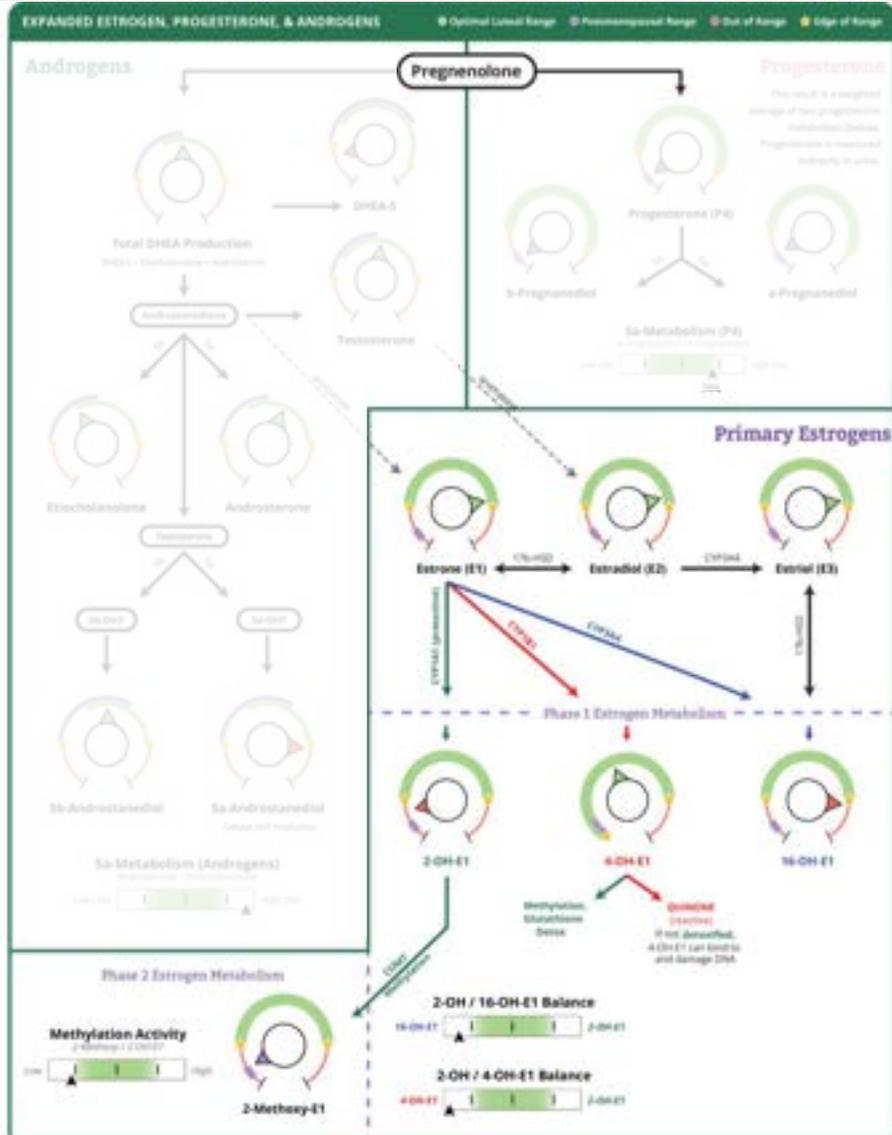# Jaclyn Smeaton, ND

Dr. Jaclyn Smeaton, ND, is the Chief Medical Officer (CMO) at Precision Analytical and a naturopathic physician focused on infertility, reproductive, and genitourinary health. Alongside her work at Hello Fertility, she is a prolific teacher in the field of reproductive endocrinology and hormones and has trained thousands of clinicians on her treatment methodology. Dr. Smeaton has extensive leadership experience in integrative medicine including as president of the American Association of Naturopathic Physicians, as an ambassador for the Academy of Integrative Health and Medicine, and a board member of the Integrative Health Policy Consortium.

Page 2

DUTCH Dozen (page 1)

- Page 1 – E2, P4, 2/4 & 2/16 Balance, Methylation

DUTCH Estrogen Advanced Insights (pages 2 & 3)

- Page 2 – Detailed Estrogen Metabolism
- Page 3 – Individual listings, including 2-OH-E2, 4-OH-E2, and Total Estrogen

DUTCH Estrogen-Related OATs (page 6)

Estrogens and Metabolites (Urine)					
Estrone (E1)	Above luteal range	26.77	ng/mg	12 - 26	1.0 - 7.0
Estradiol (E2)	Within luteal range	2.97	ng/mg	1.8 - 4.5	0.2 - 0.7
Estriol (E3)	Low end of luteal range	7.0	ng/mg	5 - 18	0.6 - 4.0
2-OH-E1	Low end of luteal range	5.62	ng/mg	5.1 - 13.1	0.3 - 2.0
4-OH-E1	Within luteal range	0.59	ng/mg	0 - 1.8	0 - 0.3
16-OH-E1	Low end of luteal range	1.03	ng/mg	0.7 - 2.6	0.2 - 0.6
2-Methoxy-E1	Low end of luteal range	3.07	ng/mg	2.5 - 6.5	0.3 - 1.4
2-OH-E2	Within luteal range	0.67	ng/mg	0 - 3.1	0 - 0.52
4-OH-E2	Within luteal range	0.17	ng/mg	0 - 0.52	0 - 0.12
Total Estrogen	Within range	47.9	ng/mg	35 - 70	3.5 - 15

Page 3

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Learning Objectives

→ Understand the purpose and clinical application of the four **estrogen and progesterone-related** DUTCH Advanced Insights.

→ Evaluate levels of **E1, E3, and Total Estrogen** and their impact on estrogenic activity.
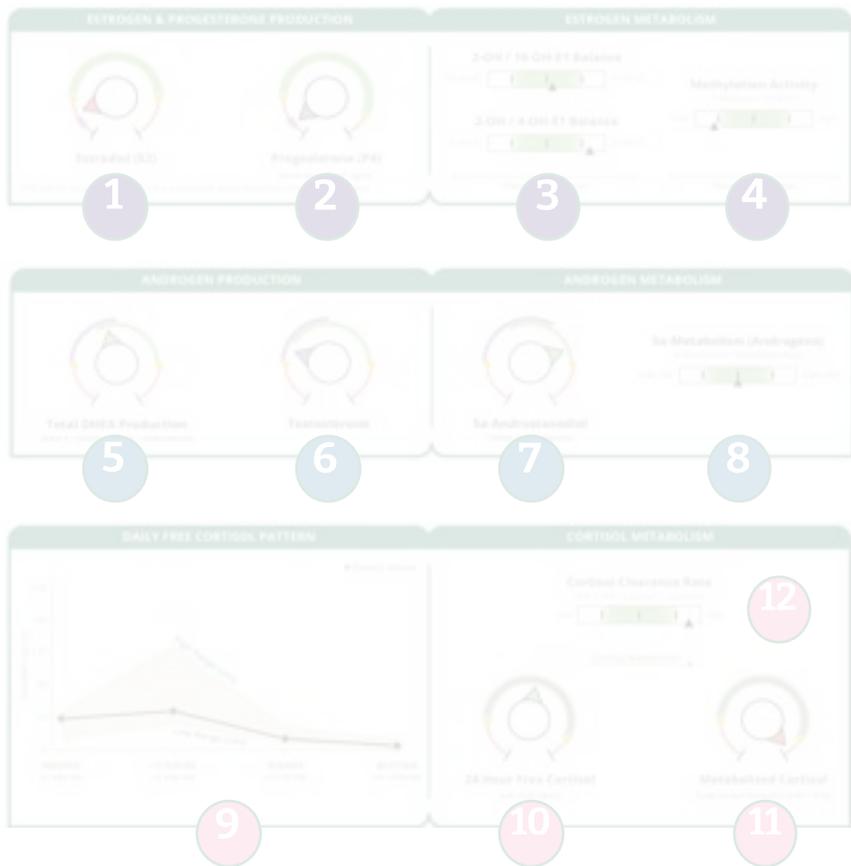
→ Assess the **progesterone preference for 5a-metabolism** and understand its GABA-related, calming effects on sleep and anxiety.

→ Analyze the efficiency of **estrogen clearance** through phases 1 and 2 by estimating the estrogen clearance rate.

→ Identify abnormalities in **estrogen-related organic acids** and understand their relevance to estrogen.

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The DUTCH Dozen

Estrogen Progesterone

1. Assess estrogen levels given the patient's reproductive status

2. Assess progesterone levels given the patient's reproductive status

3. Assess 2-OH preference in phase 1 estrogen metabolism

4. Assess methylation of 2-OH estrogens

Androgens

5. Assess adrenal androgen levels (Total DHEA)

6. Assess testosterone levels

7. Assess cellular production of 5a-DHT via 5a-androstanediol

8. Assess if there is a preference for the more potent alpha metabolism of the androgens

Cortisol

9. Assess the daily free cortisol pattern

10. Assess the daily total of free cortisol in circulation (24hr Free Cortisol)

11. Assess the total cortisol produced by the adrenal glands (Metabolized Cortisol)

12. Assess the rate of cortisol clearance from the body

DUTCH Advanced Insights

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Estrogen Progesterone

1 Assess whether E1, E3, or Total Estrogen levels add more insight into overall estrogenic activity

2 Assess if there is a preference for alpha metabolism of progesterone

3 Assess estrogen clearance through phase 1 and 2

4 Assess whether any of the estrogen-related organic acids are out of range

Androgens

5 Assess if the DHEA-S is relatively lower than the Total DHEA

6 Assess the androgen pattern to determine if urine testosterone may not accurately reflect systemic levels (UGT2B17)

7 While 5a-androstanediol best represents *cellular* 5a-DHT production, assess if 5a-DHT offers additional insight into androgenic activity

8 Assess whether any of the androgen-related organic acids are out of range

Cortisol

9 Assess if cortisone (inactive) adds more insight to the free cortisol assessment

10 Assess if there is a whole-body preference for (inactive) cortisone or (active) cortisol

11 Assess for anabolic-catabolic balance

12 Assess whether any of the cortisol-related organic acids are out of range

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The DUTCH Dozen & Advanced Insights: Estrogen and Progesterone

DUTCH Dozen
Estrogen & Progesterone

1 Assess estrogen levels given the patient's reproductive status

2 Assess progesterone levels given the patient's reproductive status

3 Assess 2-OH preference in phase 1 estrogen metabolism

4 Assess methylation of 2-OH estrogens

Advanced Insights
Estrogen & Progesterone

1 Assess whether E1, E3, or Total Estrogen levels add more insight into overall estrogenic activity

2 Assess if there is a preference for alpha metabolism of progesterone

3 Assess estrogen clearance through phase 1 and 2

4 Assess whether any of the estrogen-related organic acids are out of range

May change your DUTCH Dozen based conclusions

Provide additional information that will add to (but likely won't change) your DUTCH Dozen based conclusions
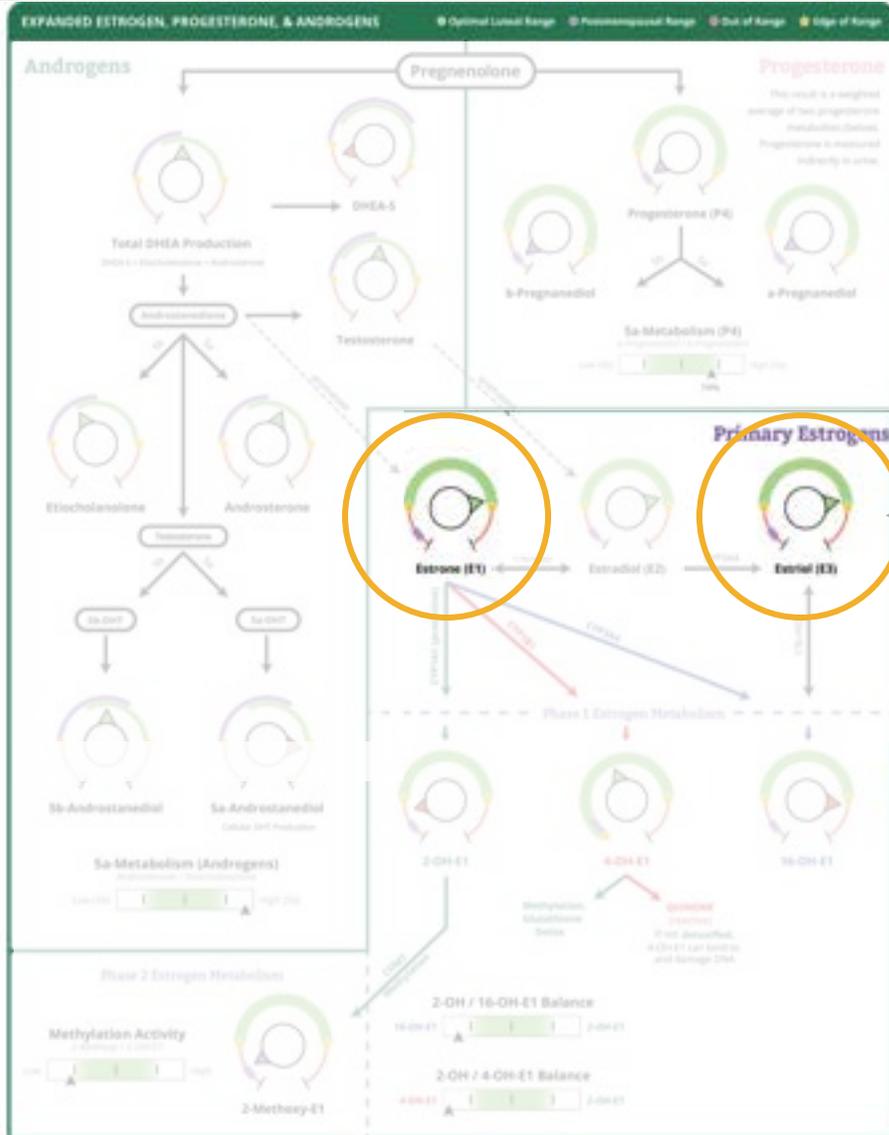
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DUTCH Advanced Insights
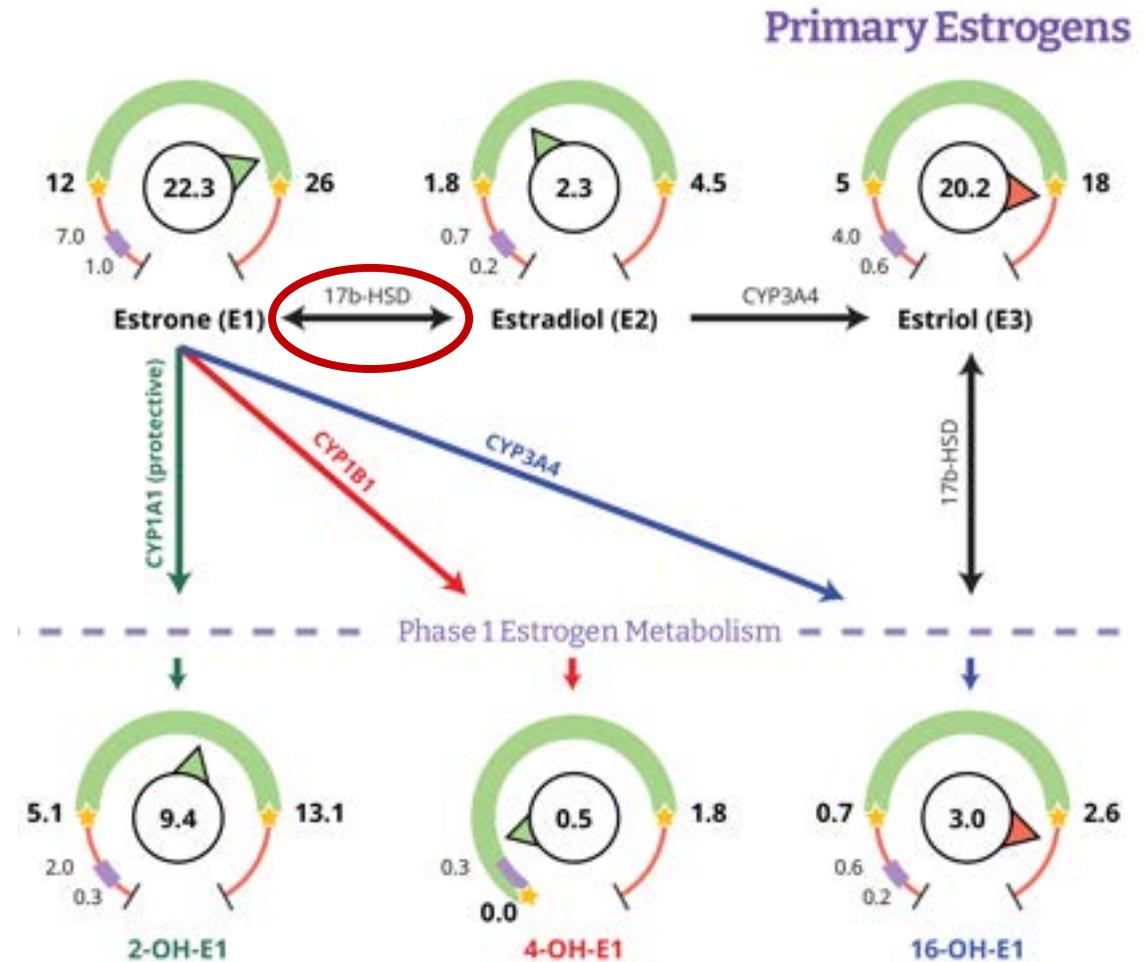## E1, E3, Total Estrogen

