Clinical Guidance

Management of Renal Disease in Pregnancy

Summary: This document is intended as a quick reference tool for the management of renal disease in pregnancy for clinicians within the South West London & Surrey Heartlands Maternal Medicine Network.

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Contents

Categories of Complex Medical Conditions in Pregnancy 2

Pre-pregnancy Counselling and Support ..... **Error! Bookmark not defined.**

2. Medication in pregnancy and lactation ..... **Error! Bookmark not defined.**

3. Pregnancy Care ..... **Error! Bookmark not defined.**

4. Specific conditions ..... **Error! Bookmark not defined.**

5. Specialist services for women with kidney disease ..... **Error! Bookmark not defined.**

Categories of Complex Medical Conditions in Pregnancy

Objective

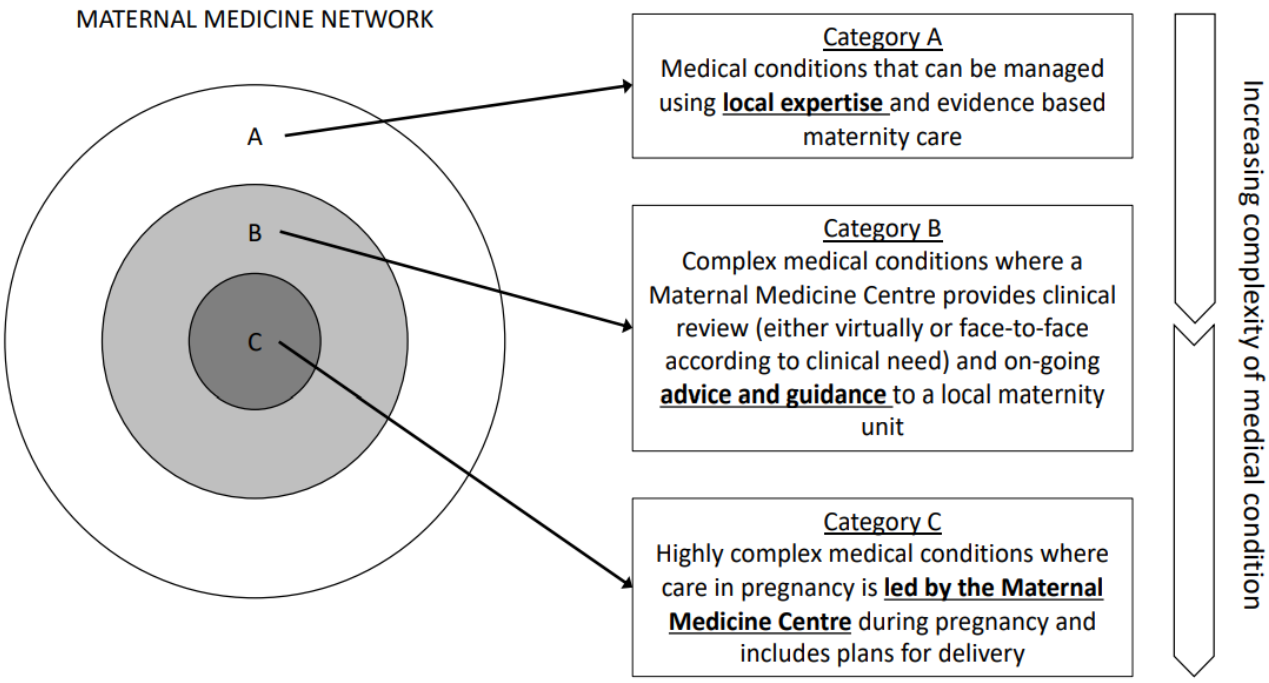
To provide evidence-based recommendations for managing renal disease in pregnant patients to optimise maternal and fetal outcomes.

Scope

This guideline applies to all healthcare providers caring for pregnant patients with renal disease.

