnancy (5–6 weeks gestation)

4.4 Surgical management of ectopic pregnancy

Table 12. Surgical management of ectopic pregnancy

Aspect	Consideration
Indications	• Woman's preference • Haemodynamic instability • Persistent excessive bleeding
Approach	• Laparoscopy is the method of choice for stable women[22] • Laparotomy may be required in cases of haemorrhagic shock
Follow-up	• GP follow-up around 2 weeks post-surgery • USS not routinely required—consider if: o β-hCG does not fall o Other clinical indications • If salpingo(s)tomy, weekly β-hCG until negative[22] o If β-hCG does not fall, consider medical treatment or salpingectomy • If salpingectomy o Unusually may see abdominal implantation especially after ruptured ectopic with haemoperitoneum o Rarely may see ongoing intrauterine gestation if undiagnosed heterotopic pregnancy o Urinary β-hCG 3 weeks after surgery • Advise early USS in next pregnancy (5–6 weeks gestation)
Advice for women	• Refer to Section 1.2 for information/advice requirements • There is no data on the optimal conception interval—clinical practice varies from next menstrual period to 3 months • Risk of recurrent ectopic pregnancy is approximately[37]: o 15% after one ectopic pregnancy o 30% after two ectopic pregnancies • Subsequent IUP rate is 38–89%[22]

5 Non-viable intrauterine pregnancy

There are no significant differences between expectant, medical and surgical management for rates of infection,[7,38] psychological outcomes,[7,38] resumption of normal activities, or subsequent fertility.[39]

5.1 Risk factors

Table 13. Risk factors associated with first trimester pregnancy loss

Risk factor group	Risk factors
Fetal/placental	• Chromosomal abnormalities[40] • Congenital abnormalities[41] • GTD
Maternal	• Maternal age: EPL 7% in 25–29 years versus 43% in 40–44 years[3,40] • Recurrent miscarriage history: risk of EPL 20–70% after three losses[42] • Anatomic factors (e.g. uterine septum) • Endocrinopathy (e.g. thyroid disease) • Immunologic factors (e.g. systemic lupus erythematosus) • Infection (e.g. cytomegalovirus) • Severe acute illness • Thrombophilia (e.g. factor V Leiden) • Uncontrolled chronic illness (e.g. diabetes, hypertension)[41] • Very high or low pre-pregnancy BMI[40]
Other	• Drug use/smoking • Teratogen exposure • Trauma (e.g. physical abuse)[41]

5.2 Expectant management of non-viable intrauterine pregnancy

Table 14. Expectant management for stable non-viable IUP

Aspect	Consideration
Indications	• Woman's preference • Most suited to the management of incomplete miscarriage[43]
Contraindications	• Suspected GTD • Haemodynamically unstable • Intrauterine device (requires removal) • Women at increased risk of haemorrhage (e.g. late in first trimester)[2] or effects of (e.g. unable to have blood transfusion or coagulopathies)[2] • Evidence of infection[2]
Risk/benefit	• More days of bleeding and a greater amount of bleeding when compared to surgical treatment[38] • The proportion of women who subsequently require surgery varies widely between 2% and 44%[38] which may be explained by management bias • Timeframe to complete miscarriage is unpredictable • In setting of missed miscarriage, complete resolution may take several weeks and overall efficacy rates are lower[43]

Ongoing management	• Arrange follow-up within 7–10 days at GP or EPAS
	• Initial evaluation by history and examination
	  o Remain vigilant for GTD and/or ectopic
	• Repeat β-hCG day 8
	• Consider USS:
	  o If clinically indicated (symptomatic)
	  o To assess for retained POC
	  o If β-hCG level has not fallen more than 90% over 7 days[44]
	• Discuss options for continued expectant management or surgical or medical management:
	  o At the woman's request
	  o If there is ongoing heavy bleeding, pain or persistent intrauterine gestational sac identified on USS
	  o If other clinical concerns identified (e.g. heavy bleeding, pain)
	• If infection suspected, recommend early surgical management with antibiotic cover
	• Recommend urinary pregnancy test at 3–6 weeks if[9 2]:
	  o No POC histopathology
	  o Failure to return to normal menstruation by 4–6 weeks
	  o Ongoing abnormal bleeding

Advice for women	• Refer to Section 1.2 for information/advice requirements • Access to a telephone and 24 hour emergency hospital admission is required or a plan for access where there is geographical/social isolation[2,7] • Expect bleeding for up to two weeks (or longer in individual cases) • Advise surgical or medical management can be chosen at a later date