1

Page 2

Estrogen Progesterone

1 Assess whether E1, E3, or Total Estrogen levels add more insight into overall estrogenic activity

- E2 is the most potent estrogen, but other estrogens such as **estrone (E1)**, and sometimes **estriol (E3)**, also contribute to overall estrogenic activity.

- **Total Estrogen** can provide insight into overall estrogen production, which may not be fully reflected in the E2 result alone.
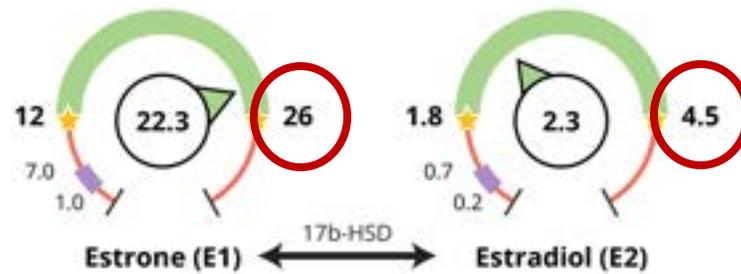
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Estrone (E1)

- E1 and Estradiol (E2) interconvert via 17b-HSD types 1 and 2.

- **E1 is much weaker than E2!**

- In order of strongest to weakest receptor binding affinity:

  - **Estradiol (strongest)**
  - **Estrone (*non-covalently binds*) & 16-OH-E1 (*covalently binds*)**
  - **Estriol**
  - **4-OH**
  - **2-OH**
  - **2-methoxy (weakest)**
    - *Low to no ER binding*

Primary Estrogens

Estrone (E1)

- E1 is **10% as potent as E2 but is typically more abundant**, about 5x higher in premenopausal women and 10x higher in postmenopausal women. This makes it a significant contributor to estrogenic symptoms (high or low), especially in menopause.

- While all estrogens are potent immune stimulators, **E1 may promote more inflammatory cytokine production** than other estrogens.

- Reviewing the relative level of E1 to E2 may give further insight into estrogenic symptoms and long-term outcomes, especially in menopause.

*Notice how the E1 range is about 5x higher than the E2 range.*

Estrone (E1)

- For example, you might think this woman with **heavy menses** has **normal estrogen activity** when looking at page #1 of her DUTCH Complete.

- But when you turn to page #2, you'll see that her **E1 is above range**.

- Her high E1 is likely increasing the estrogenic activity in her body and could explain why she is experiencing heavy menses.

- Be sure to ask about estrogen symptoms when interpreting the estrogen results!

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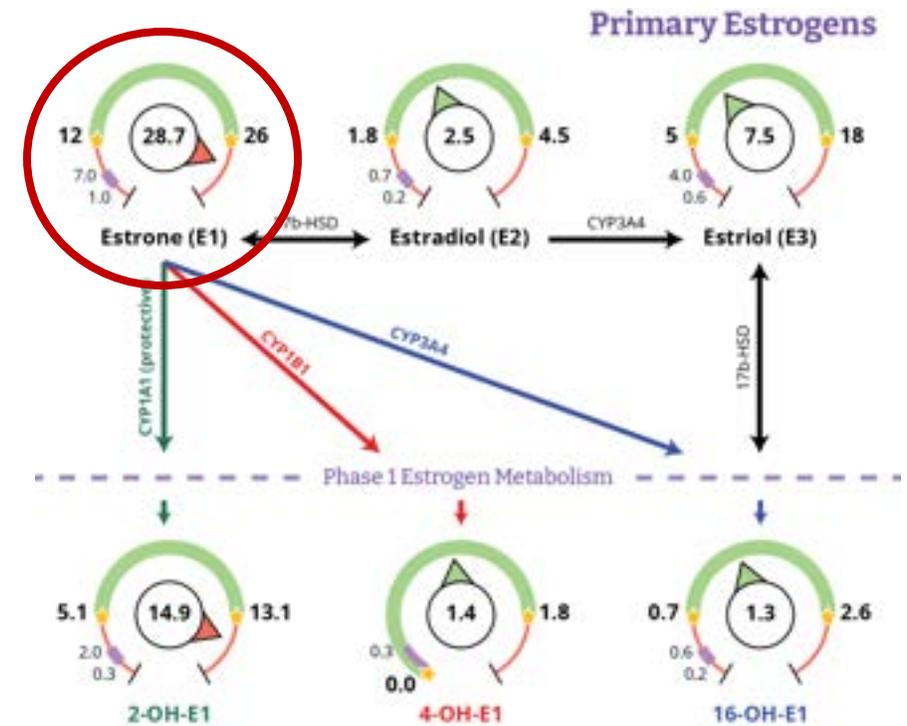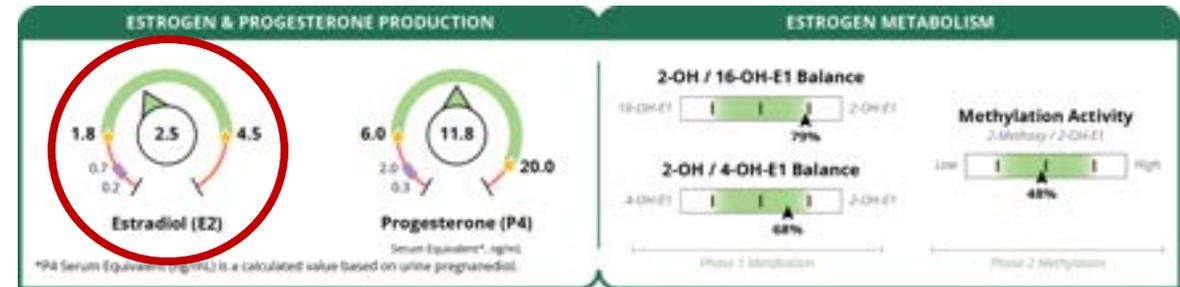
Estriol (E3)

- E3 is a **weak estrogen** that may have **anti-inflammatory** properties.

- In most conditions, E3 is not a significant contributor to estrogenic symptoms. However, when very low or elevated (**e.g., when supplemented**), it may contribute to estrogen-related symptoms.

- E3 and 16-OH-E1 have a special connection - they are **made by the same enzyme, CYP3A4**, from E2 and E1, respectively.

- Thus, **when E3 is elevated, 16-OH-E1 is typically also elevated**, and contributes to higher estrogenic activity (**and vice versa**).

- Recall that **16-OH-E1 is estrogenic**.
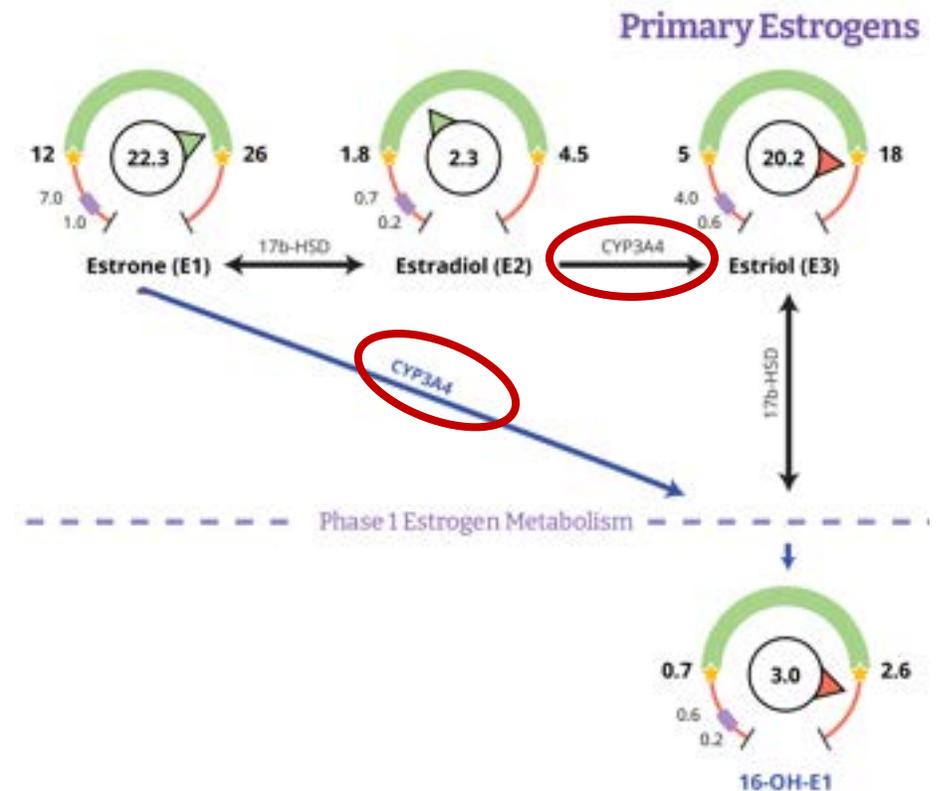
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Estriol (E3)

- CYP3A4 can be inhibited or induced:

⑪ CYP-3a4

Many common medications induce CYP-3a4, including but not limited to, phenobarbitol, phenytoin, rifampicin, and glucocorticoids.

Many common medications interfere with or competitively inhibit CYP-3a4, including but not limited to, cimetidine, tamoxifen, quinolones, and fluoxetine.

May be increased by: St. John's Wort, pesticides, caffeine, smoking, PAHs, moderate alcohol consumption, obesity.

May be decreased by: Grapefruit, resveratrol, rosemary, wild yam, peppermint oil, azole antifungals.

- For example, in patients with obesity we typically see higher E3 and 16-OH-E1 relative to E1 and E2.
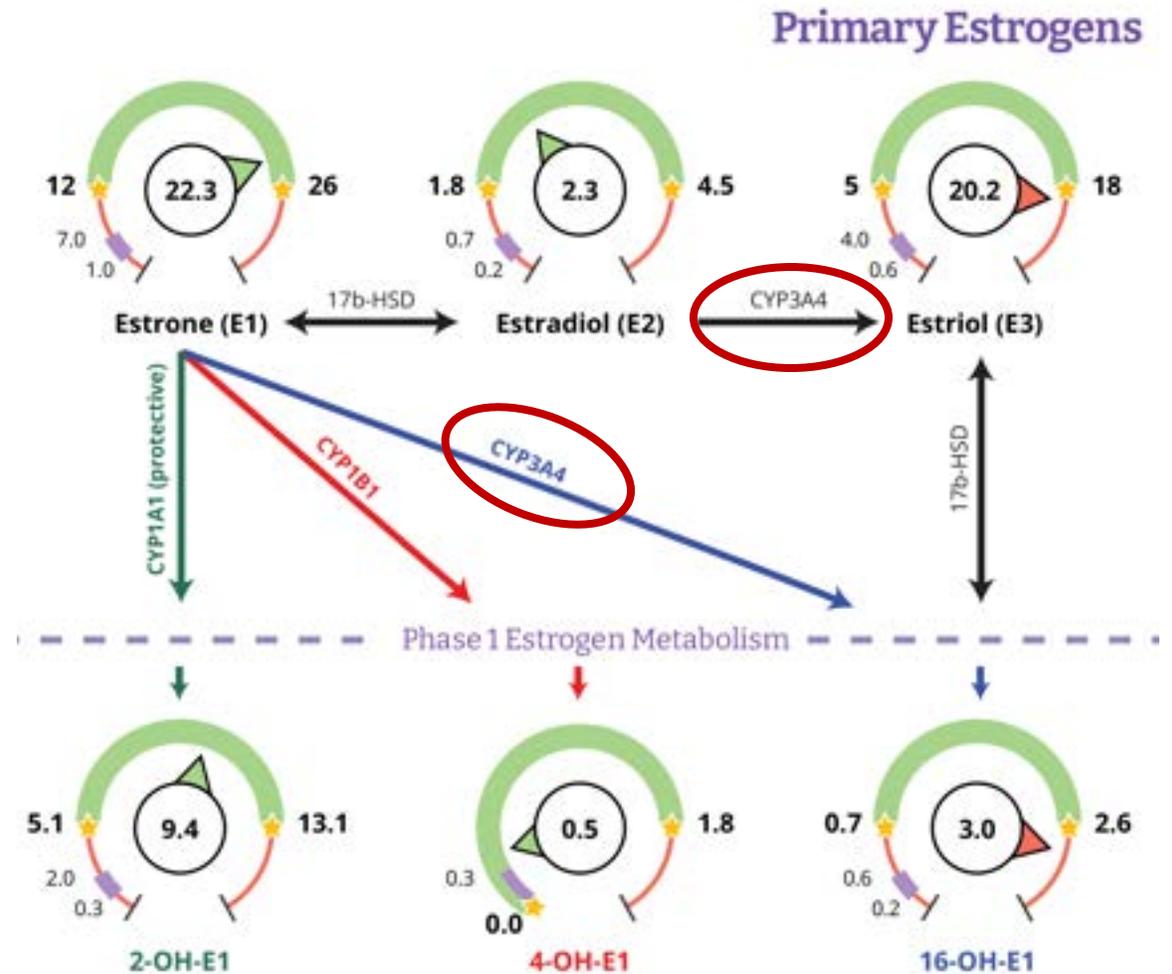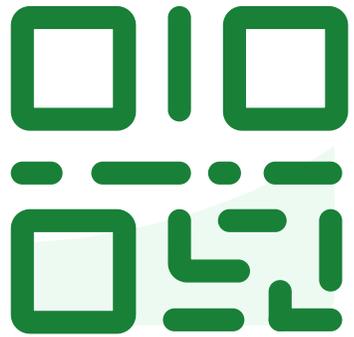
Primary Estrogens

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Game time!