Structure of Care

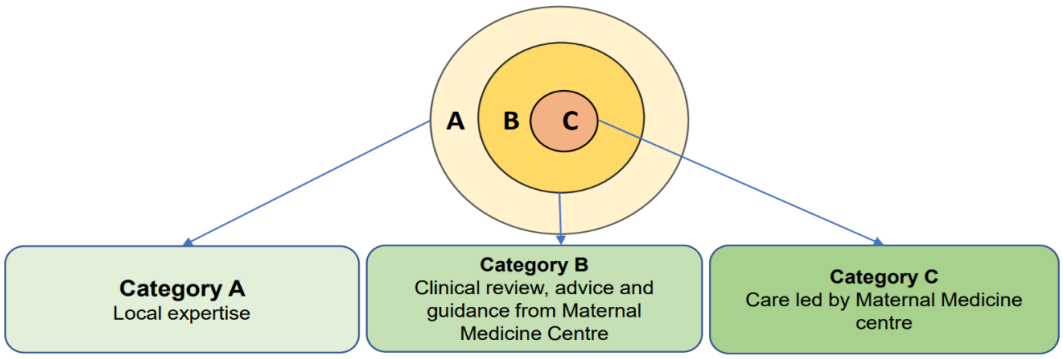
The medical conditions in pregnancy are classified as Category A, B or C depending on their complexity.



CKD can be associated with adverse maternal and fetal outcomes. The key to achieving optimum outcome in these women depends on effective preconception counselling and management by a multidisciplinary team.

CKD is classified into 5 stages based on estimated glomerular filtration rate (eGFR). Please note that eGFR is not valid for use in pregnancy. Renal function in pregnancy should be assessed using serum creatinine.

Stage 1	Normal GFR – GFR>90, urine findings, structural abnormalities or genetic traits suggestive of kidney disease
Stage 2	Mild impairment – GFR 60-89, and other findings suggestive of kidney disease
Stage 3	Moderate impairment – GFR 30-59
Stage 4	Severe impairment – GFR 15-29
Stage 5	Established renal failure – GFR <15 or on dialysis



Single Kidney	Lupus nephritis in remission or on treatment	Active lupus nephritis
Non-lupus glomerulonephritis/tubulointerstitial nephritis • No immunosuppression AND • Stable pre-pregnancy CKD stage 1-2 AND • uPCR <100 or uACR <30 AND • BP <140/90	Non-lupus glomerulonephritis/tubulointerstitial nephritis • On immunosuppression OR • Pre-pregnancy CKD stage 3 OR • uPCR >100 or uACR >30 OR • BP >140/90	Pre-pregnancy CKD 4-5
Kidney stones	Kidney transplant	Combined Kidney-pancreas transplant
Recurrent UTI (no immunosuppression)	Recurrent UTI with abnormal renal function	Dialysis
Reflux nephropathy with normal kidney function	Reflux nephropathy with abnormal kidney function (serum creatinine >78 micromol/L)	New renal vasculitis in pregnancy and vasculitis on immunosuppression
Autosomal dominant polycystic kidney disease with normal kidney function	Autosomal dominant polycystic kidney disease with abnormal kidney function	Scleroderma renal crisis
AKI responding to treatment	AKI not responding to treatment or not resolving postpartum	
AKI due to preeclampsia resolved postpartum	Previous renal vasculitis in remission, no longer on treatment	
	Previous urinary tract reconstructive surgery	
	Kidney disease on biologic treatment	
	Progressive kidney disease in pregnancy	

Pre-pregnancy Counselling and Support

- Pre-pregnancy counselling by a multi-disciplinary team including a consultant Obstetrician and Nephrologist and/or an Obstetric Physician is important to fully evaluate renal disease/other co-morbidities, to optimise medication and planning of antenatal care.
- Safe and effective contraception should be prescribed for:
  - ◊ women taking teratogenic medication
  - ◊ women with active glomerulonephritis
  - ◊ women within 1 year of renal transplantation or acute graft rejection
  - ◊ women with CKD who do not wish to conceive.
- Women with CKD should be referred for pre-pregnancy counselling before receiving assisted reproductive technology.
- Single-embryo transfer is recommended to reduce the risk of complications of multi-fetal pregnancies.
- Women with known or suspected inheritable renal diseases should be offered genetic counselling including inheritance risk, prognosis, and intervention options including pre-implantation genetic diagnosis.
- In all conditions, it is usually advisable to delay conception until the disease and drug regimen are stable.
- Women with CKD should be informed of the increased risk of complications in pregnancy including pre-eclampsia, gestational diabetes, venous thromboembolism, preterm birth, fetal growth restriction, caesarean section, and neonatal unit (NNU) admission.
- Individualised information should be provided to the woman and her family about the risks of pregnancy to her long-term health and CKD. For women with CKD stages 3 to 5, the risk of transient or permanent deterioration of background renal function, risk of requiring dialysis, acute transplant rejection, and situations where termination of pregnancy is offered should be discussed.
- There must be written communication with the Renal team and the GP including discussion about medication plans.
- Women and their caregivers must be provided with clear information on how to access specialist antenatal services in the event of a positive pregnancy test/confirmed ongoing pregnancy.
- Rapid access to termination of pregnancy services should be facilitated, if for whatever reason a woman chooses this.
- It would be advisable to make a treatment plan in the event of hyperemesis or disease exacerbation/relapse during pregnancy.