5.3 Medical management of non-viable intrauterine pregnancy

Table 15. Indications for medical management for the stable non-viable IUP

Aspect	Consideration
Indications	• Woman's preference • Missed or incomplete miscarriage to reduce need for surgery
Contraindications	• Suspected GTD[45] • Haemodynamically unstable • Increased risk of haemorrhage (e.g. late first trimester) or effects of haemorrhage (e.g. coagulopathy, unable to have blood transfusion) • Evidence of infection • Intrauterine device (requires removal)[45] • Medical contraindications (e.g. hypertension, allergy to prostaglandins[45])
Risk/benefit	• An effective alternative to surgical evacuation for first trimester EPL[46] • More effective for missed miscarriage than expectant management[43] • If incomplete miscarriage, no significant difference between medical and expectant management for rates of[8]: o Complete miscarriage o Need for surgical evacuation • Bleeding is heavier and more prolonged after medical treatment with misoprostol than with curettage[8,47]
Misoprostol*	• Misoprostol is the drug of choice[8] o Reported 80–99% effective in achieving complete miscarriage[8] • For incomplete miscarriage before 13 weeks, there is little evidence for one specific misoprostol regimen or route of administration over another[8,48] • If no local protocol, recommended regimen is: o Day 1: misoprostol 400–800 micrograms PV, oral or sublingual o Day 2 or Day 3: repeat misoprostol 400–800 micrograms PV, oral or sublingual ▪ If good history of POC passed, second dose may be omitted
Administration	• Treatment may be offered as an outpatient or day procedure[46] • Provide oral analgesia and anti-emetics as required[2,46]
Ongoing management	• Follow up with EPAS on day 2 and day 8 • Initial evaluation of success is by history and examination o Remain vigilant for GTD and/or ectopic[9] • β-hCG day 1 (day of first misoprostol), and day 8 (to confirm levels falling) • Consider USS: o If clinically indicated (symptomatic) o To assess for retained POC o If β-hCG level has not fallen more than 90% over 7 days[44] • Surgical management not indicated within one week of medical management unless[49]: o The woman requests it o There are other clinical concerns (e.g. ongoing heavy bleeding, pain) • Recommend urinary pregnancy test at 3–6 weeks if[9,50]: o No POC histology o Failure to return to normal menstruation by 4–6 weeks o Ongoing abnormal bleeding
Advice for women	• Refer to Section 1.2 for information/advice requirements • Inform women: o Bleeding heavier than menses[50] is likely o Cramping may accompany bleeding[50] o If bleeding has not commenced by 24 hours following treatment, to contact her healthcare provider to determine ongoing care[2] o Potential side-effects include pain, diarrhoea and vomiting[2]

*Refer to an Australian pharmacopeia for complete drug information

5.4 Surgical management of non-viable intrauterine pregnancy

Table 16. Surgical management of the stable non-viable IUP

Aspect	Consideration
Indications	• Woman's preference • Unsuccessful medical or expectant management • Absolute clinical indications for surgical management include:[50] o Haemodynamic instability o Persistent excessive vaginal bleeding o Evidence of infected retained tissue o Suspected GTD • Suction curettage is the recommended method[20]
Cautions	• No strict contraindications • Caution if: o Increased risk of haemorrhage (e.g. suspected arteriovenous malformation or coagulopathy) o Previous uterine perforation
Risk/benefit	• As a primary approach, surgical management results in a more immediate outcome with less follow-up[50] • Standard risks associated with procedure and anaesthesia
Cervical priming*	• Clinical experience supports the use of cervical ripening agents prior to surgical evacuation, although evidence is limited[51] • If no local protocol, recommended dose is[52]: o Misoprostol 400 micrograms PV 3–4 hours prior to surgery OR o Misoprostol 400 micrograms oral, sublingual, buccal 2–3 hours prior to surgery o Use water as lubricant
Care provision	• Suction curettage is usually performed under general anaesthetic • Provide appropriate analgesia[20] • There is insufficient evidence to support *routine* antibiotic prophylaxis prior to surgery[53] o Consider based on individual clinical indications (e.g. endometritis) • If clinically indicated, consider USS at time of suction curettage
Follow-up	• Refer to Section 1.2 for information/advice requirements • Advise GP follow-up if ongoing clinical concerns • β-hCG not routinely indicated • USS not routinely recommended
Repeat curettage	• If repeat curettage is required (experienced operator required): o Consider initial hysteroscopy to facilitate uterine evacuation and minimise risk of Asherman's syndrome o Administer antibiotics

*Refer to the Australian pharmacopeia for complete drug information

6 Second trimester pregnancy loss

Second trimester pregnancy loss represents one to two percent of recognised pregnancies.[54] A cause and effect relationship is difficult to establish and there may be multiple contributing pathologies.[41,55] There is limited evidence on the best management.[8]

Table 17. Second trimester loss

Aspect	Consideration
Potential aetiologies	**Fetal** • Chromosomal abnormalities[41] • Congenital abnormalities[41] **Maternal** • Previous second trimester loss[56] • Uterine malformations[41,56,57] • Maternal medical illness (e.g. cardiac disease, autoimmune disease, thrombophilia) • Preterm rupture of membranes • Placental complications(e.g. abruption) • Cervical insufficiency[41,56] • Infection–estimated to be implicated in 10% to 25% of cases[41]
Presentation	• Majority present as intrauterine fetal death (IUFD)[55] • May present with preterm labour or premature rupture of membranes
Assessment	• Refer to Section 2 Assessment • Perform low-vaginal and peri-anal swabs • Refer to Queensland Clinical Guidelines: *Stillbirth care*[58] protocol for maternal investigations
Care setting	• Where feasible, provide care in a setting away from women with uncomplicated pregnancies or healthy babies[57] • Provide adequate and appropriate analgesia consistent with the women's wishes[57]

6.1 Management of second trimester loss

Thoroughly discuss options with the woman and her support person/s, in the context of her unique circumstances. Where there is evidence of maternal compromise (e.g. sepsis, large placental abruption, severe or rapidly worsening pre-eclampsia), expedite birth.

