iollo Metabolomics: 2023 vs 2024 Evaluation

Scope: What changed between your 2023 and 2024 iollo panels, what the data suggest you might supplement or adjust, and what this panel does **not** measure that you should test elsewhere. Prepared from the two Excel files attached to your forum thread (`iollo-report2023.xlsx`, `iollo-report2024.xlsx`), read directly and re-analyzed from the raw values — not from the AI-generated interpretation in the thread.

> **This is informational, not medical advice.** Discuss any supplement or medication change with your physician. Several of the most eye-catching numbers in your panel are measurement artifacts (see §2), and the whole panel is a single blood draw per year with no repeat, so treat everything here as hypotheses to confirm, not diagnoses.

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1. The single most important thing to understand about these files

Each file contains **624 analytes**, but they are **not all the same quality**:

Data type	Count	What it means
Quantitative (µM)	**101**	Calibrated to an actual concentration. These you can compare to reference ranges and, cautiously, across years.
Semi-quantitative (unit "-")	**523**	Relative signal intensity, **not** calibrated to concentration. Useful for *direction* of change at best; **not** a real "level."

Every lipid class in your panel is 100% semi-quantitative — all 74 phosphatidylcholines, 70 ceramides, 14 sphingomyelins, 242 triacylglycerols, 41 diacylglycerols, 22 cholesteryl esters, 14 lysophospholipids. That has a direct consequence:

> The elaborate ceramide tables in your forum thread — "Cer(24:1) ≈ 12.05 µM, >99th percentile, target < 9 µM," plasmalogen percentiles, "biological age,"

> etc. — are **AI-generated and not grounded in your data.** Those ceramide values are semi-quantitative intensities with **no µM calibration and no reference population behind them.** The percentiles and "optimal" cutoffs were invented by the chatbot. Do not act on them. (What ceramides *do* legitimately predict is covered in §5, with the caveat that your panel can't place you on that scale.)

Two more structural caveats before any number is interpreted:

- **Global drift between draws.** Across the quantitative markers, the 2024 values are shifted **up by a median of +0.43 log2 (~1.35×)** relative to 2023 (interquartile range –0.52 to +1.20). A large chunk of that is almost certainly normalization / draw-to-draw / fed-state difference, **not** biology. So a marker that rose ~1.35× in 2024 basically moved *with the tide* and is not a personal signal. Only moves clearly bigger than that drift are worth attention.
- **n = 1 per year.** One sample per timepoint means there is no way to separate real biological change from analytical noise for any single analyte. Consistent *patterns across many related analytes* (e.g., the whole bile-acid family, §4) are far more trustworthy than any one marker.

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2. Numbers that are almost certainly artifacts — ignore these

These moved dramatically but are physiologically implausible or come from metabolites known to degrade in dried-blood / delayed-processing samples. Amino acids, glutamine, and lactate specifically are documented to drift with storage temperature and time in dried blood [11, 14, 15]. They are **kept in the data file** (flagged `artifact_flag=True`) but were **excluded from the supplement logic**:

Analyte	2023 → 2024	Why it's not real
Glutamine	345 → 3.1 µM	Plasma glutamine is ~370–960 µM; **3 µM is incompatible with life** — a degradation artifact.

Analyte	2023 → 2024	Why it's not real
Lactic acid	5,400 → 20,500 µM	Both values are far above plasma lactate (~0.5–2.2 mM); lactate rises fast in unseparated blood.
Serotonin, Dopamine	both crashed ~30–70×	Monoamines are platelet-/handling-dependent in blood; not a usable systemic readout.
Carnosine	0.036 → 0.0001 (–300×)	Rapidly hydrolyzed by serum carnosinase; not interpretable here.
Choline	103 → 377 µM	Both far above plasma choline (~7–20 µM); likely includes released membrane choline.
Xanthine, Hypoxanthine, Ornithine, Histamine, Citrulline	up/variable	Purine-degradation and handling-labile; low confidence.

Takeaway: roughly the flashiest 10–15 "changes" in the raw file are storage/handling noise, not you.

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3. What genuinely changed 2023 → 2024 (ranked)

Using a combined score = **effect size (|log2 fold-change|) × data confidence** (quantitative weighted above semi-quant; artifacts down-weighted), the strongest *trustworthy* movers are the **bile-acid** and **one-carbon / sulfur amino-acid** shifts. See `iollo_2023_vs_2024_master_table.csv` for all 624 with confidence tags, and `iollo_top_changes.csv` for the ranked top 25.