2. Medication in pregnancy and lactation

2.1 Medications considered safe in pregnancy include:

- Calcium channel blockers (including Nifedipine and Amlodipine), Methyldopa, Hydralazine, Labetalol, Propranolol, Prednisolone, Azathioprine, Tacrolimus, Cyclosporine, Hydroxychloroquine, Aspirin and Heparin. Provide women with written information regarding drug safety in pregnancy e.g. BUMPS leaflets.
- The concentrations of calcineurin inhibitors (Tacrolimus, Ciclosporin) should be checked throughout pregnancy and immediately post-partum, as blood concentrations may change.
- Medications that interfere with calcineurin inhibitor metabolism (e.g. Erythromycin, Clarithromycin) are avoided in pregnant and post-partum women taking Tacrolimus or Ciclosporin whenever possible.
- Metformin can be used in pregnancy for women with a pre-pregnancy eGFR >30 mL/min/1.73m2 and stable renal function during pregnancy.

2.2 Medications contraindicated in pregnancy include:

- ACE inhibitors (e.g. Captopril, Enalapril) and Angiotensin II receptor blockers (e.g. Candesartan, Losartan) as they are associated with an increased risk of congenital malformations and fetal renal dysfunction.
- Mycophenolate mofetil, Methotrexate, and Cyclophosphamide are teratogenic and should be avoided in pregnancy. They should be discontinued 3-6 months before conception.
- Ideally women on immunosuppressants should be switched to an alternative immunosuppressive medication with a period of at least 3 months stability on the new medication before falling pregnant.
- Women can breastfeed whilst taking Prednisolone, Hydroxychloroquine, Azathioprine, Ciclosporin, Tacrolimus, Enalapril, Captopril, Amlodipine, Nifedipine, Labetalol, Atenolol and low molecular weight heparin.

3. Pregnancy Care

3.1 Assessment of renal function in pregnancy:

- Renal function in pregnancy is assessed using serum creatinine concentrations as estimated GFR (eGFR) is not valid for use in pregnancy. A value of >78 micromol/L is considered abnormal in pregnancy.
- Women with CKD should have a formal quantification of proteinuria in pregnancy, undertaken by protein: creatinine ratio (uPCR) or albumin: creatinine ratio (uACR). Twenty-four-hour urine collection for quantification of protein is not required.

3.2 Antenatal care

- If pregnant women with CKD have not had pre-pregnancy counselling, they should be referred to the joint Obstetric Renal clinic where possible to receive the same counselling and optimisation as for women attending pre-pregnancy.
- They should be referred to the Maternal Medicine Team and Specialist Midwives for antenatal care.
- Pregnant women with CKD should have the usual trisomy screening and additional scans for fetal growth and well-being in the third trimester at 28, 32 and 36 weeks. Women with CKD exposed to teratogenic drugs in the first trimester should be referred to the Fetal Medicine Consultant.
- Women with CKD and women who themselves are kidney donors should be offered low-dose Aspirin 150 mg in pregnancy to reduce the risk of pre-eclampsia. ***This is irrespective of ASPRE screening or blood pressure readings.***
- All pregnant women taking Prednisolone and/or calcineurin inhibitors should be screened for gestational diabetes.
- The need for antenatal anaesthetic referral should be considered for all women with CKD, especially those with co-morbidities.

3.3 Blood pressure management

- The target blood pressure during pregnancy for women with CKD is 135/85 mmHg or less, and this should be documented in the woman's healthcare record – consider HBPM. Not suitable for low risk postnatal pathway.
- Pre-pregnancy anti-hypertensive treatment in women with CKD is continued in pregnancy unless systolic blood pressure is consistently < 110 mmHg systolic, or diastolic blood is pressure consistently < 70 mmHg diastolic, or there is symptomatic hypotension.
- Labetalol, Nifedipine, and Methyldopa can be used to treat hypertension in pregnancy.
- ***A diagnosis of superimposed pre-eclampsia is considered:***
  - ◊ In a woman with non-proteinuric CKD, if she develops new hypertension (systolic BP > 140 mmHg and/or diastolic BP > 90 mmHg) and proteinuria (***uPCR > 30 mg/mmol or uACR > 8 mg/mmol),*** or maternal organ dysfunction after 20 weeks gestation.