Which 25-year-old woman would you expect to have higher estrogenic activity?

1
- Obese, Smoker
- Drinks alcohol moderately
- Taking St. John's Wort for depression

2
- Healthy weight, Never-smoker
- Drinks grapefruit juice every morning
- Taking rosemary for cognition

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Question 1: Which 25-year-old woman would you expect to have higher estrogenic activity?

Game time!

Which 25-year-old woman would you expect to have higher estrogenic activity?

1
- Obese, Smoker
- Drinks alcohol moderately
- Taking St. John's Wort for depression

2
- Healthy weight, Never-smoker
- Drinks grapefruit juice every morning
- Taking rosemary for cognition

⑪ CYP-3a4

Many common medications induce CYP-3a4, including but not limited to, phenobarbitol, phenytoin, rifampicin, and glucocorticoids.

Many common medications interfere with or competitively inhibit CYP-3a4, including but not limited to, cimetidine, tamoxifen, quinolones, and fluoxetine.

May be increased by St. John's Wort, pesticides, caffeine, smoking, PAHs, moderate alcohol consumption, obesity.

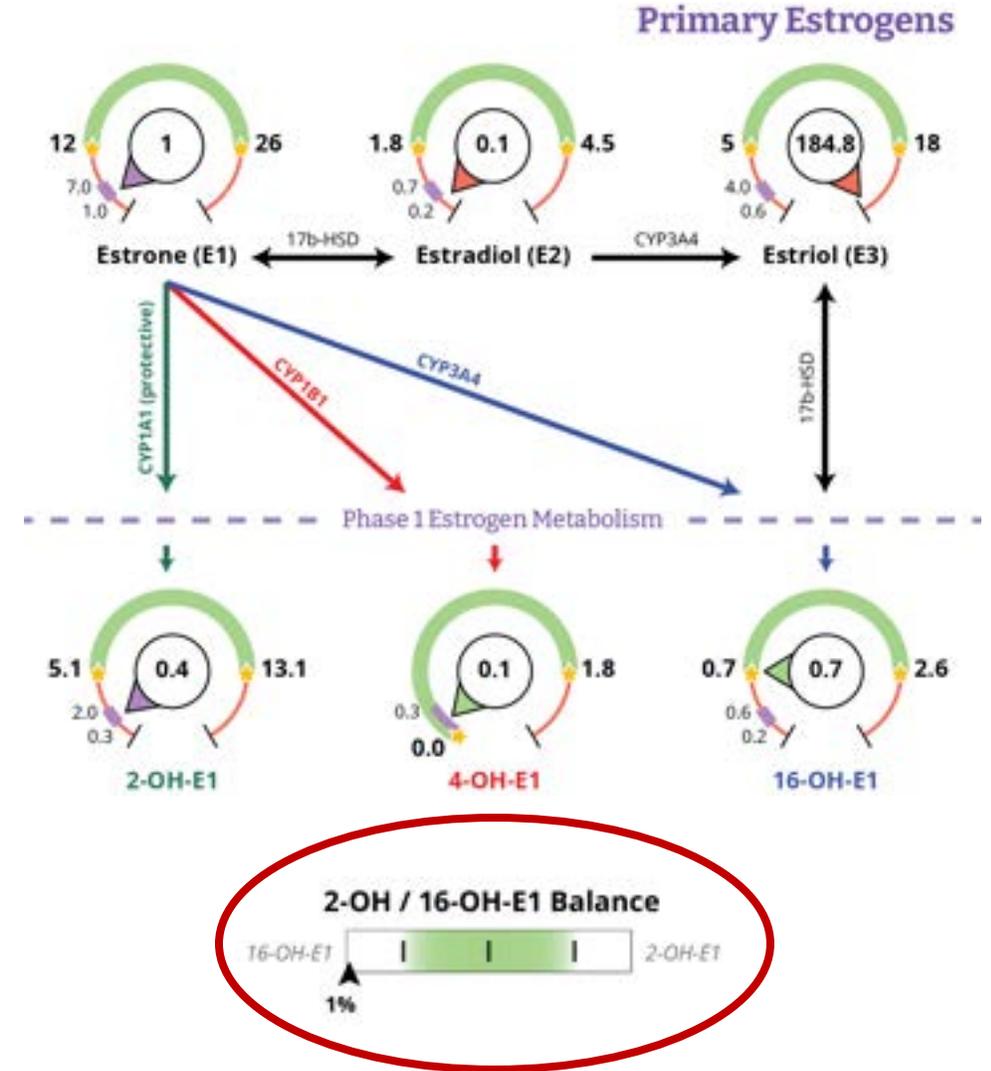**May be decreased by** Grapefruit, resveratrol, rosemary, wild yam, peppermint oil, azole antifungals.

Treating high (or low) estrogen is not as simple at manipulating enzymes!

Use caution with CYP3A4 inhibitors, as CYP3A4 is heavily involved in the phase 1 detoxification of many other compounds besides estrogen, including many pharmaceuticals. Inhibiting CYP3A4 may reduce excretion of these and affect dosing of sensitive medications.

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Estriol (E3)

- **Example: 63-year-old female took 1.5 mg oral E3 the day prior to testing.**

- If a patient is using oral estriol (E3), a portion of the E3 is metabolized into 16-OH-E1 in the **gut and liver** during first-pass.

- This tends to result in an elevated 16-OH-E1 preference that may not be reflective of **tissue** preference.

- Also, the elevated E3 will cause her **Total Estrogen** (on page #2) to be above range, which is misleading.

Total Estrogen = 187.9

Estriol (E3)

- At normal physiologic concentrations, estriol (E3) contributes negligibly to overall estrogenic activity due to its weak potency, but **supplementation** that substantially elevates circulating E3 levels can lead to significant estrogenic effects in the body.

- Transdermal and vaginal estriol are **accurately measured** on the DUTCH test in most cases, reflecting systemic (circulating) levels.

- In rare instances of vaginal contamination, the lab includes a specific alert/note on the report to flag this possibility.

- There are currently **no established clinical thresholds** or target ranges for estriol levels. Clinicians should interpret these results in the context of the individual patient's symptoms, treatment goals, and overall hormone profile.

Primary Estrogens

54-yeal-old woman
Using 0.5 mg vaginal E3

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Total Estrogen

- The Total Estrogen is calculated by adding up **ALL the estrogen metabolites** (E1 + E2 + E3 + 16-OH-E1 + 2-OH-E1 + 2-OH-E2 + 4-OH-E1 + 4-OH-E2 + 2-Methoxy-E1)

- Keep in mind that the Total Estrogen can be high with **robust, healthy estrogen metabolism**.

- Therefore, its levels do not always indicate a cause for high or low estrogen-related symptoms.

Estrogens and Metabolites (Urine)					
Estrone (E1)	Low end of luteal range	12.95	ng/mg	12 - 26	1.0 - 7.0
Estradiol (E2)	Within luteal range	2.54	ng/mg	1.8 - 4.5	0.2 - 0.7
Estriol (E3)	Low end of luteal range	6.4	ng/mg	5 - 18	0.6 - 4.0
2-OH-E1	Within luteal range	10.54	ng/mg	5.1 - 13.1	0.3 - 2.0
4-OH-E1	Within luteal range	0.97	ng/mg	0 - 1.8	0 - 0.3
16-OH-E1	Low end of luteal range	0.75	ng/mg	0.7 - 2.6	0.2 - 0.6
2-Methoxy-E1	High end of luteal range	6.48	ng/mg	2.5 - 6.5	0.3 - 1.4
2-OH-E2	High end of luteal range	2.55	ng/mg	0 - 3.1	0 - 0.52
4-OH-E2	Within luteal range	0.36	ng/mg	0 - 0.52	0 - 0.12
Total Estrogen	Within range	43.5	ng/mg	35 - 70	3.5 - 15

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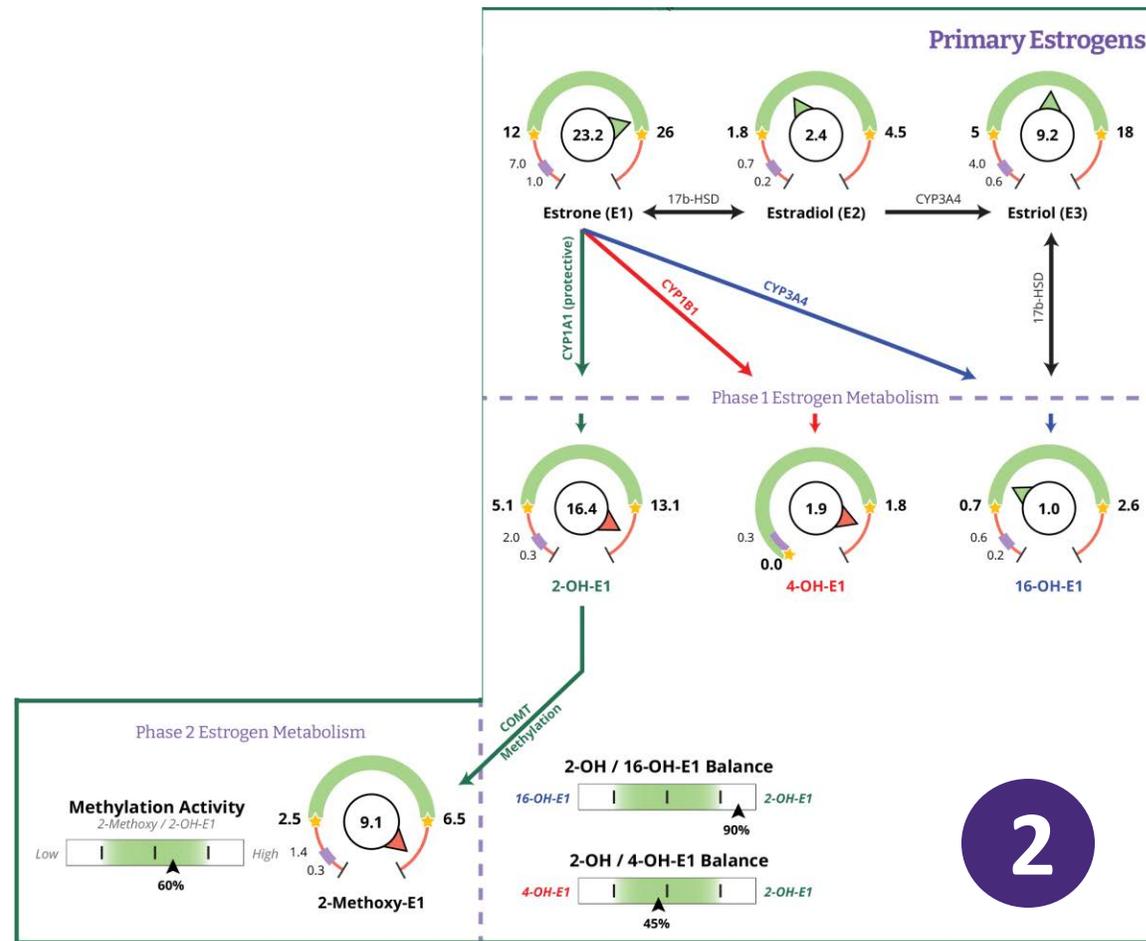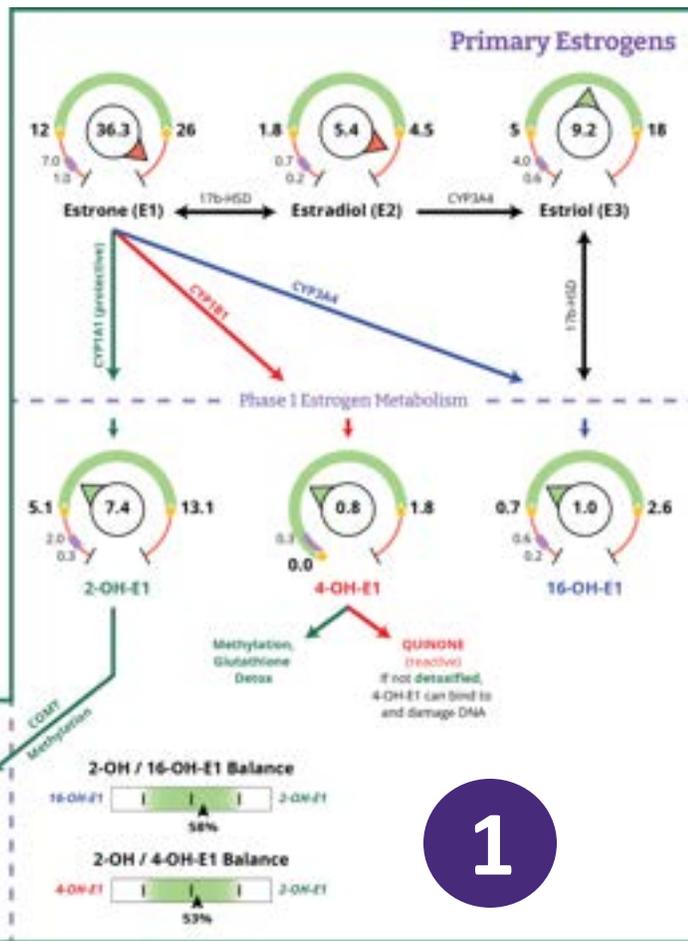
Game time!

These two women have the same high-end Total Estrogen (66.9 ng/mg). Who experiences more estrogenic activity?