Table 18. Management options

Aspect	Consideration
Management options	• Both medical and surgical management options may be appropriate, depending on gestation and individual clinical circumstances • When safe to do so, the woman may go home before returning to hospital at a mutually agreed time (or prior if clinically indicated)
Medical management*	• Appropriate for all gestations • If previous uterine surgery, risk of rupture with misoprostol reported as less than 0.28% [95% CI 0.08 to 1.0][59] • If cervix is closed and membranes are intact, mifepristone and misoprostol are first-line agents for induction of labour[57] o Misoprostol alone may also be used o If no local protocol, refer to Queensland Clinical Guideline: *Therapeutic termination of pregnancy*[60] • If membranes are ruptured and/or the cervix is dilated, consider misoprostol or intravenous oxytocin if required[57]
Third stage	• Active management is recommended • If not complete within 30 minutes: o Notify medical officer o Empty bladder o Consider oxytocin infusion • If not complete within one hour, consider manual removal of placenta • Anticipate and prepare for PPH[57] • Retain cord, membranes and placenta for histopathology[57]
Surgical management	• May be necessary in cases of persistent excessive bleeding, haemodynamic instability, evidence of retained POC, suspected GTD[57] • Generally suitable for gestations up to 15 completed weeks o Between 12 and 15 weeks, experienced practitioner required[61] • May be suitable beyond 16 weeks where baby has died at an earlier gestation and surgery is deemed to be safe
Lactation suppression	• Milk production can occur as early as 16 weeks o Early milk production is more likely in multigravidas and women who have breastfed previously[62] • Where lactation suppression is indicated, recommend conservative and comfort measures (e.g. minimal breast stimulation, cold compresses and analgesia)[62] • Pharmacological agents o There is weak evidence that pharmacologic treatments are better than no treatment for suppressing lactation[63] o Exercise caution when considering use of lactation inhibiting medication and consult with relevant health professionals (e.g. pharmacists, lactation consultants)
Follow-up	• Arrange follow-up appointment with obstetrician[57] • Consider postnatal USS to assess for uterine malformations where indicated • Inform GP and provide a clinical summary • Refer to the Queensland Clinical Guideline: *Stillbirth care*[58] for follow-up maternal and fetal investigations (e.g. autopsy, pathology)

*Refer to the Australian pharmacopeia for complete drug information

7 RhD immunoglobulin

Collect blood group and antibody screen for all women with early pregnancy complications.[64]

Table 19. Assessment for RhD immunoglobulin

Aspect	Recommendation
Context	• Approximately 21% of women in Queensland are RhD negative blood type[65] • The majority of fetal bleeds are less than 5 mL of red blood cells (4% are greater than 1 mL whole blood)[66] • There is limited evidence about the risk of sensitisation with bleeding before 12 weeks, but has been reported as early as 6 weeks gestation[66]
Contra-indications[67]	• RhD positive women • RhD negative women with preformed anti-D antibodies • Previous sensitivity or allergy to RhD immunoglobulin (RhD-Ig) • Woman declines
Indications 1–12+6 weeks gestation	• Recommend to women without contraindications following[64,66] o Miscarriage o Termination of pregnancy o Ectopic pregnancy o Chorionic villous sampling o Hydatidiform mole
Indications 13+0 weeks and beyond	• Recommend to women without contraindications following[66]: o Chorionic villous sampling, amniocentesis, cordocentesis or fetoscopy o Abdominal trauma considered sufficient to cause fetomaternal haemorrhage (FMH) (even if Kleihauer negative, as 0.001 mL fetal blood sensitises an RhD negative mother) ▪ Refer to Queensland Clinical Guideline: *Trauma in pregnancy*[68] o Each occasion of revealed or concealed antepartum haemorrhage o External cephalic version (performed or attempted) o Miscarriage or termination of pregnancy
Quantifying FMH	• If gestation less than 12+6 weeks, quantification of FMH is not required after a sensitising event[69] • If gestation 13 weeks or more, quantify the magnitude of the FMH with the Kleihauer test to ensure an adequate dose of RhD-Ig is offered o Each 100 IU of RhD-Ig protects against 1 mL fetal red cells (2 mL whole blood)[70] • If the Kleihauer test is negative, a further dose of RhD-Ig is not required • If the Kleihauer test indicates FMH is greater than that covered by the RhD-Ig dose administered, give an additional dose(s) within 72 hours sufficient to provide immunoprophylaxis • Flow cytometry (the most accurate quantitative test for FMH) may be performed by the laboratory at their discretion • Interpret with caution in women with persistent fetal haemoglobin (e.g. African women, especially if sickle cell traits)

