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Recommendation	Evidence quality	Strength	Rationale for the recommendation
Consider planned birth at 38–39 weeks' gestation in women with moderate ICP with peak bile acids 40–99 micromol/L and no other risk factors; advise them that the overall risk of stillbirth is similar to the background risk until 38–39 weeks' gestation	**1+**	**A**	Systematic review with individual patient data meta-analysis reporting risk of stillbirth, stratified by peak maternal bile acid concentration
Consider planned birth at 35–36 weeks' gestation in women with severe ICP with peak bile acids 100 micromol/L or more; advise them that the risk of stillbirth is higher than the background risk	**1+**	**A**	Systematic review with individual patient data meta-analysis reporting risk of stillbirth, stratified by peak maternal bile acid concentration
Advise women that the presence of co-morbidities (such as gestational diabetes, pre-eclampsia, multifetal pregnancy) appear to increase the risk of stillbirth and may influence decision-making around timing of planned birth	**2+**	**C**	Evidence from national surveillance case control study supported by other case series demonstrating increased stillbirth risk with comorbidities

Active care in ICP, usually referring to planned birth around 38 weeks' gestation, came into practice in many settings, including the UK, despite inadequate evaluation of its benefit or an understanding of which women with ICP might be at increased risk of adverse perinatal outcomes. Previous studies had reported on cohorts of women with ICP, often after introduction of active care, and speculated that low stillbirth risk is related to such a policy,[46,47] but few had evaluated prognostic factors to allow better stratification to tailor timing of birth. *[Evidence level 1+]*

A large systematic review and individual patient data meta-analysis of women with ICP has reported that the risk of stillbirth is 0.13% in women with peak bile acids less than 40 micromol/L, which is not higher than background population risk.[7] Although the risk of stillbirth remains low throughout gestation for these women, the benefits of continuing the pregnancy after 40 weeks' gestation may be outweighed by the risk, therefore it is reasonable to discuss with the woman or pregnant person whether they wish to continue the pregnancy or have a planned birth. *[Evidence level 1+]*

The risk of stillbirth in women with peak bile acids of 40–99 micromol/L was 0.28%. This was not higher than overall background population risk,[7] but did appear to increase at around 38–39 weeks' gestation. Although the number of affected pregnancies is small and the confidence intervals wide, it is reasonable to offer planned birth at this gestation for women and pregnant people with peak bile acids of 40–99 micromol/L, or earlier if other comorbidities (such as gestational diabetes or pre-eclampsia) are present. *[Evidence level 1+]*

For women with peak bile acids 100 micromol/L or more, the risk of stillbirth is 3.44%, which is higher than background population rate, and the risk appears to increase from 35–36 weeks' gestation. This information should be shared with the woman or pregnant person and planned birth considered, based on other factors and the woman's preferences. This is in keeping with other studies using different methodologies, including a retrospective cohort study of 1 604 386 pregnancies assessing composite perinatal mortality risk[48] and a decision modelling study concluding that 36 weeks' gestation was optimal.[49] *[Evidence level 1+]*

In women with ICP and peak bile acids 40 micromol/L or more, co-morbidities may be associated with a greater risk of stillbirth.[29] The presence of and risks related to co-morbidities should be taken into account when considering the timing of planned birth. *[Evidence level 1+]*

8.2 | Mode of birth

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Advise women that ICP in itself does not impact their choice around mode of birth and that these decisions should be based on usual obstetric practice for that woman	**2+**	**D**	Choices around mode of birth should follow routine obstetric practice

Women and pregnant people with ICP do not have increased rates of assisted or operative birth compared with women without ICP.[50] Mode of birth should therefore be based on usual obstetric or medical indications. If planned early birth is indicated, induction of labour should be considered unless other reasons for caesarean birth are present. *[Evidence level 2+]*

8.3 | Monitoring in labour

Recommendation	Evidence quality	Strength	Rationale for the recommendation
• **Offer continuous electronic fetal monitoring (CEFM) to women with peak bile acids 100 micromol/L or more.** • **There is insufficient evidence for or against CEFM in women with peak bile acids below 100 micromol/L. A shared decision can be made based on co-morbidities and preferences.** **Advise women that the presence of risk factors (such as gestational diabetes, pre-eclampsia, multifetal pregnancy) appear to increase the risk of adverse perinatal outcomes and that these conditions themselves may necessitate monitoring during birth or in conjunction with ICP may influence decision-making around monitoring in labour.** **Advise women that meconium-stained liquor is more common in moderate and severe ICP, and that this will influence decision-making around CEFM**	4	D	Recommendation based on extrapolation from assessment of fetal risk associated with stillbirth and other adverse perinatal outcomes, highlighted by systematic review