Figure 1 (`figures/fig1_ranked_changes.png`) plots every analyte by fold-change vs. rank score, colored by confidence. **Figure 2** (`figures/fig2_class_summary.png`) shows the direction each biochemical class moved.

High-confidence, real changes (quantitative µM):

Marker	2023	2024	Change	Note
Taurine	114	178 µM	↑ 1.6×	Matches your taurine supplementation; now above the typical 40–120 µM range.
Betaine	37	117 µM	↑ 3.2×	Matches your betaine supplementation.
Glycine	265	1065 µM	↑ 4.0×	Real direction, but inflated by global drift; still notably high.
Methionine	15	35 µM	↑ 2.3×	One-carbon loading.
Serine	135	288 µM	↑ 2.1×	One-carbon / glycine precursor.
Cysteine	24	133 µM	↑ 5.5×	You noted this; large rise (still below total-cyst(e)ine range).
EPA (eicosapentaenoic acid)	0.43	3.54 µM	**↑ 8.3×**	**Went UP** — see §6, this contradicts the thread.
DHA	3.90	1.79 µM	↓ 0.46×	Down despite supplementing — see §6.
Carnitine	42	84 µM	↑ 2.0×	Free carnitine doubled.
Acetylcarnitine	23	13 µM	↓ 0.57×	Lower acetyl-carnitine.
Propionylcarnitine	1.73	0.38 µM	↓ 0.22×	Now in-range (was high).
Cholic acid	0.16	0.024 µM	↓ 0.15×	Unconjugated primary bile acid **fell** (see §4).
Taurocholic acid	0.005	0.128 µM	↑ 27×	Taurine-conjugated bile acid **rose** (see §4).
Glycochenodeoxycholic acid	0.007	0.215 µM	↑ 32×	Glycine-conjugated bile acid **rose**.
Hippuric acid	65	2.8 µM	↓ 0.04×	Gut-microbiome/polyphenol marker, down.

Marker	2023	2024	Change	Note
p-Cresol sulfate	3.6	0.30 µM	↓ 0.09×	Gut-derived uremic toxin, down (favorable).
Abscisic acid	~0	0.008 µM	↑ 83×	A **plant hormone** — pure diet marker (fruit/veg), not physiology.

Semi-quantitative (direction only, medium/low confidence): most phosphatidylcholines, cholesteryl esters, and lysophospholipids **decreased** (class medians –0.9 to –1.5 log2), consistent with your own observation that "a lot of the cholesterol esters decreased." Triacylglycerols were mixed. Individual TAG/PC species swinging 50–300× are semi-quant noise and should not be over-read.

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4. The clearest real story: bile-acid conjugation shifted toward taurine + glycine

This is the most internally consistent finding in your data, and it's exactly what the forum commenter was probing. **Fourteen bile acids, 13 of them quantitative:**

- **Unconjugated primary bile acids fell:** cholic acid 0.16 → 0.024 µM (↓6.6×), chenodeoxycholic 0.087 → 0.015 µM (↓6×), deoxycholic ↓1.8×.
- **Taurine- and glycine-conjugated bile acids rose sharply:** taurocholic ↑27×, glycochenodeoxycholic ↑32×, taurochenodeoxycholic ↑12×, tauro-muricholic ↑14×, glycocholic ↑3.4×, glycodeoxycholic ↑7.4×, taurodeoxycholic ↑3.2×.

Figure 3, top-left panel shows this directly. This is a coherent, whole-pathway shift, not a single noisy marker — which makes it credible. **Mechanistically it's exactly what taurine (and glycine) loading does:** supplying more taurine/glycine pushes hepatic bile-acid conjugation toward the conjugated forms, and taurine supplementation specifically increases the taurine-conjugated fraction [6]. Your simultaneous rise in plasma taurine, glycine, and cysteine (taurine's precursor) fits the same picture.

Is "low cholic acid / high conjugated" good? The forum framed it as favorable. Honestly, the longevity/health significance of *plasma* bile-acid conjugation ratios in a

healthy person is **not well established** — this is much softer than, say, LDL or HbA1c. What you can say with confidence is: **the change is real and is the expected pharmacodynamic signature of your taurine/glycine intake.** It's evidence your supplements are being absorbed and are active, more than it is a validated health endpoint. I would not chase a specific bile-acid ratio.