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Question 2: These two women have the same high-end Total Estrogen (66.9 ng/mg). Who experiences more estrogenic activity?
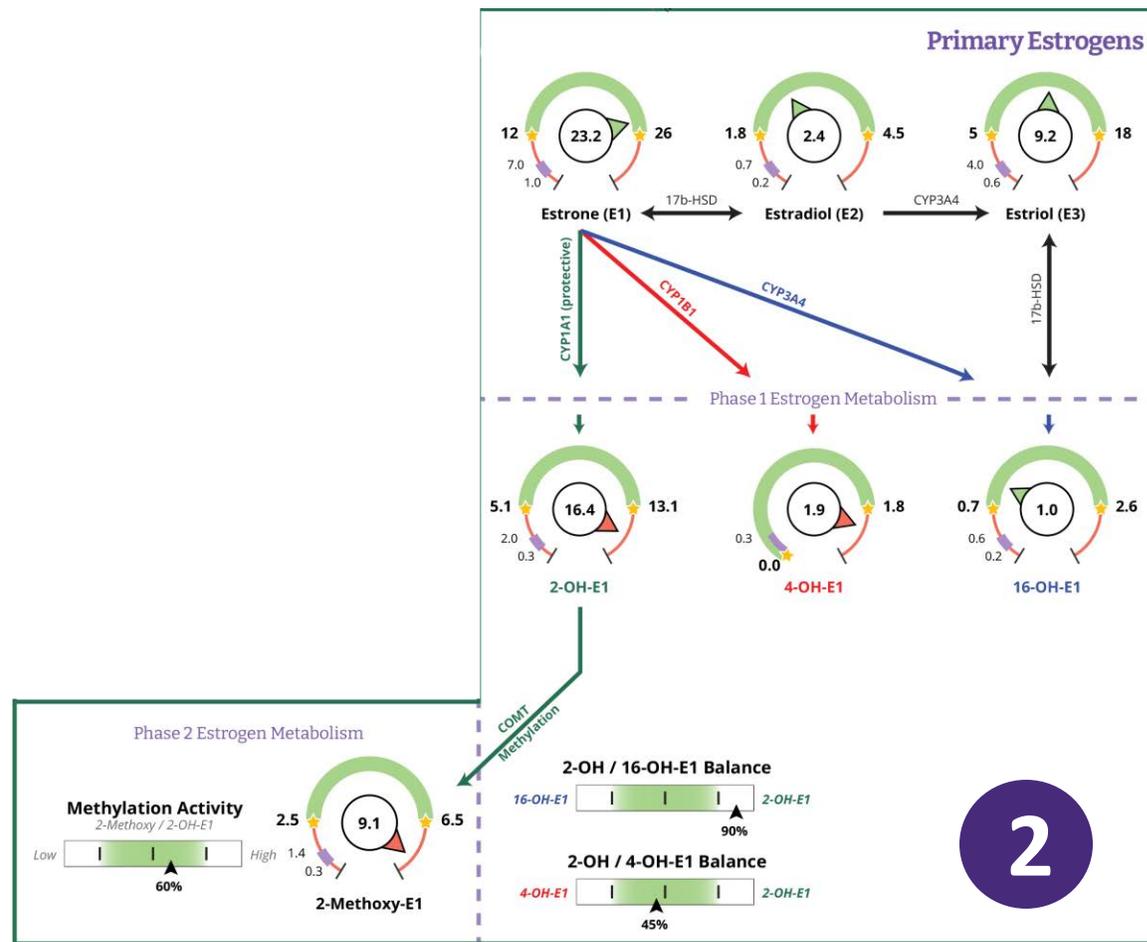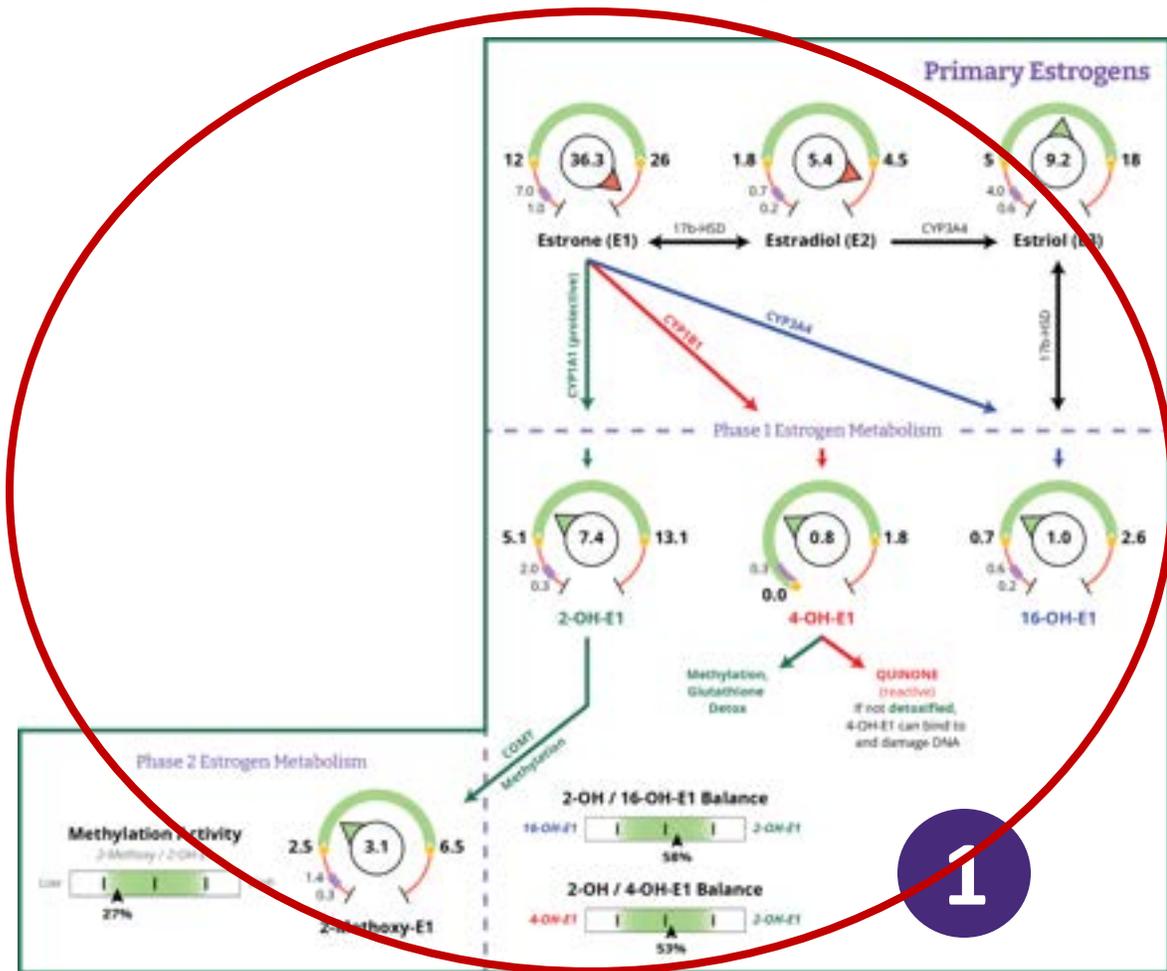
Game time!

These two women have the same Total Estrogen (66.9 ng/mg). Who experiences more estrogenic activity?

Summary of E1, E2, E3, 16-OH-E1:

| Estrone (E1)	Estradiol (E2)	Estriol (E3)	16-OH-E1
• 10% as potent as E2 but typically more abundant • 5x higher in pre-menopausal women • 10x higher in postmenopausal women than E2 • Non-covalent binding	• Most potent estrogen	• Weak estrogen • May have anti-inflammatory properties • Made via CYP3A4	• Potency similar to that of E1 due to its covalent binding • Estrogenic/Proliferative • Made via CYP3A4

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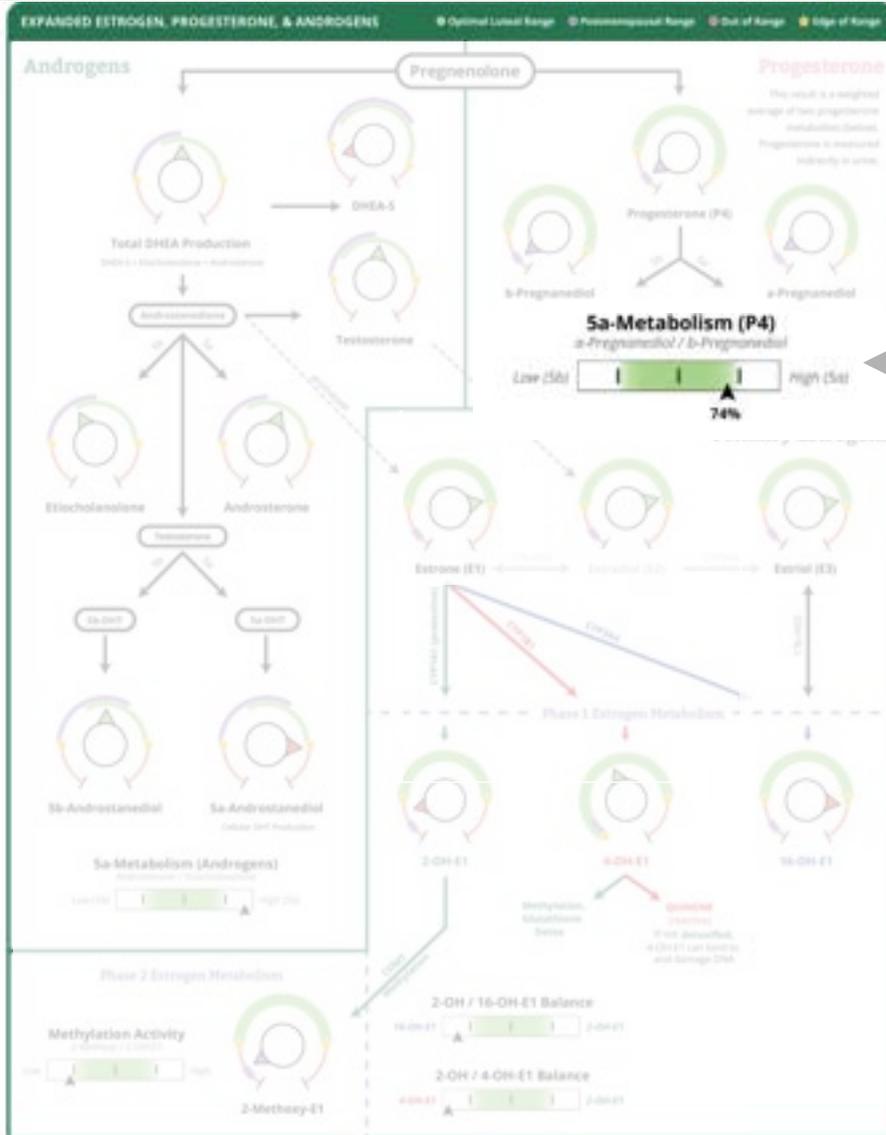
Page 2

Advanced Insights
Estrogen & Progesterone

② Assess if there is a preference for alpha metabolism of progesterone
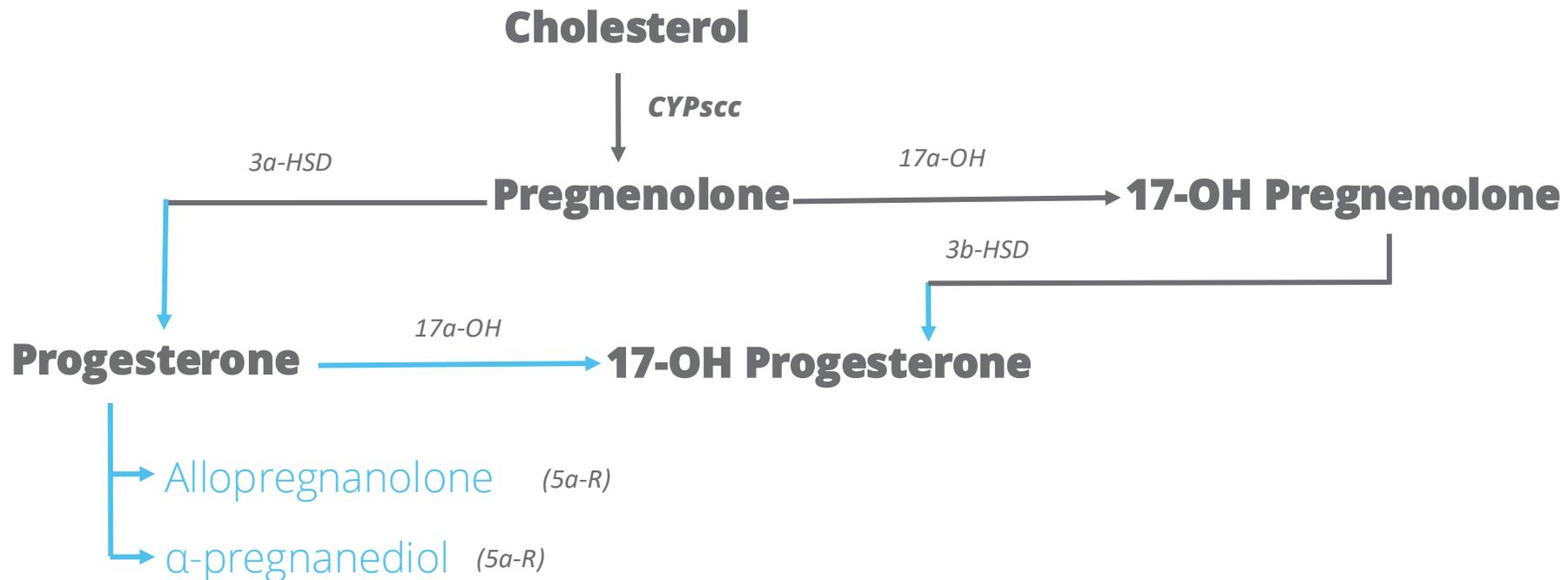
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- **The 5a-Metabolism (P4) Slider** is the most effective tool for assessing whether progesterone is primarily metabolized through the alpha pathway (into a-pregnanediol) or the beta pathway (into b-pregnanediol).

5a-Metabolism (P4)
a-Pregnanediol / b-Pregnanediol

Low (5b) | I   I   I | High (5a)

91%

- Understanding this preference can be valuable, as **alpha progesterone metabolites**, such as allopregnanolone and a-pregnanediol, modulate **GABA** receptors, potentially supporting **mood** and **sleep**.

  - The GABA(A) receptor is the primary **inhibitory** neurotransmitter receptor in the brain.

  - GABA(A) receptor activation slows down nerve cell activity and produces a **calming effect**.
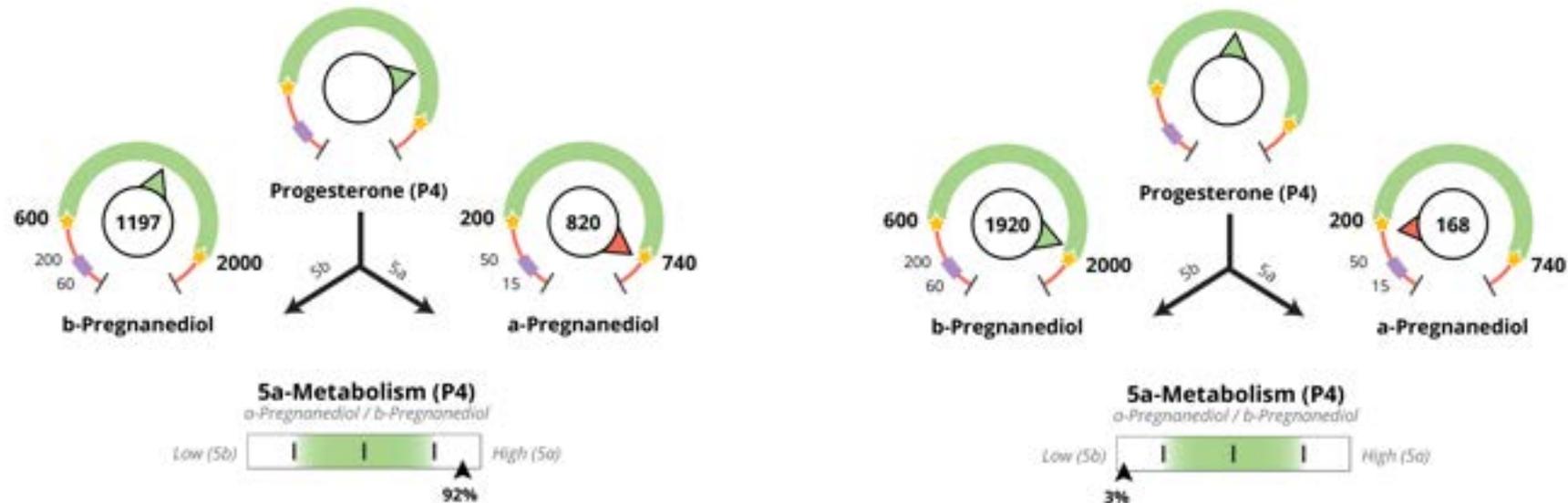
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- While **allopregnanolone** has significantly stronger sedating effects than **α-pregnanediol**, internal DUTCH data shows a **strong correlation between their levels**.