7.1 Administration of RhD immunoglobulin

Table 20. Administration of RhD immunoglobulin

Aspect	Consideration	
Information	• Inform women that RhD-Ig is a blood product • Obtain consent for administration as for other blood products	
Timing/route	• Administer RhD-Ig as soon as possible after each sensitising event (always within 72 hours) • If not offered within 72 hours, a dose offered within 9–10 days may provide protection[71] • Deep intramuscular injection (IMI)	
Intravenous Rophylac®	• Not indicated for routine prophylaxis in RhD negative women • May be indicated for use in large FMH where administration of IM RhD-Ig is either contraindicated or not practical or for inadvertent or emergency transfusion of RhD positive blood to an RhD negative female of childbearing potential[72] • Rophylac® 1500 IU administered IV will suppress the immunising potential of up to 15 mL of RhD positive red cells[72]	
BMI greater than 30 kg/m^2	• Consider the adequacy of injection site and length of needle used[73] • No additional routine testing or dosing required[73] • If BMI greater than 30 kg/m^2 and FMH greater than 6 mL, intravenous administration may be considered for any additional doses ○ Increases bioavailability and facilitates more rapid clearance of fetal cells	
Dose of IMI RhD-Ig*	**For each sensitising event**	**Dose (IMI)**
	• Singleton pregnancy of 1–12+6 weeks gestation	250 IU
	• Multiple pregnancy (any gestation) • Gestation uncertain but possibly 13 or more weeks • Gestation 13+0 weeks or beyond	625 IU

*Refer to the Australian pharmacopeia for complete drug information

7.2 Threatened miscarriage

Table 21. Threatened miscarriage

Gestation	Consideration
1–12+6 weeks	• Insufficient evidence to support routine use of RhD-Ig for bleeding in an ongoing pregnancy[56] • If there is heavy or repeated bleeding, or bleeding associated with abdominal pain, significant abdominal trauma or a visible subchorionic haematoma, individualise RhD-Ig administration according to clinical circumstances[66,69]
13+0 weeks and beyond	• Quantify FMH at one or two weekly intervals[69] • If a new sensitising event is suspected in addition to continued bleeding, (e.g. change in symptoms or pattern or severity of bleeding) manage as an additional sensitising event • If Kleihauer is positive on any test, give an additional dose of RhD-Ig sufficient to provide immunoprophylaxis[69]

8 Gestational trophoblastic disease

GTD is classified as two premalignant diseases (complete hydatidiform mole (HM) and partial HM) and as four malignant disorders (invasive mole/persistent trophoblast neoplasia, choriocarcinoma, placental site trophoblastic tumour (PSTT) and epithelioid trophoblastic tumour (ETT)). The latter four malignant conditions are often collectively referred to a gestational trophoblastic neoplasia (GTN).[74]

Table 22. Gestational Trophoblastic Disease

Aspect	Considerations
Clinical presentation	• Most common presentation is abnormal vaginal bleeding • More common in Asia (as high as 2 per 1000 pregnancies) compared with Europe and North America (less than 1 per 1000 pregnancies[75]
Diagnosis	• Complete HM are more likely than partial HM to be identified by their characteristic USS features • Normal USS does not exclude the diagnosis of a HM[76] • A quantitative β-hCG is recommended • Definitive diagnosis is made by histological examination of the POC[76]

Interventions	• Register women with the Queensland Trophoblast Centre (QTC)
	• Suction curettage with concomitant administration of IV uterotonic agents (e.g. oxytocin) is required[75]
	• Although there is limited evidence, misoprostol for pre-surgical cervical priming may be considered
	• If GTD is demonstrated by histopathology following medical or expectant management:
	  ○ Close follow-up indicated
	  ○ If ongoing bleeding, β-hCG not clearing, or USS indicates retained POC, then surgery may be indicated

Persistent trophoblastic disease	• In a series of 686 women, 4.7% with partial HM and 16.5% of complete HM, developed persistent disease which required treatment[77]
	• Risk increases progressively with the time taken to reach negative β-hCG after evacuation (more than 100 fold when the interval exceeded 12 weeks[77])
	• Consider persistent disease where there is:
	  ○ Increased, stationary or inadequately falling β-hCG trend on three consecutive weeks at any time following surgical evacuation
	  ○ Continued PV bleeding and detectable β-hCG
	  ○ Evidence of metastases in the presence of detectable β-hCG

Follow-up	• Aim is to exclude persistent GTD[78] • Recommend effective contraception to avoid pregnancy during follow-up • Perform β-hCG levels 6 weeks after any future pregnancy • If β-hCG decreases spontaneously in HM, routine chest x-ray not required **Partial HM** • Weekly serum β-hCG levels until negative for three consecutive weeks • Conception may be attempted immediately after three consecutive negative β-hCG results • Annual follow-up for five years with QTC **Complete HM** • Weekly serum β-hCG until negative for three consecutive weeks • Then monthly for 6 months after the third negative result • Conception may be attempted immediately after the six months of consecutive negative β-hCG results are finalised • Annual follow-up for five years with QTC

Queensland Trophoblast Centre (QTC)	• Mortality with GTD treated at a trophoblast centre was 2.1% compared to 8% among women referred after failure of primary treatment[79]
	• Register all women with the QTC at the Royal Brisbane and Women's Hospital, Queensland 4029
	• Contact QTC:
	  ○ For any clinical concerns
	  ○ In all cases of persistent GTD
	• Further information and contact details available at: http://www.health.qld.gov.au/rbwh/services/gtd-unit.asp

9 Psychological support

Early pregnancy loss is an experience common to many women, and yet it is simultaneously an intensely personal, private, intimate and individual experience.[80] It is important for longer term health and wellbeing, that a woman's psychological needs are not overlooked, and that any symptoms of grief, depression and anxiety are recognised and acknowledged by health professionals.[81]