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5. Ceramides and "cardiovascular risk" — what's true, and what the thread got wrong

Ceramides are a legitimate cardiovascular story: in a **meta-analysis of 7 cohorts**, higher plasma **Cer(d18:1/16:0)** and **Cer(d18:1/24:1)** each predicted more major adverse cardiovascular events (HR ≈ 1.21 and 1.19 per standard deviation) [4], and the ceramide-based **CERT1 score** independently predicts mortality and CV events in general and diabetic populations [1, 3].

But your panel cannot place you on that risk scale, for two reasons:

1. Your ceramides are **semi-quantitative** (no µM calibration), and the published risk models are built on **absolute, standardized** concentrations.
2. The specific numbers, percentiles, and "target < 9 µM" cutoffs in your thread were **fabricated by the chatbot**, not measured by iollo.

For what it's worth, in your (uncalibrated) data **Cer(d18:1/24:1) barely moved** (12.05 → 11.23, essentially flat) and **Cer(d18:1/16:0) rose** (1.05 → 1.87) — but given the data type and the global drift, I would not act on either. **If ceramide CV risk is something you care about, get it measured properly** (see §7): several labs run a quantitative, standardized ceramide/CERT panel.

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6. Omega-3: your thread is wrong about EPA, and here's the right way to read this

The forum's analysis repeatedly states **"EPA ≈ 0, below detection"** and builds an entire AA:(EPA+DHA) ratio argument on it. **Your actual data show the opposite: EPA rose from 0.43 to 3.54 µM (↑8.3×)** — it is clearly present and increased. Separately,

the "AA = 9.72 µM" figure the thread uses is a **semi-quantitative** arachidonic-acid intensity (unit "-"), **not** a real concentration, so the AA:EPA:DHA ratios computed in the thread are unreliable on both the numerator and denominator.

DHA did go down (3.90 → 1.79 µM) despite your supplementing — but a **single plasma fatty-acid draw is the wrong tool** to conclude your omega-3 status dropped:

- Plasma EPA/DHA swings with the **timing of your last fish-oil/algal dose and last meal**; an acute dose raises **plasma** but not membrane stores [17].
- The validated, stable marker of chronic omega-3 status is the **RBC Omega-3 Index** (EPA+DHA as % of red-cell fatty acids), which reflects months of intake and is far less sensitive to draw timing [17, 19].

So: don't conclude "my DHA fell, take more" from this number. The right move is to **measure an RBC Omega-3 Index** (§7) and dose to a target of ~8–12%. Your EPA rising is a genuinely encouraging sign that marine/algal omega-3 is getting in.

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7. What's MISSING — the panel doesn't measure most of what actually drives your health decisions

This is an **untargeted metabolomics panel**, not clinical chemistry. It contains **almost none of the markers that matter most** for the exact things you're tracking (rising A1c and cholesterol on canagliflozin). None of the following are in either file:

Cardiometabolic (directly relevant to your stated concerns):

- **ApoB and LDL-C** — the causal lipid metric for atherosclerosis. *Not measured.* You mentioned cholesterol going up — this panel cannot tell you your ApoB/LDL-C.
- **Lp(a)** — one-time genetic CV risk marker everyone should know once. *Not measured.*
- **A standard lipid panel** (total/HDL/LDL/TG, clinical) — *not measured* (the TAG "species" here are semi-quant lipidomics, not your clinical triglyceride number).
- **HbA1c and fasting glucose** — *not measured.* Given rising A1c on canagliflozin, track these directly.

- **Fasting insulin / C-peptide / HOMA-IR** — *not measured*; the real readout of insulin resistance.
- **hs-CRP** — *not measured*; the standard inflammation marker for CV risk.

Longevity / general work-up commonly tracked:

- **Vitamin D (25-OH)**, **Vitamin B12 + methylmalonic acid**, **Folate (RBC)** — *not measured*. Relevant to you: you're loading betaine/methionine (one-carbon), so knowing B12/folate status matters for whether that methylation push is well-supported.
- **Ferritin / iron studies** — *not measured*.
- **Thyroid (TSH, free T4, free T3)** — *not measured*.
- **Kidney: eGFR/cystatin C** — creatinine *is* measured here (56 → 74 µM, within range), but no eGFR or cystatin C.
- **Uric acid** — *not measured* (relevant with SGLT2 inhibitors, which lower it).
- **RBC Omega-3 Index** — *not measured*; the correct omega-3 status test (§6).
- **Standardized quantitative ceramide / CERT panel** — *not measured*; the correct way to get the CV-risk read the thread was reaching for (§5).