Cholesterol

CYPscc

3a-HSD   *17a-OH*

Pregnenolone → **17-OH Pregnenolone**

3b-HSD

17a-OH

Progesterone → **17-OH Progesterone**

→ Allopregnanolone   *(5a-R)*

→ α-pregnanediol   *(5a-R)*

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- Favoring the **alpha pathway** pushes more progesterone into the alpha metabolites, like a-pregnanediol and allopregnanolone, which increases GABA(A) receptor (**calming**) activity.

- Therefore, woman who favors the alpha pathway on the left may experience more calming effect from her luteal progesterone than the woman on the right who favors the beta pathway.
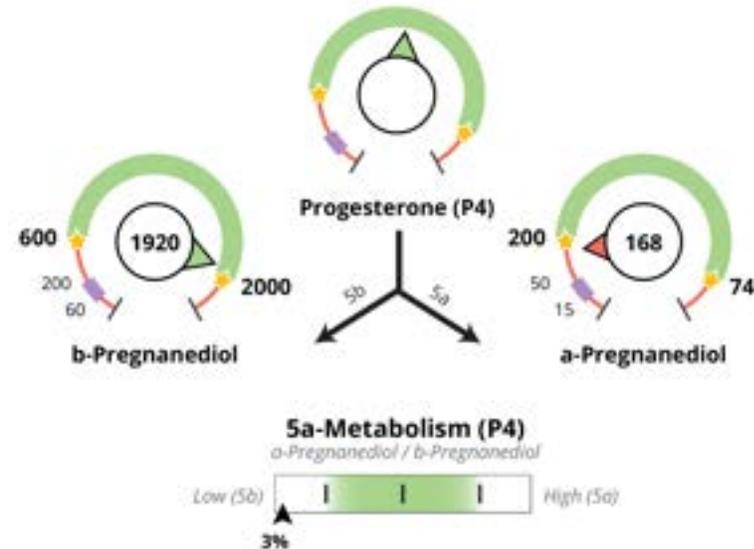
- 5a-reductase inhibitors can also block alpha progesterone metabolism.

5a-Reductase Blockers

- Beta-sitosterol
- EGCG from green tea
- PUFAs
- Pygeum
- Reishi mushroom
- Saw palmetto
- Stinging nettle root
- Zn (balance Cu)
- Rx: Finasteride, etc.

Progesterone (P4)

600   1920   2000
200
60
b-Pregnanediol

5b   5a

200   168   740
50
15
a-Pregnanediol

5a-Metabolism (P4)
a-Pregnanediol / b-Pregnanediol

Low (5b)   High (5a)

3%

Think about it!

Game time!

Your 28-year-old patient with anxiety is taking saw palmetto for hair loss. What do you tell her?

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- An alpha (or beta) preference may not always be clinically significant, especially if progesterone levels are low.

- For example, even though this 59-year-old woman has a **strong alpha preference**, because her progesterone is very low, she is not getting much GABA modulation (calming effects) from her low a-pregnanediol levels.

- In this case, the slider bar is not very clinically useful.
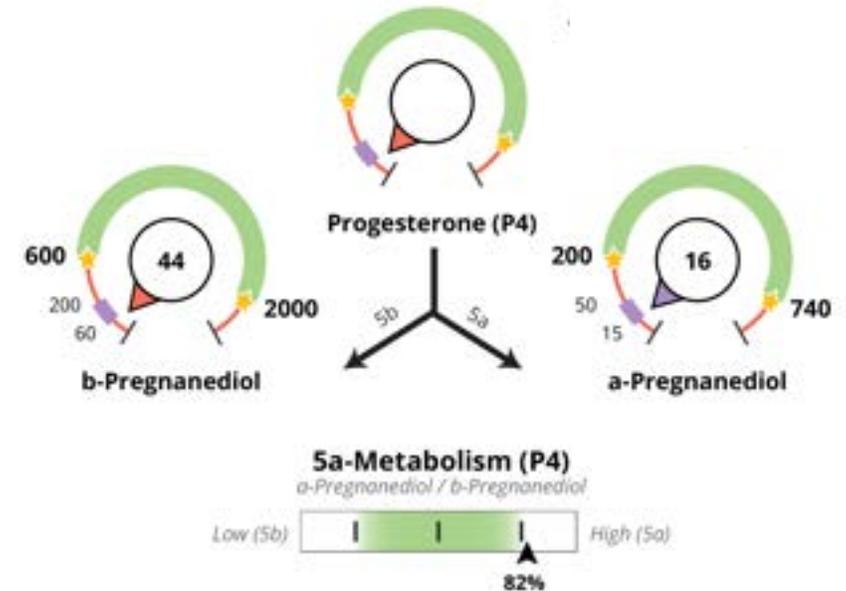
- Progesterone metabolism is <u>very relevant</u> for patients using oral progesterone (OMP).
- For example, when OMP is supplemented, women favoring the beta pathway (as shown below) may need a higher dose than women favoring the alpha pathway to see similar improvements in mood and sleep.
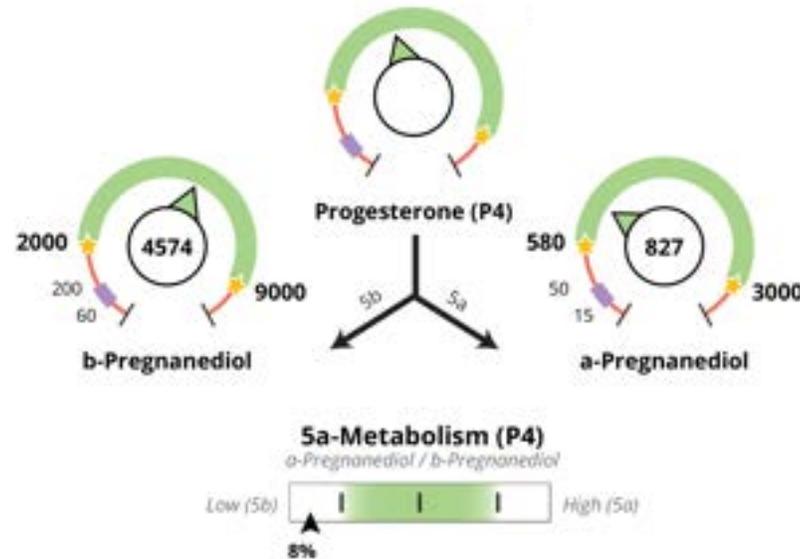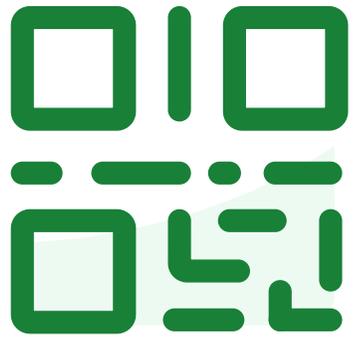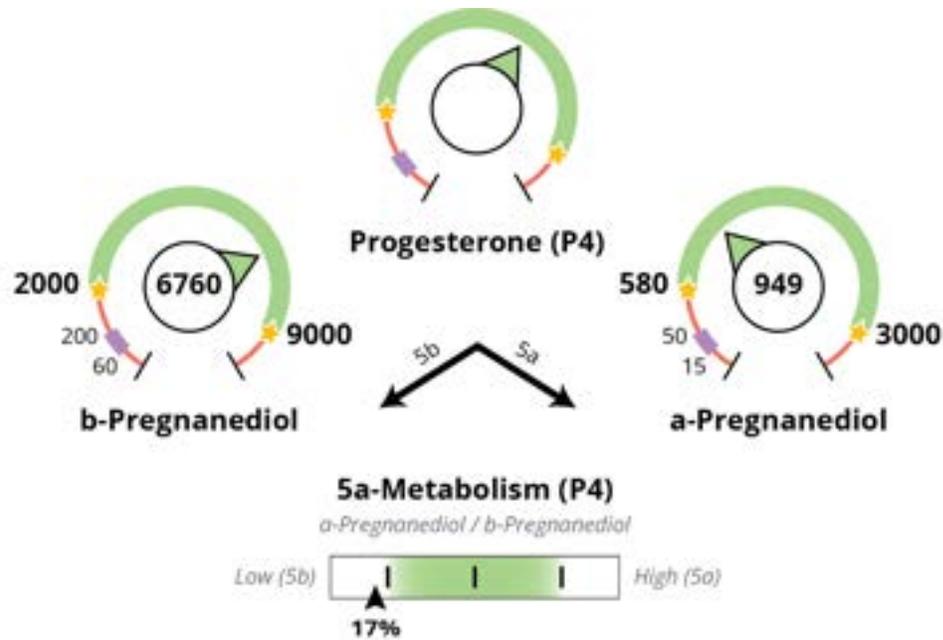
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Game time!

Both women below are taking 100 mg oral micronized progesterone (OMP) at bedtime. Which woman would you expect to experience more calming effects from the OMP?

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Question 3: Both women below are taking 100 mg oral micronized progesterone (OMP) at bedtime. Which woman would you expect to experience more calming effects from the OMP?
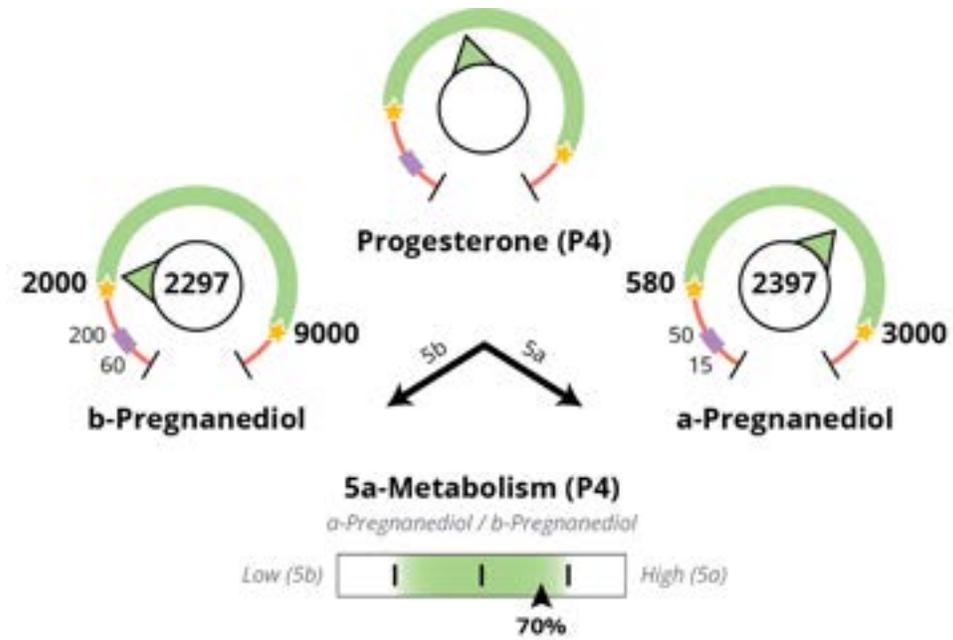
Game time!

Both women below are taking 100 mg oral micronized progesterone (OMP) at bedtime. Which woman would you expect to experience more calming effects from the OMP?
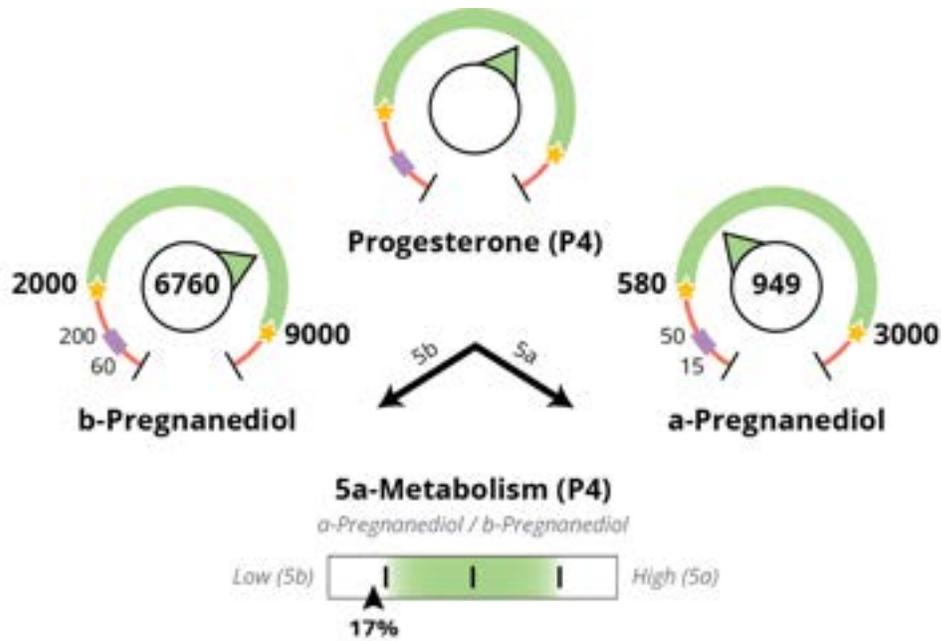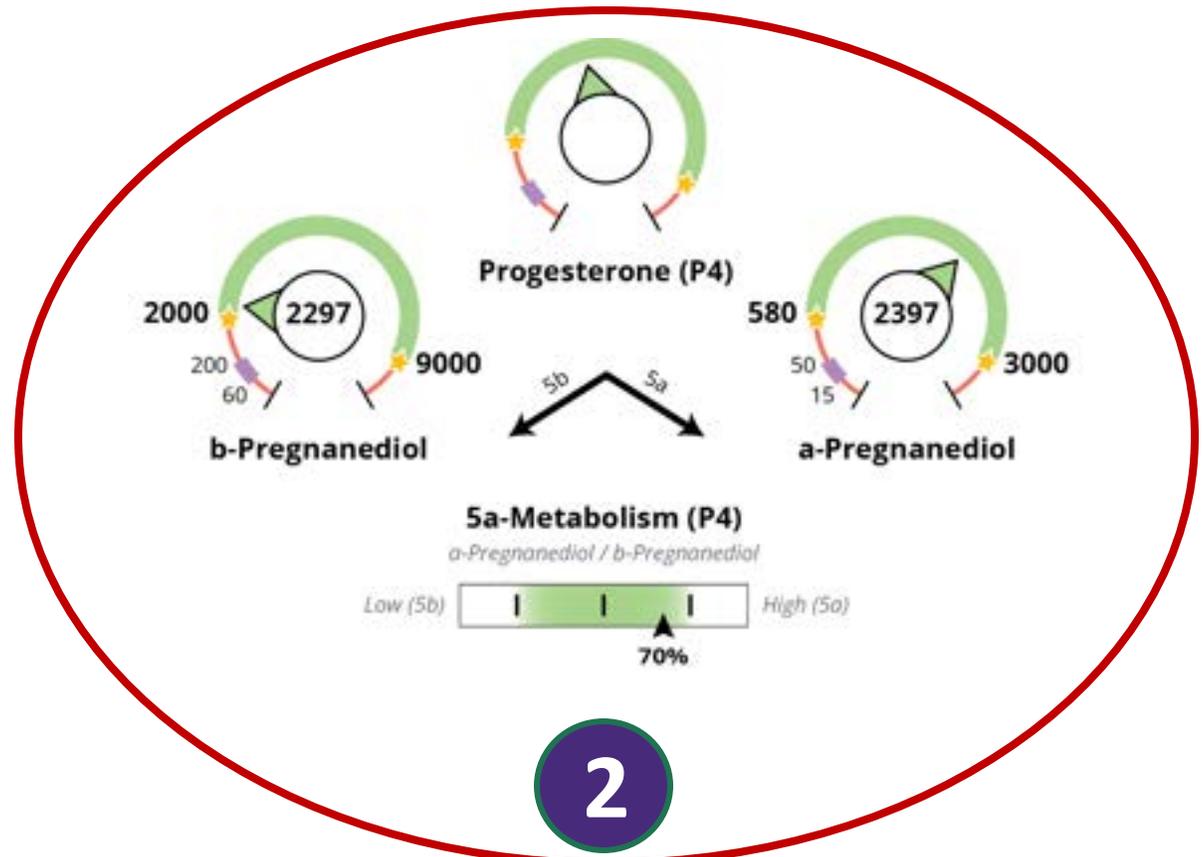
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DUTCH Advanced Insights
Estrogen Clearance Rate

3

Page 2

Estrogen Progesterone

3 Assess estrogen clearance through phase 1 and 2

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- The estrogen clearance rate can be estimated by comparing the parent estrogen levels with the phase 1 & 2 metabolite levels.