9.1 Context and experience of early pregnancy loss

Table 23. Context and experience of early pregnancy loss

Aspect	Consideration
Context	• Approximately one third of women experience at least one EPL[4] • Historically, maternal grief following a EPL was presumed to be mild and short lived, but has been more recently recognised as significant as losing any loved one[81]
Unique challenges of EPL	• Often sudden and unexpected, limiting the opportunity for anticipatory grieving and practical preparation[81] • Encompasses both the loss of a baby, and the loss of future dreams and possibilities[80,82,83] • The loss is largely invisible and hidden (as distinct from loss later in pregnancy) • May be largely unacknowledged by family, friends and society in general contributing to a feeling of isolation and secrecy[81,84] • Frequently no formal or public commemoration, funeral or ritual to mark the loss • Often a sense of taboo, stigma and silence which can make it difficult to move through the grieving process[81,82,85] • Society can trivialise the impact and downplay the need for women to mourn their loss[4] • Can be perceived as a failure of her own body[80] • Often no known cause, contributing to a sense of confusion, failure, and self-blame ○ Ascribing an explanation for the loss can bring some resolution and reduce feelings of personal responsibility and guilt[80,86,87] • The meaning women attach to their pregnancies varies, and in turn affects the way they interpret an EPL. Feelings range from relief through to devastation[4] • Partners may experience and respond differently to the loss
Care setting	• Minimise waiting times, particularly in public areas such as waiting rooms • Consider each woman's unique situation and context (e.g. previous history of EPL, multiple pregnancy, geographical challenges) • Where feasible, offer inpatient care away from maternity units where other mothers and babies are located • Offer and facilitate the presence of a support person for all care provision as appropriate • Non-directive pregnancy support counselling services are provided under Medicare to a person who is currently pregnant or has been pregnant in the preceding 12 months[88]

9.2 Communicating with parents

Table 24. Psychological support considerations

Consideration	Recommendation
General principles	• Ensure both parents are present at discussions if feasible, and offer inclusion of a support person where appropriate • Ensure both written and verbal information given is consistent[89] • Avoid speculation regarding the cause and explain that the cause of EPL often remains unexplained • Express sorrow for what has happened ○ Offering sympathy is not an admission of guilt or error • Be open and honest in dealings with parents • Allow time for parents to ask questions, consider treatment options and make decisions • Repeat important information as stress and grief may interfere with comprehension and recall of information

Sharing information	• Information is critical in increasing knowledge and understanding, and in facilitating control and coping whilst also decreasing distress, fear and anxiety[84,90]
	  ○ 93% of women reported that seeking of information was a helpful strategy for coping with their loss[83]
	• Information about the prevalence of EPL may help women come to terms with loss and reduce feelings of guilt, shame and personal failure[82,91]
	• Offer practical information (including written resources) on issues including:
	  ○ What their baby remains may look like (where appropriate)
	  ○ The grieving process
	  ○ Options for the disposal of baby remains [refer to Section 11]

Communication tips[91]	• Do:
	  ○ Use the word “baby” (as opposed to “fetus” or “POC”)
	  ○ Say “I am sorry for your loss”
	  ○ Call baby by given name (if named) when making/creating memories
	  ○ Refer to parents as mum and dad to the baby
	• Do not say:
	  ○ You can always have another baby[82]
	  ○ You’re lucky to have other children
	  ○ It was for the best or everything happens for a reason
	• Do not try to “cheer them up”
	• Inform parents that well-meaning family and friends may say hurtful things

Breaking bad news	• Take great care in being sensitive when delivering bad news. Moments such as these frequently remain engraved in women’s memories, and they are often able to reconstruct the scene and words used in detail[80] • The most experienced practitioners are required for these difficult conversations • Train sonographers and other health professionals in breaking bad news sensitively[2,91] • Inform parents of diagnosis in a timely manner • Provide a private environment and ensure confidentiality • Provide opportunity for parents to see absence of heartbeat on screen in USS where appropriate • Offer USS results in writing and/or a photo as a memento • Communicate empathetically, clearly and honestly • Use empathetic but unambiguous language (e.g. ‘your baby has died’) • When appropriate, reassure the woman that the loss was not due to anything she did or did not do • Listen reflectively to the parents and give comprehensive answers to questions • Provide support after hearing bad news such as quiet time and opportunity to contact close family/friends

9.3 Supportive care

Table 25. Supportive care

Aspect	Consideration
General principles	• Emotional care is central to women's perception about the quality of care received • Treat women with early pregnancy complications with dignity and respect, being aware that women will react in different ways[2] • Empathy, compassion, warmth, kindness, patience, gentleness and understanding[91] are essential characteristics for health care providers • Take the time to listen and be present and support the woman to mourn and experience the event in her own way[80] • Recognise the loss and acknowledge the importance of this baby no matter how early the loss occurs • Inform parents that they can make their own decisions as to what happens to their baby[91]
Grief and mourning	• Allow time for the woman to respond to her loss and offer her a space to discuss her feelings[90,92] • Express genuine concern and demonstrate emotional awareness • Counsel women regarding the potential to experience symptoms of grief, depression and anxiety following an EPL[90,92] • Provide information about accessing additional psychological support in the future