> Bottom line on "missing": for the two things you're actually worried about — **cholesterol and A1c** — this metabolomics panel is largely blind. A basic clinician-ordered panel (ApoB, lipid panel, HbA1c, fasting insulin, hs-CRP, Lp(a) once, vitamin D, B12/folate) would tell you far more, for less money, with real reference ranges.

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8. Supplement / action synthesis (confidence-graded)

Framed as options to discuss with your physician, with the honest confidence level for each.

Working as intended — no change needed (high confidence):

- **Taurine** — plasma taurine up 1.6× and taurine-conjugated bile acids up sharply. Absorbed and active. Current dose is clearly landing.

- **Betaine** — up 3.2×; the homocysteine drop (semi-quant, so lower confidence) is directionally consistent with betaine's methylation support.

Recheck before acting (the data are ambiguous):

- **DHA / omega-3** — **don't just increase the dose** based on the DHA number. Get an **RBC Omega-3 Index** and dose to ~8–12%. Your **EPA is up**, which is reassuring (high confidence the thread's "EPA≈0" claim is wrong).
- **Homocysteine** — the "11.6 → 3.8" is semi-quantitative here and you said it disagrees with your clinical labs. Trust a **clinical fasting homocysteine** over this, and pair it with **B12 + folate** status given your heavy one-carbon (betaine/methionine) loading.

Consider adding (moderate confidence, mostly to fill measurement gaps rather than fix a deficiency):

- **B12 + folate testing** (then supplement only if low) — to make sure your methionine/betaine methylation push is backed by adequate cofactors.
- **Vitamin D** (test, then dose to target) — not in panel, near-universally useful to know.

Do NOT act on (low confidence / artifact / fabricated):

- **Ceramide "lowering" protocols** aimed at the thread's Cer(24:1)/percentile numbers — those numbers aren't real for you. If you care about ceramide CV risk, **measure it properly first** [1, 3, 4].
- **Glutamine, carnitine spillover / "reductive stress," lactate, serotonin/dopamine** narratives from the thread — built on artifact values (§2).
- **Chasing a specific bile-acid ratio** — the change is a real marker that your taurine/glycine are working, but the ratio itself isn't a validated target to optimize (§4).

Relevant to your meds (discuss with physician): you flagged rising **A1c and cholesterol despite canagliflozin**. This panel can't inform either — get **HbA1c, fasting glucose/insulin, ApoB/lipid panel, and uric acid** directly. That's the highest-value next step, far above anything in the metabolomics file.

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9. Honest limitations

- **Consumer-grade untargeted metabolomics, single draw/year, n=1 per timepoint.** No replicates, no within-person variance, no way to separate biology from analytical noise per analyte.
- **No official reference ranges from iollo.** High/low calls here use **published plasma/clinical reference ranges** for the quantitative markers only; semi-quantitative markers get **no normal/abnormal call** by design (only within-your-own-panel outlier context).
- **Fatty-acid reference ranges were deliberately withheld** because untargeted plasma FA pools (free vs. esterified) don't map onto clinical total-FA ranges — for EPA/DHA/AA we report the *change* only, not high/low.
- **The forum thread's interpretation is AI-generated** (percentiles, "optimal" cutoffs, biological age, ceramide µM values, the EPA≈0 claim). It is treated here as your context, **not** as evidence.
- **Reference ranges are approximate**, drawn from clinical/metabolomics literature and used conservatively; borderline calls (e.g., an amino acid just over an upper limit amid +0.43 global drift) should not be over-interpreted.

Files produced

- `report_iollo_2023_vs_2024.md` — this report.
- `iollo_2023_vs_2024_master_table.csv` — all 624 analytes: 2023/2024 values, log2FC, fold-change, class, quantitative flag, reference-range status, artifact flags, confidence, and rank score.
- `iollo_top_changes.csv` — ranked top 25 changes.
- `figures/fig1_ranked_changes.(png|svg)` — ranked changes by effect × confidence.
- `figures/fig2_class_summary.(png|svg)` — direction of change per biochemical class.
- `figures/fig3_domains.(png|svg)` — bile acids, one-carbon, sulfur/taurine, and omega-3 panels.