Parent Estrogens

- E1
- E2

Phase 1 & 2 Metabolites

- 2-OH-E1
- 4-OH-E1
- 16-OH-E1
- E3
- 2-Methoxy-E1
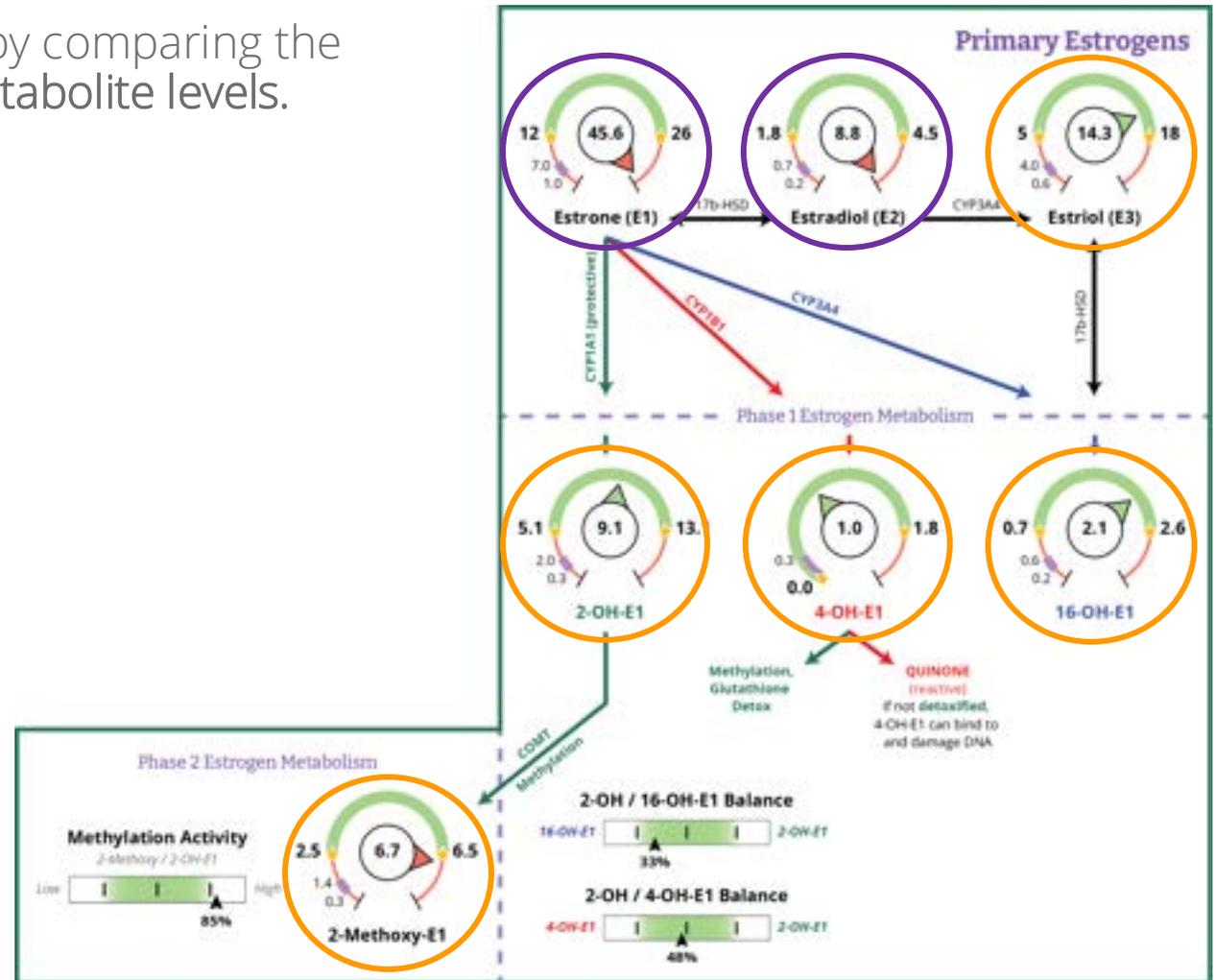
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- If the parent estrogens are **much higher** than the phase 1 and 2 metabolites, then the patient may have **slow estrogen clearance** (and vice versa).

- **Slow estrogen clearance may put patients at higher risk of estrogen excess conditions.** On the contrary, fast estrogen clearance may put patients at a lower risk of estrogen excess conditions.

The Bathtub Detox Analogy:

Phase 1 is the water filling up the tub

- Is the right type of water filling up the tub (2-OH vs. 4-OH and 16-OH). How fast or slow is it filling up?

Phase 2 is the drain

- How open or closed is the drain? Is it open wide enough?

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Estrogen clearance issues are sometimes not apparent when looking at page 1 of the DUTCH report.

- For example, this 32-year-old female complains of **breast tenderness** and **moderate PMS**.
- Her phase 1 ratios might look good on page 1, ***but***…
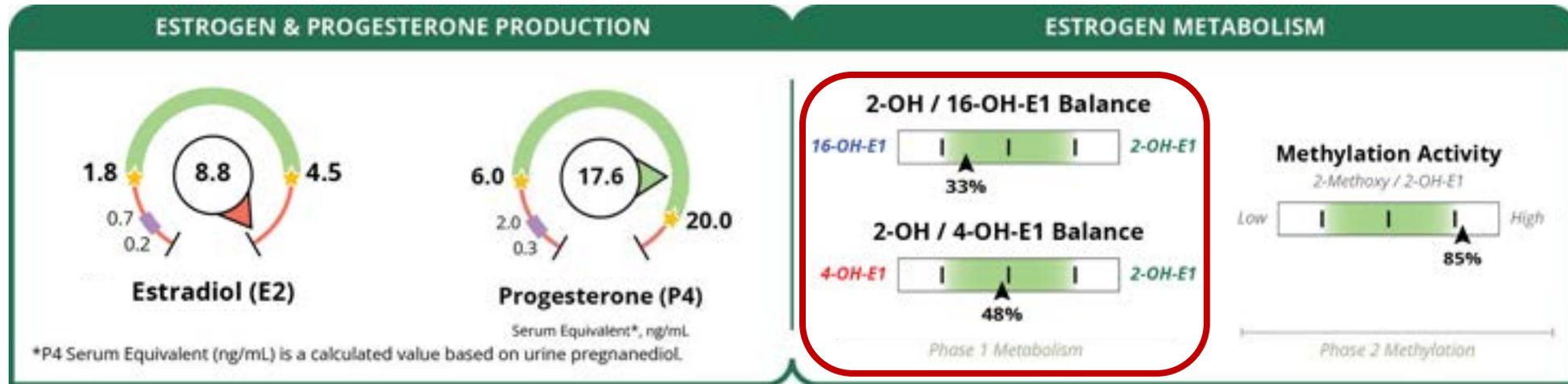
....when we look at page 2, we can see she has **slow estrogen clearance**, which could be worsening her estrogen excess symptoms.

- How do we know she has slow estrogen clearance?

- Her E1 and E2 are almost double above range!

- However, her phase 1 metabolites (2-OH-E1, 4-OH-E1, 16-OH-E1, E3) are within range.

- Her phase 2 metabolite (2-Methoxy-E1) is slightly above range because she is methylating well.

What might her results look like if she had normal estrogen clearance?
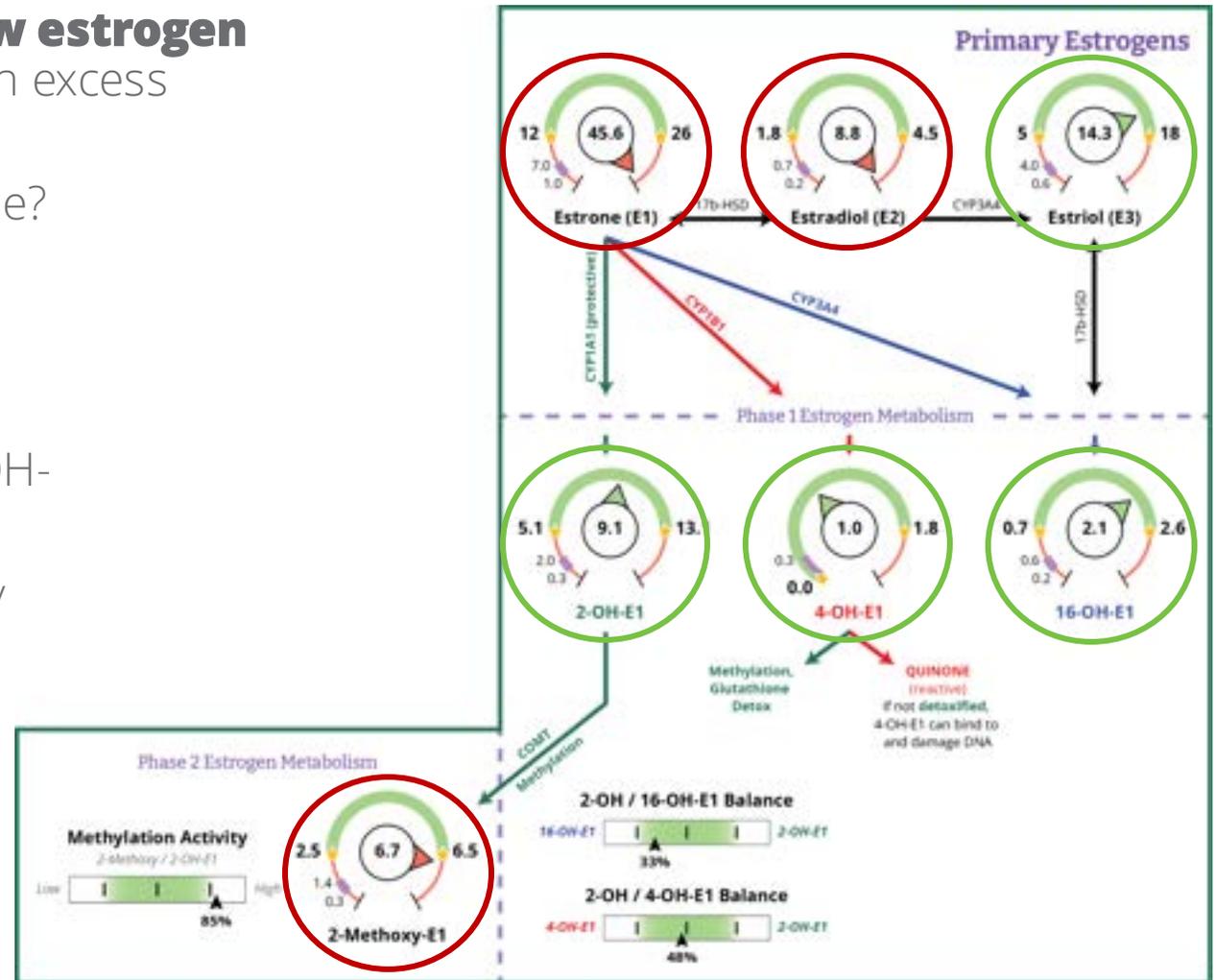
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If she had normal estrogen clearance…

- E1 and E2 levels may be lower because she's clearing her estrogen at a normal rate now (compared to a slower rate on the previous slide).

- Phase 1 and 2 metabolites might be higher as she is more effectively clearing E1 and E2 into circulation (as compared to the previous slide).

What might her results look like if she had fast estrogen clearance?
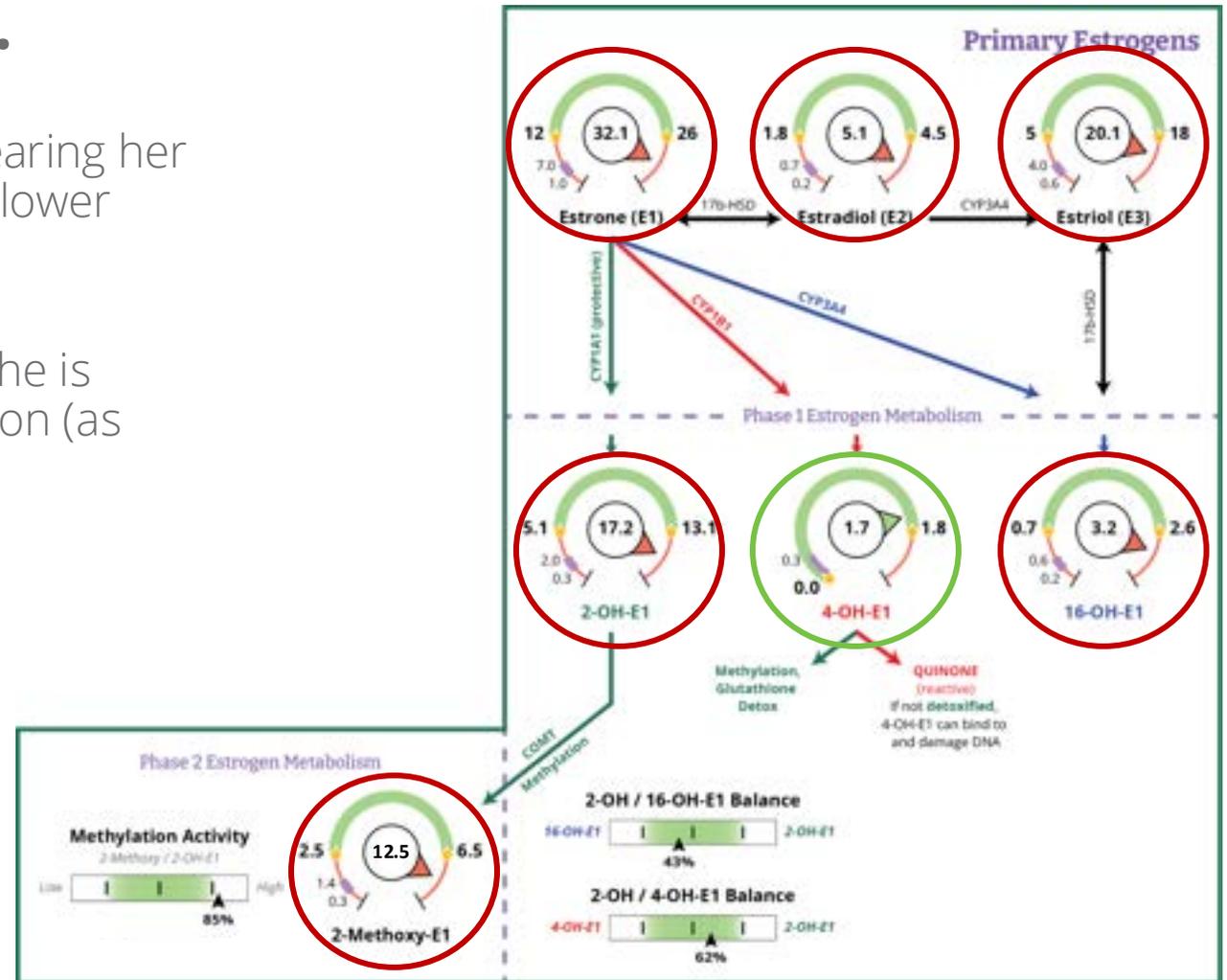
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If she had fast estrogen clearance...