9.4 Creating memories

Table 26. Memory creation

Aspect	Consideration
Individual preferences	• Parents may or may not wish to create memories of their pregnancy/baby • Discuss options for memory creation with the parents as appropriate to the gestational age, circumstances and cultural preferences • Obtain parental consent prior to creating/gathering mementos (as may not always be culturally appropriate) • Where immediate memento creation is declined, offer to provide mementos to parents (or family) in a sealed envelope for future access ○ Storing mementos with hospital records is not recommended as they may be lost or misplaced especially as electronic medical records become more common and replace hard copy records

Seeing the baby	• Where desired, give parents the opportunity to see and/or hold their baby
	  ○ Some women wish to avoid this, whereas others may place importance on seeing their baby[91,93]
	  ○ Prepare the woman/family for what they may see
	• Following second trimester loss, it may be possible to collect memories such as photographs, handprints and footprints, or to bath the baby
	  ○ Complete all swabs and tests on baby before bathing
	• Offer options to include extended family (e.g. photographs of family groups, relatives/siblings)

Mementos	• Suggestions to support memory creation include:
	  ○ Apply for an EPL recognition certificate from the Department of Births, Deaths, Marriages and Divorces[94]
	  ○ Create a keepsake box to keep sentimental items in
	  ○ Collect mementos such as USS photos, initial positive pregnancy test, hospital identification tags, cot card, sympathy cards, toys or clothes that had been purchased for the baby
	  ○ Name the baby
	  ○ Choose a keepsake (e.g. jewellery, ornament, or special quilt)
	  ○ Create a memorial (e.g. special plant or seat in garden)[91]
	  ○ Keep a journal of events, thoughts and feelings, or notes or poems to or about baby

9.5 Psychological morbidity

Table 27. Psychological morbidity

Aspect	Consideration
After EPL	• Suicide is the leading cause of maternal death in Queensland and Australia[24,95] ○ One of eight maternal suicides in Queensland in 2012–2013 occurred following an EPL[95] • A Finnish study reported significantly higher suicide rate following EPL (18.1 per 100 000) than after birth (5.9 per 100 000) or in the general population (11.3 per 100 000)[96] • 50% suffer some form of psychological morbidity[81] • 40% suffer symptoms of grief immediately[81,90] including sadness, longing for the lost baby, a desire to discuss the loss with others and search for a meaningful explanation • Depressive symptoms occur in 12–55% and a similar proportion of women fit the criteria for a major depressive disorder following miscarriage[81,90] • Elevated anxiety symptoms reported in 20–40%[81,90] • Pathological grief (characterized by despair, deep feelings of worthlessness and hopelessness, and difficulty resuming normal interactions and activities of daily life)[81] can develop • Exacerbation of pre-existing mental health issues
Risk factors for psychological morbidity	• History of mental illness[85] • Stress and negative life events around time of loss[85] • Dissatisfaction with primary care provider[85] • Lower level of education[85] • No living children at the time of pregnancy loss[90] • Lack of social support[90] • High levels of self-criticism[97] • Later gestational age[97]
Prevention	• Assess for psychological risk factors and refer to mental health services when required[92] (e.g. suicidal ideation) • Assess each woman's response to EPL, and individualised care[89,92] • Remember that an EPL, while common within the clinical setting, is a significantly distressing event and that nearly half of women experience psychological morbidity[86,89,90] • Be proactive rather than reactive in meeting emotional and physical needs to avoid the woman feeling forgotten, alone or abandoned[89,92]

10 Recurrent early pregnancy loss

While recurrent early pregnancy loss is defined as three or more consecutive miscarriages, consider the individual circumstances of each woman when determining if further investigation is warranted after EPL (e.g. the woman's age in relation to her opportunity to achieve a live birth).

Table 28. Recurrent early pregnancy loss

Aspect	Consideration
Care provision	• Specialist gynaecological consultation is recommended • If underlying medical conditions are suspected, refer to specialist physicians as indicated • Individualise the investigation of recurrent EPL based on a comprehensive history of both partners and the clinical circumstances • Investigation is often disappointing with many unanswered questions regarding aetiology, evaluation and management

Risk factors	• Epidemiological factors
	  ○ Advanced maternal age: risk 51% at 40–44 years; 93% at greater than 45 years[98]
	  ○ Risk of EPL increases after each successive loss (40% after three consecutive losses)
	• Anatomical factors (e.g. congenital uterine malformations)
	• Endocrine factors (e.g. diabetes mellitus, thyroid, polycystic ovary syndrome)
	• Genetic factors[98]
	  ○ Chromosomal abnormalities of the embryo account for 30–57% of further EPL
	  ○ Chromosomal anomaly present in one partner in 2–5% of couples[98]
	• Antiphospholipid antibodies: present in 15% of women with recurrent EPL
	• Infective agents
	• Inherited and acquired thrombophilia

Standard investigations	• Full Blood Count • ELFT • Thrombophilia screen • Fasting homocysteine and MTHFR (methylenetetrahydrofolate reductase) • Antiphospholipid antibodies • Thyroid function tests • Fasting insulin • Fasting blood glucose level • POC for fetal karyotyping • Parental chromosomes • Pelvic USS to assess anatomy of the uterus and fallopian tubes • Sperm testing
Potential treatments	• As indicated by individual clinical circumstances • May include low dose aspirin, enoxaparin, progesterone pessaries, or steroids

11 Sensitive management of fetal tissue/remains

The decisions parents make after EPL can have a significant impact on the grieving process. Even where there is no legal requirement for a funeral, burial or cremation, parents may still desire this option or return months, or even years, later to enquire about the manner in which their baby was disposed of.[99]