- ◊ In women with proteinuric CKD if they develop new hypertension (systolic BP > 140 mmHg and/or diastolic BP > 90 mmHg) or maternal organ dysfunction after 20 weeks gestation.
- ◊ In a woman with chronic hypertension and proteinuria, if she develops maternal organ dysfunction after 20 weeks gestation.
- ◊ In women with chronic hypertension and proteinuria who develop sustained severe hypertension (systolic BP > 160 mmHg and/or diastolic BP > 110 mmHg, or doubling of the dose of anti-hypertensive agents) and/or a substantial rise in proteinuria (doubling of uPCR or uACR compared to early pregnancy).

- Angiogenic markers (PlGF ± sFlt-1) should be considered as an adjunct to diagnose suspected preterm pre-eclampsia.

3.4 *Venous thromboembolism*

- Women with nephrotic-range proteinuria (uPCR > 300 mg/mmol or ACR > 250 mg/mmol) should be offered thromboprophylaxis with low molecular weight heparin in pregnancy and the post-partum period unless there is a specific contraindication such as the risk of labour or active bleeding.
- Non-nephrotic range proteinuria in pregnancy is a risk factor for thrombosis and thromboprophylaxis should be considered if additional risk factors are present.

3.5 Anaemia

- Routine screening and treatment of anaemia, including a booking ferritin, should be offered to all women, and early iron replacement administered as indicated.
- In women with CKD, decreased erythropoietin levels and shortened red cell survival are common. Where indicated, following discussion with the specialist Renal team, erythropoietin treatment should be offered to improve anaemia.
- IV iron replacement to achieve serum ferritin >200 is usually required before EPO therapy.

3.6 Bone health

- Women with CKD who are vitamin D deficient should be given vitamin D supplementation in pregnancy.
- Calcimimetics and non-calcium-based phosphate binders should be discontinued in pregnancy.

3.7 Renal biopsy

- A renal biopsy can be performed in the first and early second trimesters if a histological diagnosis will change the management in pregnancy.

3.8 Planning birth

- Timing/mode of birth should be guided by obstetric factors in women with stable kidney disease CKD 1/2.
- In the presence of associated hypertension, birth should be offered by 39 weeks. Earlier induction may be associated with improved maternal and fetal outcomes in women with CKD 3 or more, or in women with deterioration in renal function.
- In pregnancies complicated by SGA, gestational hypertension or pre-eclampsia, timing/mode of birth should be offered at 37-38 weeks, if not indicated sooner.
- A care plan should be documented prior to 36 weeks in women where there are special considerations likely to affect birth/post-partum management.
- These include:
  - ◊ The need for senior/additional surgical support in the event of a caesarean section – this is particularly relevant in women who have had a renal transplant
  - ◊ Anaesthetic considerations
  - ◊ Care plan for the management of LMWH
  - ◊ Plan for IV hydrocortisone where indicated
  - ◊ Plan for insulin therapy

- ◊ Additional considerations in women with CKD who are at risk of volume depletion or volume overload.
- ◊ A plan for medications in the immediate postnatal period