If the woman or pregnant person has existing obstetric or medical conditions that influence decision-making around fetal monitoring in labour, these should be taken into account when planning intrapartum care. In women with mild ICP (peak bile acids 19–39 micromol/L) and no other risk factors, intrapartum care can follow national guidelines.[33] In women with moderate ICP (peak bile acids 40–99 micromol/L), the decision should be made on an individualised basis, explaining that the benefit of continuous electronic fetal monitoring is uncertain; the presence of any other risk factors should be taken into account. In women with severe ICP (peak bile acids 100 micromol/L or more), in light of evidence that there is a risk of adverse perinatal outcomes in these women, continuous electronic fetal monitoring should be offered. Women with moderate and severe ICP are more likely to have meconium-stained liquor, and this will influence the need for continuous electronic monitoring in labour. *[Evidence level 4]*

8.4 | Analgesia in labour

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Offer women with uncomplicated ICP standard analgesia and anaesthesia options for birth	4	D	Choice of analgesia should be based on routine clinical practice

There are no studies that have indicated that women or pregnant people with ICP require different options for analgesia and anaesthesia for birth and national guidance should be followed.[33] Three cohort studies of 223 women,[17] 531 women[15] and 745 women[18] with ICP described above in Section 4.2, who had routine coagulation testing reported no cases of prolonged prothrombin time in women with uncomplicated clinical presentations. The small number of abnormal results occurred in women with alternative diagnoses (such as acute fatty liver of pregnancy). *[Evidence level 4]*

8.5 | Third stage of birth

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Advise women that there is no evidence of an increased risk of postpartum haemorrhage if they have uncomplicated ICP	2–	D	Care of third stage should follow routine clinical practice

A case–control study (64 cases)[50] and case-cohort study (348 cases)[51] both showed no increased risk of postpartum haemorrhage in women with ICP. Standard care using national guidance for the third stage of birth should be followed.[33] *[Evidence level 2–]*

9 | WHAT FOLLOW-UP SHOULD BE OFFERED TO WOMEN WHO HAVE HAD A PREGNANCY AFFECTED BY ICP?

Recommendation	Evidence quality	Strength	Rationale for the recommendation
For women who have uncomplicated ICP, follow-up should be arranged at least 4 weeks after birth to confirm resolution of ICP. Advise them that they should anticipate itching and raised maternal bile acid concentrations to resolve after birth	4	D	Good practice to arrange follow up

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In women who have had ICP, itch usually stops after birth, often in the first few days, and liver function tests and bile acid concentrations should return to normal within a few weeks. At postnatal follow-up, the healthcare professional should ensure that itching has resolved and should confirm that maternal bile acid concentrations and liver function tests have normalised. If itching or biochemical abnormalities persist beyond 6 weeks postpartum, consider other diagnoses depending upon the history and examination findings. Referral to a hepatologist may be required. *[Evidence level 4]*

9.1 | What advice should be offered for future contraceptive or hormonal options?

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Advise women that ICP itself does not influence their choice of contraception or hormone replacement therapy	**4**	**D**	Choice of contraception should follow UK Medical Eligibility Criteria (UKMEC) guidance
For women with ICP and previous cholestasis secondary to combined hormonal (oestrogen-containing) contraception, advise them to use progestogen-only or non-hormonal methods	**4**	**D**	This is in line with UKMEC guidance
In women with previous ICP requesting HRT, consider offering if there are no other contraindications to use	**4**	**D**	Extrapolated from UKMEC guidance on exogenous oestrogen use

As with all women and pregnant people, discussion about methods of contraception should begin during the antenatal period[21] and continue in the early postpartum days.[52] This should include the health benefits of spacing pregnancies, consideration of medical conditions and/or patient characteristics affecting contraceptive choice (such as venous thromboemblism risk factors, breastfeeding, medical history), the reliability and benefits of long-acting reversible contraceptive methods, and the additional use of condoms if there is a risk of sexually transmitted infections and HIV.[53] *[Evidence level 4]*

The 2016 UK Medical Eligibility Criteria (UKMEC) for Contraceptive Use advises that copper-bearing intra-uterine devices, levonorgestrel-releasing intra-uterine systems, progestogen-only implant, progestogen-only injectable, and progestogen-only pill can be used without restriction in women with a history of ICP (UKMEC category 1).[53]