Table 29. Sensitive disposal of fetal remains

Consideration	Recommendation

Birth registration	• It is compulsory to register the birth of a baby born in Queensland if any of the following conditions are met. Baby is:
	  ○ Born alive (a baby whose heart has beaten after delivery of the baby is completed[100])
	  ○ 20 weeks or more gestation
	  ○ 400 g or more
	• If birth registration is compulsory (i.e. one or more of the above conditions are met), a death certificate and burial or cremation are also compulsory and perinatal data collection is required
	• If birth registration is not compulsory (i.e. none of the above conditions are met), then a death certificate, burial or cremation, and perinatal data collection are not required
	• Inform parents that an 'Early pregnancy loss recognition certificate' can be obtained free of charge from the Registry of Births, Deaths Marriages and Divorces

Management options	• Queensland Health facilities may release a deceased fetus which does not require burial or cremation to the parents, provided that:
	  ○ The facility is satisfied there is no risk of transmission of notifiable conditions
	  ○ Parents have been informed as to the manner in which the fetal tissue/remains may be lawfully disposed of
	• Options for disposal include:
	  ○ Hospital disposal by cremation
	  ○ Transfer to a funeral director for private arrangements
	  ○ If there are no prohibiting local council requirements, burial on private property

Facility responsibilities	• Develop local options and protocols to facilitate sensitive disposal of fetal remains including (but not limited to):
	  ○ Identification of local council requirements (if any) regarding burial on private property
	  ○ Release of fetal remains to parents and subsequent return for hospital cremation
	  ○ Documentation in case of community queries regarding the transport and/or disposal of fetal remains
	• Document in the health record, the arrangements that are made for fetal tissue disposal

Information provision	• Inform parents clearly and sensitively of the options available • Allow time for decision making (including when disposal occurs) and provide written information where possible • If parents choose to take fetal remains home, provide information about temperature and timeframes for optimal preservation (e.g. intermittent refrigeration) and expected look and feel • Advise that cremation of fetal tissue does not often produce any ashes to scatter[101] • Respect the wishes of parents who may not want to be involved

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Appendix A: Early pregnancy assessment service

Aspect	Consideration
Benefits of dedicated EPAS	• Streamlining of care and improved efficiency and higher quality of care • Reduction in admissions and shorter inpatient hospital stay for those requiring admission • Greater satisfaction from women regarding their perceived quality of care*

Service provision	• May be provided by
	  ○ Obstetricians and gynaecologists
	  ○ GP obstetricians
	  ○ GPs in community/rural settings
	  ○ Nurse Practitioners with relevant skill-set
	• Network with a dedicated EPAS for consultation and referral as required

Service requirements	• An appointment system
	• A discrete waiting area and appropriate consultation room
	• USS equipment (including transvaginal probe) or access to USS evaluation
	• Easy access to laboratory facilities for:
	  ○ RhD antibody testing
	  ○ Selective serum ß-hCG
	  ○ Ideally progesterone estimation
	• Be available on a daily basis Monday to Friday
	  ○ If possible available on weekends and after hours

Governance	• Establish governance and accountability for clinical practice • Identify defined lines of communication • Determine clinical inclusion/exclusion criteria based on the Clinical Service Capability Framework • Establish written pathways for clinical management • Provide guidance for appointment booking (i.e. referral only or self-referral) • Establish referral and transfer of care pathways within and external to the service
Documentation	• Access to standardised written patient information • Referral and transfer of care (discharge) letters available

*Tsartsara E, Johnson MP. Women's experience of care at a specialised miscarriage unit: an interpretative phenomenological study. Clinical Effectiveness in Nursing 2002;6:55-65.

Appendix B: Sonographic anatomy, landmarks and documentation

Sonographic landmarks: TVS is recommended for the accurate assessment of early pregnancy

Aspect	Findings
Gestational sac	• Earliest sonographic finding in pregnancy • Use Mean sac diameter (MSD) to determine gestational age before crown rump length (CRL) can be clearly measured • Usually visible (with TVS) from 4 weeks and 3 days after LNMP • True gestational sac is eccentrically placed within the endometrial cavity and surrounded by 'echogenic ring' on TVS ○ Intra-cavity fluid (previously called 'pseudo gestational sac') is in the midline of the endometrial cavity, displacing the anterior and posterior surfaces of the endometrial cavity • With a positive pregnancy test and no signs of intra or extra uterine pregnancy on TVS, pregnancy is identified as PUL
Yolk sac	• Yolk sac is usually first structure visible within the gestational sac and usually visible by 5.5 weeks gestation or MSD of 8–10 mm • Presence of yolk sac is definitive evidence to differentiate a sac into a gestational sac • Number of yolk sacs usually indicates the number of amniotic sacs in the case of twin pregnancies (i.e. two yolk sacs indicated a diamniotic pregnancy, MCMA twins have one yolk sac)
Embryo and cardiac activity	• The fetal pole (embryonic disc) is usually visible by 5–6 weeks gestation • CRL at 6 weeks and 0 days is 4 mm • During the embryonic period (weeks 6–10) the CRL increases about 1 mm per day • Cardiac activity is routinely detected by 6 to 6.5 weeks gestation • Before 6 weeks gestation, the cardiac rate will be slow (i.e. between 100 and 115 beats per minute, and increases rapidly after 6 weeks
Corpus luteum	• Can vary greatly in appearance, from solid to cystic forms, up to 3cm in size • Peripheral vascularity often detected
Early first trimester dating	• Gestational sac (no yolk sac, embryo or heartbeat) = 5 weeks • Gestational sac and yolk sac (no embryo, no heartbeat) = 5.5 weeks • Gestational sac and yolk sac (living embryo, CRL less than 5 mm (too small to measure) = 6 weeks • When CRL available, use Australasian Society of Ultrasound Medicine measurements to date the pregnancy

