SUPPLEMENTAL MATERIAL

(i) **Fasting serum C4** (sampled in the morning because of diurnal variation) measured by high-performance liquid chromatography with tandem mass spectrometry[23], based on the method adapted from Gälman et al.[24] Serum 7α-OH-4-cholesten-3-one (C4) is a downstream product of cytochrome P450 7A1 (CYP7A1), thus a surrogate for hepatic BA synthesis and a validated test for BAM. Increased serum C4 had a sensitivity of 90% and a specificity of 79% in diagnosing BAM, compared with the ^{75}seleno-homocholyltaurine (SeHCAT) whole body retention test[25]. It had 98% negative predictive value and 74% positive predictive value for diagnosis of BAM[26], making the assay attractive as a screening test to rule out BAM. The lower limit of detection of serum C4 using this assay is 0.04ng/ml[23]. The upper limit of normal is 47.1ng/mL.

(ii**) Total and main fecal BA excretion** (per 48h on 100g fat diet) measured by high-performance liquid chromatography/tandem mass spectrometry[5, 11], an assay adapted from a BA quantification method in human plasma[27]. The extraction, analysis and analytical performance of this test have been documented[5]. Each of the individual main BAs (CA, CDCA, DCA and LCA) has 0.06μmol (in methanol extract) as lower limit of detection. The 90th percentile for total fecal BA excretion in healthy volunteers is 2337μmoles/48h[10].

(iii**) Fecal fat** per 24h was measured at Mayo Clinic's Department of Laboratory Medicine using nuclear magnetic resonance spectrometry. Normal fecal fat was 2-7g per 24h.

(iv) Total **fecal weight** per 48h was obtained by weighing of the whole 48h stool collections.

(v) **Overall CT by scintigraphy [geometric center (GC)] at 24 (GC24) and 48 hours (GC48).** The precise procedure and performance characteristics of the measurement of colonic transit by scintigraphy[28], as well as responsiveness to pharmacological effects of medications[19, 20] have been extensively described.