3.9 Peri-partum care

- CKD is not an indication for caesarean birth (unless specific circumstances - complex congenital anomalies etc). Women with CKD should be reassured that vaginal birth is a safe and suitable choice for the majority. Their informed choice following counselling in line with NICE guidance should be supported.
- Continuous electronic fetal monitoring is recommended for women with CKD.
- All women with CKD should have observations taken and documented during any hospital admission. This includes temperature, heart rate, blood pressure, respiratory rate, oxygen saturation, and level of consciousness. An early warning score should be calculated and actioned appropriately.
- There is no contraindication to the use of labour analgesia including epidural. For women prescribed LMWH, a haematology care plan should be documented at 36 weeks, or earlier if necessary.
- Additional assessment should be undertaken for women with an elevated early warning score, for women considered to be high risk, and for any women in whom there is any clinical concern. This includes jugular venous pressure, chest auscultation and urine output monitoring (in-dwelling catheter not usually required) in addition to routine parameters.
- Fluid balance should be managed judiciously with the aim of maintaining normal fluid volume and avoiding dehydration and pulmonary oedema, with input from clinicians with expertise in fluid balance and renal disease if necessary.
- **A specific assessment of the increased risk of pulmonary oedema should be undertaken in women with CKD and pre-eclampsia.**
- In women taking >7.5mg Prednisolone daily, an individualised plan for intrapartum steroid cover should be documented. Intravenous Hydrocortisone 50-100mg 6-hourly may be used where stress-dose cover is indicated, with dose tailored to usual steroid dose, clinical condition and mode of birth, until oral medication can be recommenced.
- An arterial line may be indicated, and this should be specified in the anaesthetic care plan.
- Blood loss should be assessed as accurately as possible.
- Limitation of second stage is not needed.
- Ergometrine and Syntometrine are often contraindicated due to pre-existing hypertension and/or pre-eclampsia.
- ***When MgSO4 is administered*** (fetal neuroprotection or severe pre-eclampsia), clinicians should be alert to the possibility of magnesium toxicity in women with impaired renal function and consider using lower doses for maintenance MgSO4 therapy.

3.10 Postnatal care

- Non-steroidal anti-inflammatories should not be given.
- LMWH should be continued for 6 weeks post-partum in women with significant risk factors for VTE or where antenatal VTE prophylaxis was recommended.
- Women with CKD should have a planned early post-partum renal review.
- Women with a new diagnosis of CKD during pregnancy should be referred to a nephrology clinic and advised of the possibility of requiring a renal biopsy.
- Women with CKD should be prescribed medications that are compatible with breastfeeding whenever possible.
- Women with CKD should be offered safe and effective contraception post-partum. These include the progesterone-only pill, progesterone sub-dermal implant, and the progesterone intra-uterine system (Mirena IUS). Emergency contraception is safe in CKD and transplant patients. Combined OCP are 3rd line but not excluded.
- Depot progestogens can have variable interactions with Tacrolimus and Cyclosporine.

4. Specific conditions

4.1 Renal transplantation

- Women with renal transplants should ideally wait until their kidney function is stable on medications that are safe in pregnancy before conceiving, which is usually more than one year after transplantation.
- Plans for delivery in a woman with a renal transplant should be discussed with the local surgical transplant team.
- The mode of delivery in women with renal transplant is based on obstetric indications and maternal preference.
- Caesarean delivery in a woman with a renal transplant should be performed by the most senior obstetrician available, ideally a consultant. The location of the transplanted kidney should be established as part of the birth plan for delivery, ideally with the input of the surgical transplant team. This information and the birth plan should be readily available to the obstetric team. Additional considerations should be taken in cases where preterm delivery is required.
- Women with kidney-pancreas transplants, kidney-liver transplants, and dual kidney transplants should be managed during pregnancy and delivery by a multi-disciplinary team including transplant physicians and surgeons, at a transplant centre.

4.2 Dialysis

Women receiving maintenance dialysis before pregnancy

- Women established on dialysis before pregnancy should receive pre-pregnancy counselling including the options of postponing pregnancy until transplantation (when feasible) and the need for frequent dialysis before and during pregnancy. Women established on peritoneal dialysis before pregnancy may need to convert to haemodialysis during pregnancy.
- **Initiating dialysis during pregnancy**:
    - ◊ Haemodialysis should be initiated in pregnancy when the maternal urea concentration is 17-20 mmol/L, and the risks of pre-term delivery outweigh those of dialysis initiation. Gestation, renal function trajectory, fluid balance, biochemical parameters, blood pressure, and uraemic symptoms should be considered in addition to maternal urea concentration and an individualised plan made.

4.3 Lupus nephritis and vasculitis

- Women with lupus or vasculitis should be advised to wait until their disease is quiescent for at least 6 months before conceiving.
- They should be advised to take Hydroxychloroquine in pregnancy unless it is contraindicated.
- Women with lupus should be monitored for disease activity during pregnancy.
- Women who are positive for anti-Ro (SSA) or anti-La (SSB) antibodies should be referred for fetal echocardiography in the second trimester.
- Women with anti-phospholipid syndrome and a history of a confirmed thromboembolic event or previous adverse obstetric outcome (excluding recurrent early fetal loss) should receive low molecular weight heparin in pregnancy and for six weeks post-partum.
- Steroids, Azathioprine, calcineurin inhibitors, intravenous immunoglobulin, and plasma exchange can be used to treat lupus in pregnancy.