- E1 and E2 levels may be **even lower** (and perhaps within range!) compared to the previous slide because she's clearing her estrogen at a **fast** rate.

- Phase 1 and 2 metabolites would be **even higher** as she clears E1 and E2 out of circulation and into phase 1 at a fast rate.
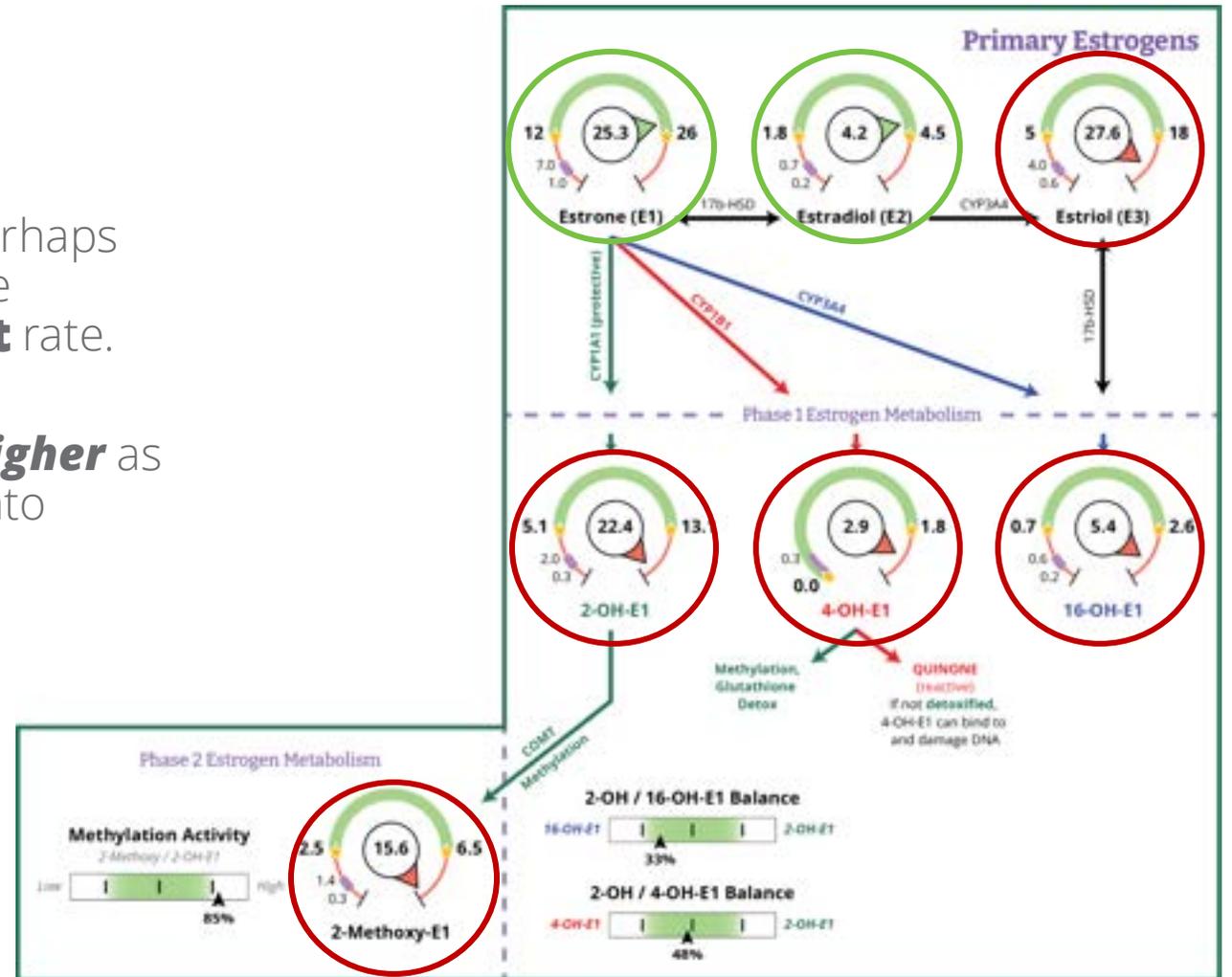
Summy of progression from slow to fast estrogen clearance (focusing in on phase 1):

Slow   Normal   Fast

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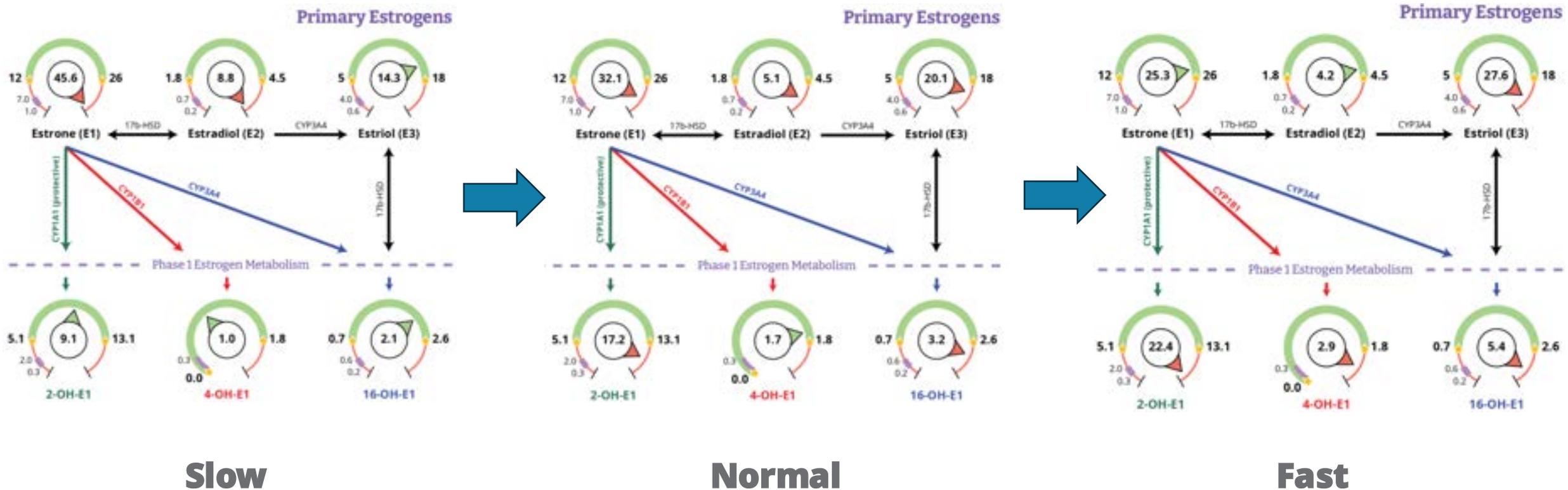
What improves estrogen clearance?

- **Many providers use 3,3'-diindolylmethane (DIM) or indole-3-carbinol (I3C) to increase the estrogen clearance rate.**

- DIM can reduce circulating parent estrogens (E1, E2) via increased phase I metabolism through the 2-OH pathway.

- Estrogens metabolized into 2-OH-E1/E2 are associated with reduced long-term risk of breast cancer according to observational studies.

- When used in relative estrogen dominant conditions, DIM has been found to anecdotally reduce heavy menses, breast tenderness, and bloating.

- Typical dosing 50-500 mg daily.

For references see "2OH Metabolites and Reduced Risk of Breast Cancer" in the Reference section

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- Precision Analytical has three published studies on DIM, two in 2025: one in premenopausal women and the other in postmenopausal women using a TD E2 patch.

- Both studies found that **DIM lowered estrogen and 16-OH-E1 levels, increased 2-OH levels, and improved the 2/16 balance**.
  - *This is significant because 16-OH-E1 is estrogenic, and 2-OH is anti-proliferative!*

- However, the study in premenopausal women additionally showed that DIM **increased 4-OH levels** and **only slightly improved the 2/4 balance**.
  - *This is significant because 4-OH is genotoxic; Thus, use caution with DIM and I3C supplementation.*

Menopause
The Journal of The Menopause Society
Articles & Issues ⌄   Collections ⌄   Videos   For Authors ⌄   Journal Info ⌄

ORIGINAL STUDIES

The impact of 3,3'-diindolylmethane on estradiol and estrogen metabolism in postmenopausal women using a transdermal estradiol patch
Newman, Mark S. MS; Smeaton, Jaclyn ND

Newman and Smeaton BMC Complementary Medicine and Therapies   (2024) 24:405
https://doi.org/10.1186/s12906-024-04708-7

BMC Complementary Medicine and Therapies

RESEARCH   Open Access

Exploring the impact of 3,3'-diindolylmethane on the urinary estrogen profile of premenopausal women

Mark Newman[1*] and Jaclyn Smeaton[1]

Newman M et al. BMC Complement Med Ther. 2024 Nov 22;24(1):405.

Newman MS et al. Menopause. 2025 Jul 1;32(7):630-639.
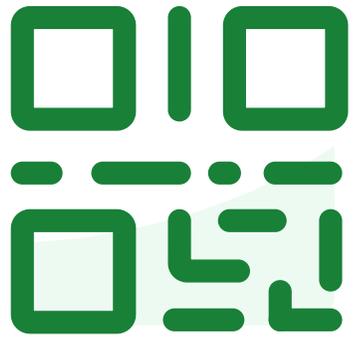
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Join at slido.com
#DUTCHFEST4

Game time!

This 53-year-old PMP woman using TD E2 cream tested **before and after** DIM. Which report represents her hormone detox patterns while taking DIM?

slido.com
#DUTCHFEST4
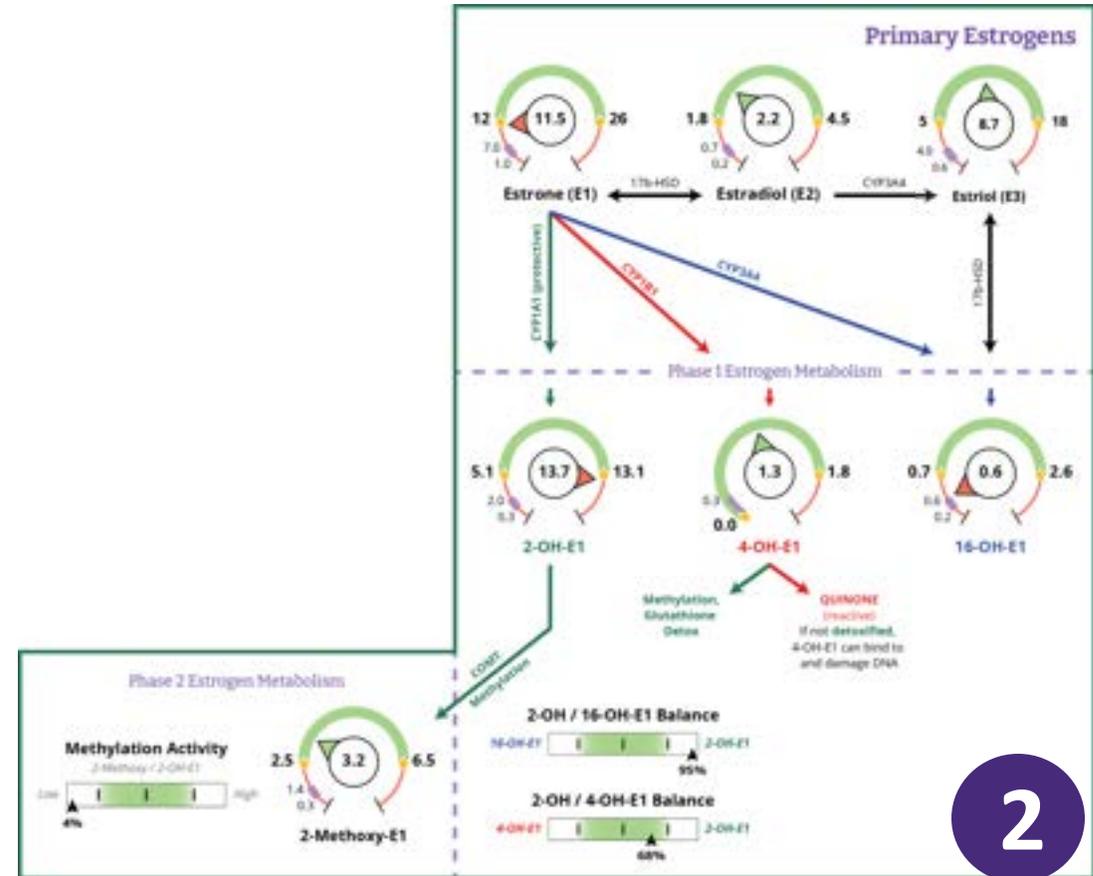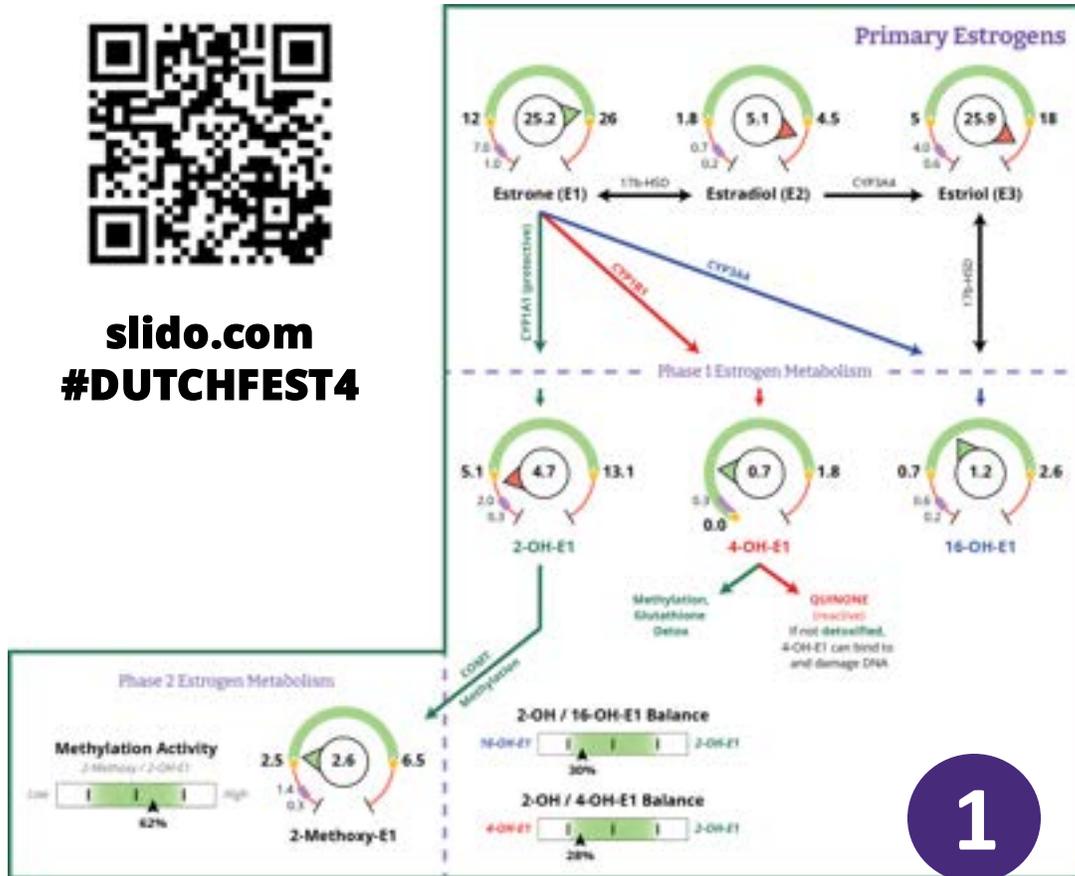
Question 4: This 53-year-old PMP woman using TD E2 cream tested before and after DIM. Which report represents her hormone detox patterns while taking DIM?

