Information for Clinicians

Biochemistry Department

7-alpha-hydroxy-4-cholesten-3-one (7αC4) for the investigation of Bile Acid Diarrhoea (BAD)

Background

Bile acids are synthesised from cholesterol in the liver and excreted in bile to aid digestion of fat. In healthy individuals, up to 95% of bile acids are reabsorbed in the terminal ileum through enterohepatic circulation. In bile acid diarrhoea (BAD) bile acid resorption is significantly reduced.

Bile acid diarrhoea (BAD), also known as bile acid salt malabsorption or bile salt malabsorption, can be categorised by pathophysiology:
Type 1 – reduced bile acids resorption from ileal resection or inflammation
Type 2 – increased bile acid synthesis (disruption to the enterocyte negative feedback mechanism) (mostly idiopathic)
Type 3 – altered bile acid homeostasis secondary to other GI pathology e.g. cholecystectomy, coeliac disease, microscopic colitis, abdominal radiotherapy, chronic pancreatitis

BAD is estimated to have prevalence in the general population of 1% and likely to be an under-diagnosed condition, with ~ 30% of patients labelled with diarrhoea-predominant IBS likely to be undiagnosed BAD. Once recognised, BAD can be effectively treated with bile acid sequestrants.

The serum marker, 7-alpha-hydroxy-4-cholesten-3-one (7αC4) is an intermediary product in the liver synthesis of bile acids, cholic acid and chenodeoxycholic acid. Fasting 7αC4 levels provide a measure of bile acid production and is recommended as a non-invasive, cost-effective, convenient screen for BAD.

Fasting 7αC4 can be used as an alternative to the gold standard nuclear medicine ^{75}Se-homocholic acid-taurine (^{75}SeHCAT) scan, which requires patients to ingest ^{75}SeHCAT and attend for 2 full body gamma scans 7 days apart to determine retention of the isotope, with low percentage retention being a sensitive and specific test for BAD. 7αC4 levels are inversely correlated to ^{75}SeHCAT retention.

<u>Based on published studies, using fasting serum 7αC4 as a frontline test for BAD, is estimated to reduce requirement for ^{75}SeHCAT scans by more than 50%.</u>

© Royal United Hospitals Bath NHS Foundation Trust 16.10.2026

Patient suitability

Serum 7αC4 testing should be performed in relevant adults, as assessed by gastroenterologists only; clinicians should await 7αC4 results prior to referral for a ^{75}SeHCAT. Collect an early morning (8:00–10:00 am) serum sample following a 12-hour fast. Samples need to reach the RUH laboratory and be separated within 12 hours of collection, the RUH lab will refer the sample to Wythenshawe Hospital, Manchester for analysis (quoted TAT 14 days). See Appendix 1 for patient preparation instructions.

False negatives:

- **Statins** – advise stop for 5 days prior to sample collection
- **Liver disease** – do not perform in patients with advanced liver disease/cirrhosis

False positives:

- **Non-fasted samples** – collect serum following 12h overnight fast
- **Samples taken after 10am** – 7αC4 increases due to diurnal variation
- **Alcohol** – suggest abstain for 24h prior to testing
- **Bile acid sequestrants** – ideally test 7αC4 before trialling treatment (otherwise stop for 24h)
- **Hypertriglyceridaemia**

GLP-1 agonists – may have variable effects – consider stopping.

Interpretation

Serum 7αC4 (nmol/L)	Interpretation	Action
<50	BAD unlikely	Investigate alternative causes of chronic diarrhoea
50 – 142	Equivocal	Proceed to ^{75}SeHCAT scan
>142	BAD likely	Treat with bile acid sequestrants

Literature quoted sensitivity for BAD is 46% at 7αC4 >142 nmol/L, specificity at this level is 96%.

References

Atkins *et al*. Development and validation of a novel 7α-hydroxy-4-cholesten-3-one (C4) liquid chromatography tandem mass spectrometry method and its utility to assess pre-analytical stability. Clin. Chem Lab. Med. 2024. 63(1):154-163.

Farrugia A, Arasaradnam R. Bile acid diarrhoea: pathophysiology, diagnosis and management. Frontline Gastroenterol. 2020. 12(6):500–507.

Borup C *et al*. Biochemical Diagnosis of Bile Acid Diarrhea: Prospective Comparison with the ^{75}Seleno-Taurohomocholic Acid Test. Am. J. Gastroenterol. 2020. 115(12):2086-2094

Borup C *et al*. Correction to: Biochemical Diagnosis of Bile Acid Diarrhea: Prospective Comparison with the ^{75}Seleno-Taurohomocholic Acid Test. Am. J. Gastroenterol. 2022. 117(11):1885-1886

Arasaradnam RP, Brown S, Forbes A, et al. Guidelines for the investigation of chronic diarrhoea in adults: British Society of Gastroenterology, 3rd edition. Gut. 2018. 67(8):1380–1399.

Mayo Clinic Laboratories Test Catalog: 7AC4 - Overview: 7AC4, Bile Acid Synthesis, Serum (accessed March 2026)

© Royal United Hospitals Bath NHS Foundation Trust 16.10.2026

Appendix 1

Patient Information – preparing for your 7αC4 blood test

Please book an appointment for a blood test at your GP surgery (or use the RUH walk-in Phlebotomy Service in B9) between 8am and 10am in the morning, following a 12 hour fast.

Before the blood test, please avoid:

- Statins (medicine for cholesterol) for 5 days
- Bile acid sequestrants e.g. cholestyramine or colesevelam for 24 hours
- Alcohol for 24 hours
- Food and drink for 12 hours (water is allowed)

Amendment History

Issue	Status	Date	Reason for Change	Authorised
1.0	Approved	September 2026	New guideline	Dr M O'Doherty

© Royal United Hospitals Bath NHS Foundation Trust 16.10.2026