Sourced primarily from Australasian Society of Ultrasound Medicine guidelines. Available from *http://www.asum.com.au/*

Standard ultrasound documentation

Aspect	Information required
Approach	• Specify if TVS or TAS to aid interpretation
Patient history	• LNMP if known and estimated date of delivery by LNMP • Any USS performed in the current pregnancy and the results • Whether β-hCG (urine or serum) performed and when
Intrauterine:	• Presence of intrauterine sac and if visualised whether single or multiple • Mean sac diameter in mm and estimated gestation • Presence of yolk sac • Presence of fetal pole and the length • Presence of fetal heart movement and/or rate in beats per minute (bpm) • Presence and size of any peri-gestational bleed • Gestational age in weeks and days and estimated date of delivery by this USS • Presence and size of retained POC • If multiple pregnancy, number of yolk sacs and chorions, and thickness of dividing membrane • Possible ectopic intrauterine implantation (cornual, intramural, cervical, scar, ectopic)
Extrauterine:	• Ovary—left and right • Adnexa—left and right • Presence of free fluid and volume (minimal, moderate, extensive) if any

Appendix C: Methotrexate regimens for ectopic pregnancy

Follow local protocols for the safe administration/disposal of cytotoxic medications and equipment.
Refer to the Australian pharmacopeia for complete drug information.

Intramuscular injection (IMI) methotrexate	
Indications	• Unruptured tubal ectopic pregnancy with **all** of the following: ○ β-hCG less than 3000 IU/L ○ Fetal sac less than 3.5 cm ○ NO fetal cardiac activity
Dose calculation	• Dose is calculated per square meter of Body Surface Area (BSA) ○ BSA = the square root of [Height (cm) x Weight (kg) divided by 3600] • No consensus on methotrexate dose capping, but commonly capped at 2 m^2 BSA (equivalent to methotrexate 100 mg IMI) ○ If capped, morbidly obese women may require an additional dose ○ If BSA greater than 2 m^2 seek expert advice
Prior to commencement	• FBC, ELFT, β-hCG prior to each dose of methotrexate • Antiemetic 30 minutes prior to methotrexate (i.e. ondansetron 8 mg IV (or oral) OR granisetron 3 mg IV)
Post-dose	• Monitor woman for 30 minutes post methotrexate administration for hypersensitivity reactions (rare), consider antihistamine or steroid cream • Give ondansetron 4 mg BD PRN for 2 days
Day 1 (Treatment day)	• β-hCG • Methotrexate 50 mg/m^2 BSA IMI (rounded to the nearest 5 mg)
Day 4	• β-hCG
Day 7	• β-hCG • If day 7 β-hCG reduction is less than 15% of day 4 β-hCG, (or if no day 4 level, then less than 25% of day 1 β-hCG) give a second dose of methotrexate 50 mg/m^2 BSA IMI
Day 14	• β-hCG • If day 14 β-hCG reduction is less than 15% of day 7 β-hCG, give a third dose of methotrexate 50 mg/m^2 BSA IMI
β-hCG	• Monitor the β-hCG weekly until less than 5 IU/L

Intravenous injection (IVI) methotrexate	
Indication	• Any stable ectopic pregnancy at the discretion of the physician, particularly if **any** of the following: ○ β-hCG greater than 3000 IU/L ○ Fetal sac greater than 3.5 cm ○ Presence of cardiac activity
Prior to commencement	• β-hCG, FBC, ELFT • Ensure adequate hydration • 24 hours prior (or as soon as practical) ensure urinary pH greater than 7.0 ○ Give two sachets of sodium citrotartrate 6 hourly and prn ○ Test each urinary void during treatment and prior to discharge
Commence as inpatient	• Antiemetic 30 minutes prior to methotrexate (i.e. ondansetron 8 mg IV (or oral) OR granisetron 3 mg IV) • Loading dose of methotrexate 100 mg IV stat, over 5–10 minutes • Then methotrexate 200 mg IV infusion in 500 mL 0.9% sodium chloride over 12 hours
Post loading dose folinic acid *(inpatient or outpatient)*	• Give ondansetron 4 mg BD PRN for 2 days • Give folinic acid 15 mg oral (leucovorin) at each of the following times (**timing is critical**): ○ 30 hours post-loading dose of methotrexate ○ 42 hours post loading dose of methotrexate ○ 54 hours post loading dose of methotrexate ○ 66 hours post loading dose of methotrexate • Confirm timings with follow-up telephone call the day after discharge
β-hCG	• Monitor the β-hCG weekly until less than 5 IU/L

NB: In some circumstances, alternative treatment may involve USS guided direct injection of methotrexate into ectopic pregnancy (plus or minus feticide). Seek expert advice.

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