4.4 Diabetic nephropathy

- Women with diabetic nephropathy should have optimisation of blood glucose, blood pressure, and proteinuria before conception.
- Women with diabetic nephropathy should continue angiotensin-converting enzyme inhibitors until conception, with regular pregnancy testing during attempts to conceive.
- Schedule of care, surveillance, and management of women with diabetic nephropathy should be taken according to national guidelines for diabetes in pregnancy, in addition to specialist monitoring of renal disease in pregnancy.

4.5 Urinary Tract Infection (UTI)

- Women with reflux nephropathy, congenital anomalies of the kidneys and urinary tract (CAKUT), women with CKD taking immunosuppression, and women with a history of recurrent UTI should be offered antibiotic prophylaxis during pregnancy after a single UTI in pregnancy, including asymptomatic bacteriuria.
- Pre-pregnancy UTI prophylaxis can be continued in pregnancy using agents known to be safe.

4.6 Reflux nephropathy and Congenital Abnormalities of the Kidney and Urinary Tract (CAKUT)

- Women with previous bladder surgery (re-implantation of the ureter, bladder reconstruction, all complex paediatric urology) should be discussed during pregnancy with a Urologist with expertise in bladder reconstruction to evaluate options for delivery.
- Antenatally detected abnormalities in the fetal kidneys and/or urinary tract should be discussed with fetal medicine and paediatric nephrology specialists to determine appropriate neonatal management.

New diagnosis of CKD in pregnancy (raised serum creatinine and/or proteinuria before 22 weeks)

Initial investigations should include:

- MSU to exclude UTI
- uPCR to quantify proteinuria
- Baseline FBC, U&Es, LFTs, antinuclear antibodies, ds-DNA, lupus anticoagulant (complement and immunoglobulin analysis may also be indicated).
- Renal USS
- Review VTE risk and consider LMWH if there is significant proteinuria.
- Treat hypertension to maintain BP < 140/90mmHg.
- Consider renal biopsy in the first and early second trimester of pregnancy if a histological diagnosis will change management. The risks of renal biopsy after 22 weeks usually outweigh the benefits.
- Offer birth at 37-38 weeks unless indicated sooner.
- Ensure postnatal follow-up is arranged to confirm/exclude persistent proteinuria and arrange appropriate renal referral.

5. Specialist services for women with kidney disease

Joint Obstetric Renal Clinic ANC at St Georges Hospital and St Helier Hospitals

- This is a specialized service for women with kidney disease or severe hypertension who are pregnant. A team including Obstetricians, Nephrologists, and specialist midwives contribute to the service. The service provides pre-conceptual, antenatal, intra-partum, and postnatal care. The aim is to provide individualized, woman-centred care.
- **How does the service work?**
  The team runs a clinic on an afternoon every 4th Thursday at St George's and every first Wednesday of the month at St Helier.
  If women are admitted to the hospital, they are cared for by the same team on the ward.
- **Where does the clinic run?**
  The clinic is held in the Antenatal Clinic on the ground floor of Lanesborough Wing at St George's and on the ground floor of the Women's Health Department at St Helier.
- **Who should be referred to the clinic?**
  - ◊ Any women with known or suspected kidney disease prior to pregnancy, should be seen in the pre-conception clinic.
  - ◊ Women already booked at ESTH, with known kidney disease should be referred as early in pregnancy as possible.
  - ◊ Women with moderate or high-risk kidney disease who are booked at other hospitals should be referred, although some may continue their care in their local hospital if this seems appropriate.
- **How do I refer a woman to this clinic?**

- ◊ SGH: Women under Kingston and SGH are usually referred here.
  Please contact the specialist midwives on baton mobile 07766800345 or 02086721255 ext. 6204/4760 or email maternalmedicine@stgeorges.nhs.uk. Please provide as much detail as possible.
- ◊ ESTH: Women under ESTH, Croydon, Ashford and St Peter's, East Surrey and Royal Surrey hospitals are usually referred here.
  Please contact the specialist midwives on 07919978922 or 02082962764 or email esth.matmed.midwives@nhs.net. Please provide as much detail as possible.

- Please remember to complete a Refer-a-Patient (RaP) form on the portal.

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