Combined hormonal contraception can be used in women with ICP (UKMEC 2) provided they do not also have a history of contraception related cholestasis. It was previously thought that women with a history of ICP may have an increased risk of developing cholestasis when using oestrogen-containing hormonal contraception, but this is unlikely for the majority of women. The 2016 UKMEC states that in women who have had ICP the advantages of using these oestrogen-containing methods outweigh this theoretical risk (UKMEC category 2)[53] and women may thus choose to use this method. Resolution of itching and liver function tests and bile acid concentrations returning to normal levels should be confirmed before commencing this method. *[Evidence level 4]* Advise women to attend for review if recurrence of itch and abnormal liver function tests occur while using combined hormonal contraception, this would give a diagnosis of contraceptive-related cholestasis (UKMEC 3) and alternative contraception options should be discussed. *[Evidence level 4]*

For women with an atypical presentation of ICP, atypical postnatal clinical course, where other diagnoses are suspected, or where itching and liver function tests have not resolved, a personalised approach to contraceptive choice should be undertaken, with provision of information about avoidance of pregnancy with active liver disease.

For menopausal women considering hormonal replacement therapy (HRT), national recommendations should be followed.[54] Current UKMEC guidance is that oestrogen-containing contraception can be used in women with a history of ICP. It therefore seems reasonable to offer the lower physiological dose of oestrogen found in HRT, with review of use if women develop itching or other signs of cholestasis.

9.2 | How should women be cared for in future pregnancies?

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Advise women with a history of ICP that they have an increased chance of recurrence of ICP in subsequent pregnancies	**3**	**D**	Good practice to inform women of likelihood of recurrence
Perform a baseline liver function test and bile acid concentration with booking blood investigations	**3**	**D**	Good practice to establish baseline values

Women and people of reproductive age who have had a pregnancy complicated by ICP have an increased chance of ICP in a subsequent pregnancy compared to the general pregnancy

population, but the precise magnitude of this is unclear, as quoted rates of recurrence are based on small studies (e.g. of 18 women[55] and 69 women[56]) and the results may not be generalizable to a wider UK population with ICP. At booking in subsequent pregnancies, baseline measurement of liver function tests and bile acid concentrations should be performed in order to establish that these are normal. They should only be repeated if clinically indicated. *[Evidence level 3]*

10 | RECOMMENDATIONS FOR FUTURE RESEARCH

- In women with ICP:
  - Which maternal or fetal prognostic tools and/or monitoring modalities predict adverse perinatal outcome (including preterm birth and stillbirth)?
  - Should women with ICP be tested for gestational diabetes (and by what method)?
  - What is an effective treatment for itching?
  - What is an effective treatment to prevent adverse perinatal outcomes?
- In pregnant women with raised bile acids, what is the natural history of bile acid concentrations without treatment?
- What is the ongoing risk of adverse pregnancy outcome in women whose bile acid concentrations normalise?
- What is the cause of itching in women without raised bile acids, and what is an effective treatment for their itching?

11 | AUDITABLE TOPICS

- Proportion of women with raised bile acid concentrations offered timing of birth in line with RCOG Green-top Guideline. (>90%)
- Proportion of women with uncomplicated raised bile acid concentrations having additional investigations routinely performed. (<10%)
- Proportion of women with raised bile acid concentrations offered ursodeoxycholic acid in line with RCOG Green-top Guideline. (<5%)
- Proportion of women with severe ICP (peak bile acids ≥100 micromol/L) offered continuous electronic fetal monitoring during labour. (>90%)

These targets have been set in recognition of the need for individualised care particularly in women with comorbidities and atypical ICP.

12 | USEFUL LINKS AND SUPPORT GROUPS

- Information for healthcare professionals
  - Maternal use of medication in pregnancy (UK Teratology Information Service) (http://www.uktis.org/html/maternal_exposure.html)
  - http://www.uktis.org/html/maternal_exposure.html
- Information for women and families
  - Research based charity and support group ICP Support (http://www.icpsupport.org/)
  - RCOG. *Intrahepatic Cholestasis of Pregnancy*. Information for you (https://www.rcog.org.uk/for-the-public/)
- Information for women and their families on use of medicines in pregnancy
  - http://www.medicinesinpregnancy.org/

CONFLICT OF INTERESTS

JG, CLK and LC have declared no conflicts of interest.

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