Polling Question

Game time!

This 53-year-old PMP woman using TD E2 cream tested **before and after** DIM. Which report represents her hormone detox patterns while taking DIM?

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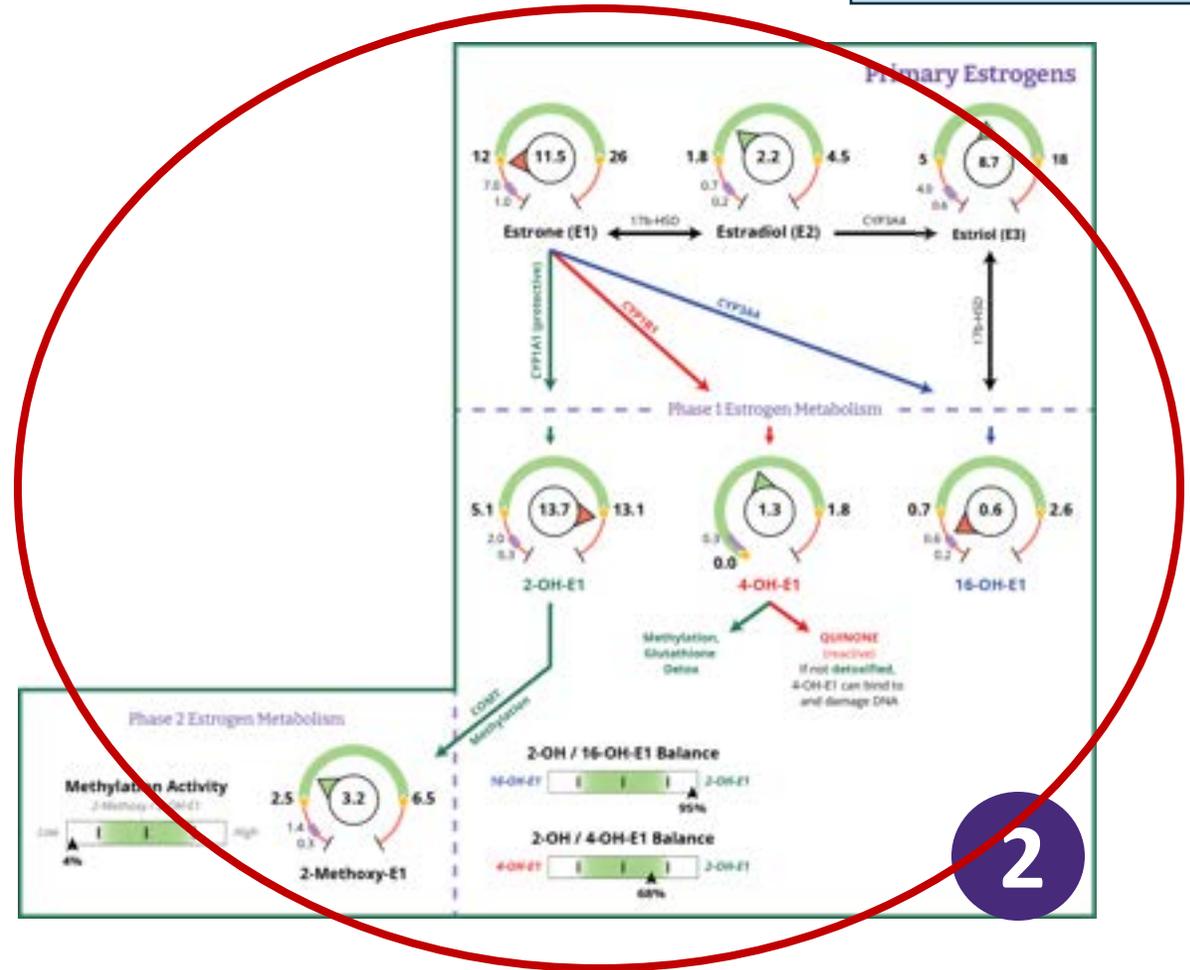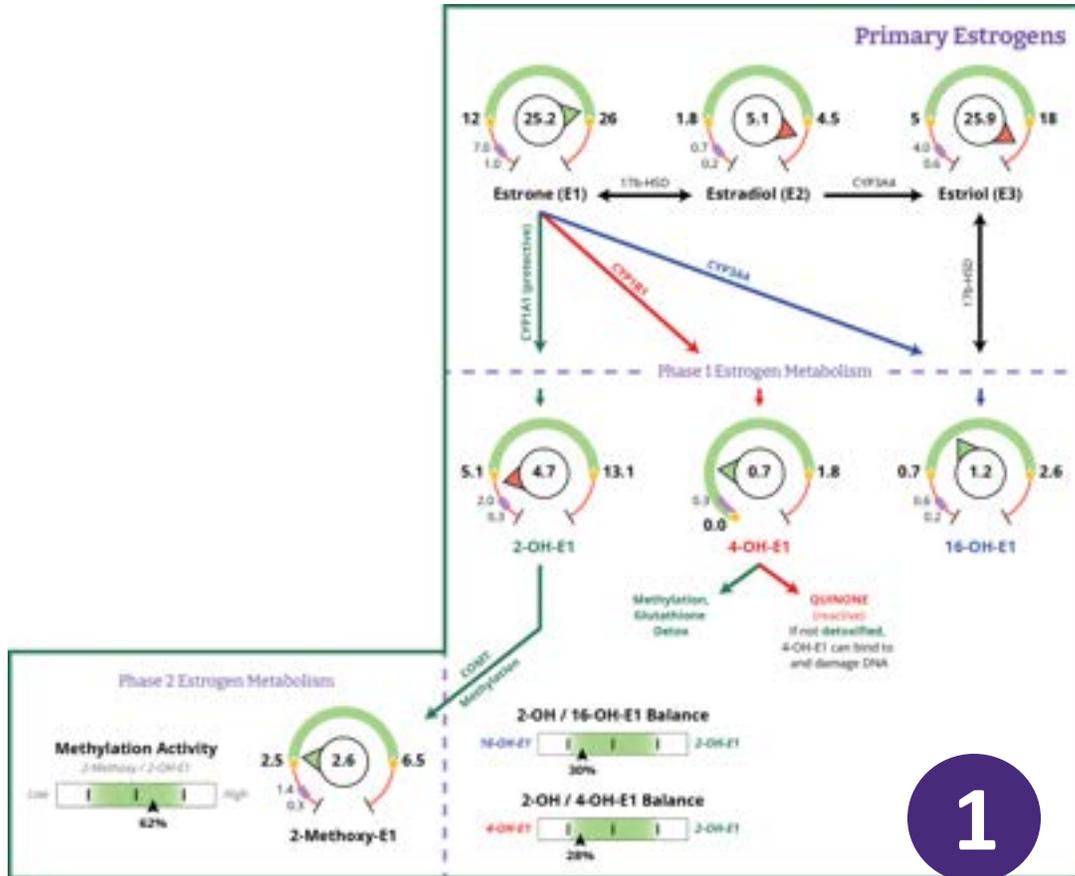
- Because DIM effectively "pushes" E1 and E2 into phase 1, mostly down the 2-OH pathway, it can increase the estrogen clearance rate.

- Because it lowers E1 and E2 and 16-OH-E1 it can lower estrogen activity in estrogen-sensitive tissues (such as breast, uterus, and ovaries) and lower the estrogenic burden in the body.

- ***Caution***: Ensure phase 2 (methylation) and phase 3 elimination (gut/stool/bile) are functioning properly or phase 1 metabolites (2-OH and 4-OH) can "back up" and "build up" in phase 1, which is not ideal as 4-OH metabolites are unstable and can cause oxidative damage.

E1 & E2 → **DIM (+)** →

Phase 1	Phase 2	Phase 3
Hydroxylation	**Conjugation (e.g., methylation)** ✓	**Elimination** ✓

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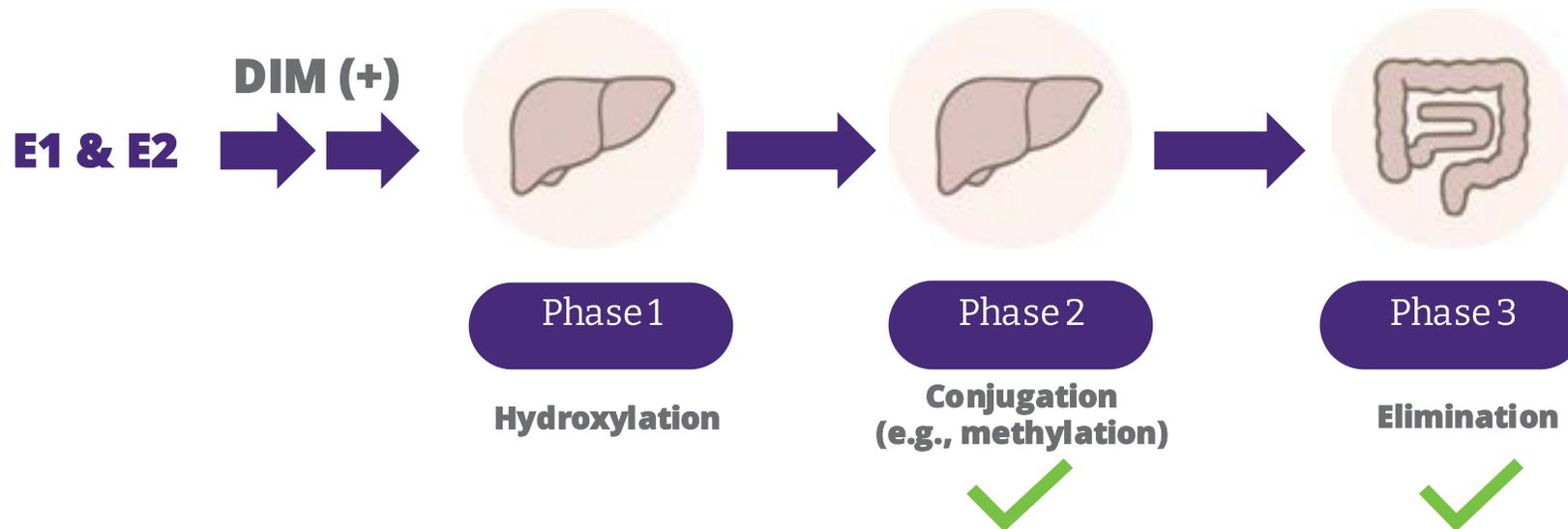
Think about it!

Game time!

45-year-old female with regular cycles, **hot flashes**, **night sweats**, and **vaginal dryness**. Fast estrogen clearance due to taking DIM.

• Would you tell her to continue the DIM?

• Would you support her methylation?

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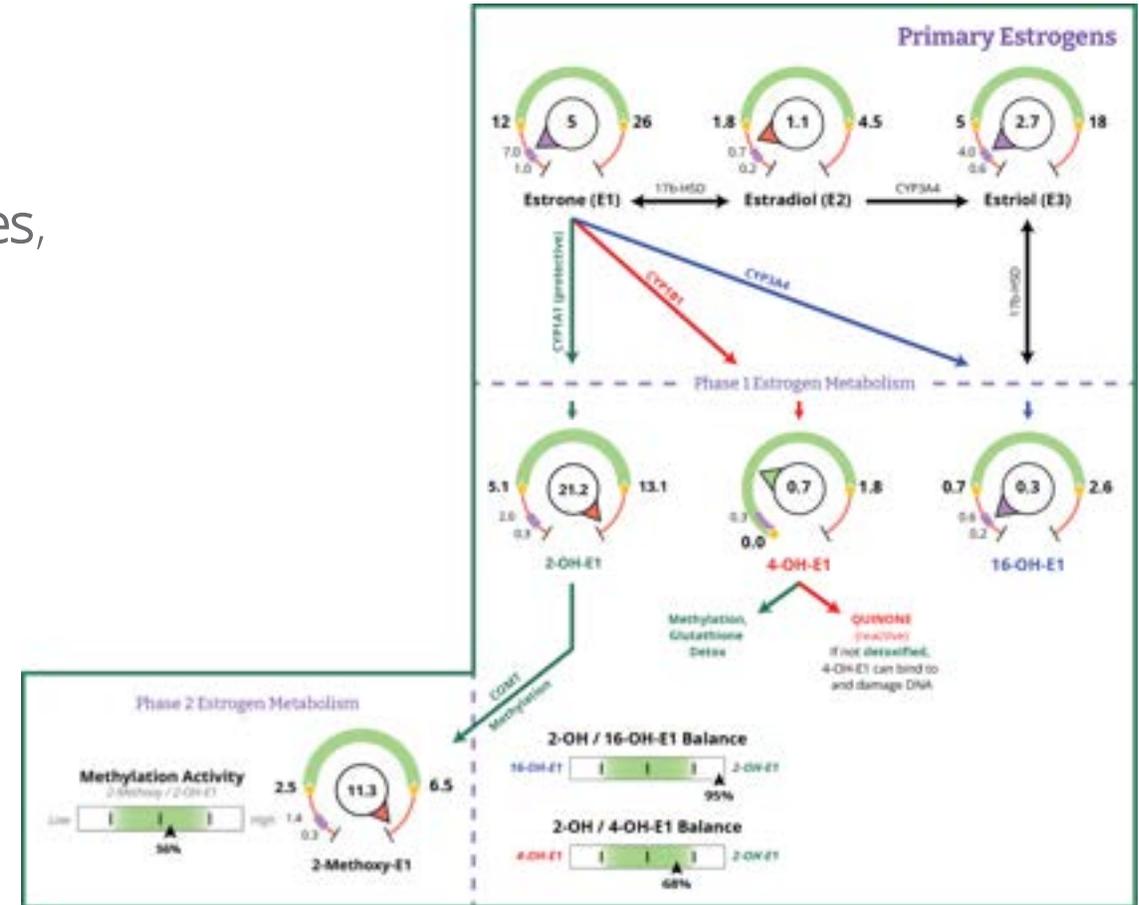
A Word of Caution

- DIM is generally considered "chemoprotective" but use caution when influencing metabolic pathways.

- For example, DIM increases CYP1A1 activity and research shows that increased activity in CYP1A1 and CYP1A2 due to certain SNPs can increase cancer risk through their role in the bioactivation of pro-carcinogens.

Polycyclic aromatic hydrocarbons (PAHs) and other similar toxins are inert until activated by CYP1A1 and CYP1A2 into toxic and highly reactive intermediate metabolites that are carcinogenic.

CYP1A1
CYP1A2

DIM (+)

Toxic intermediates

Phase 1
Hydroxylation

Phase 2
Conjugation (e.g., methylation)

Phase 3
Elimination
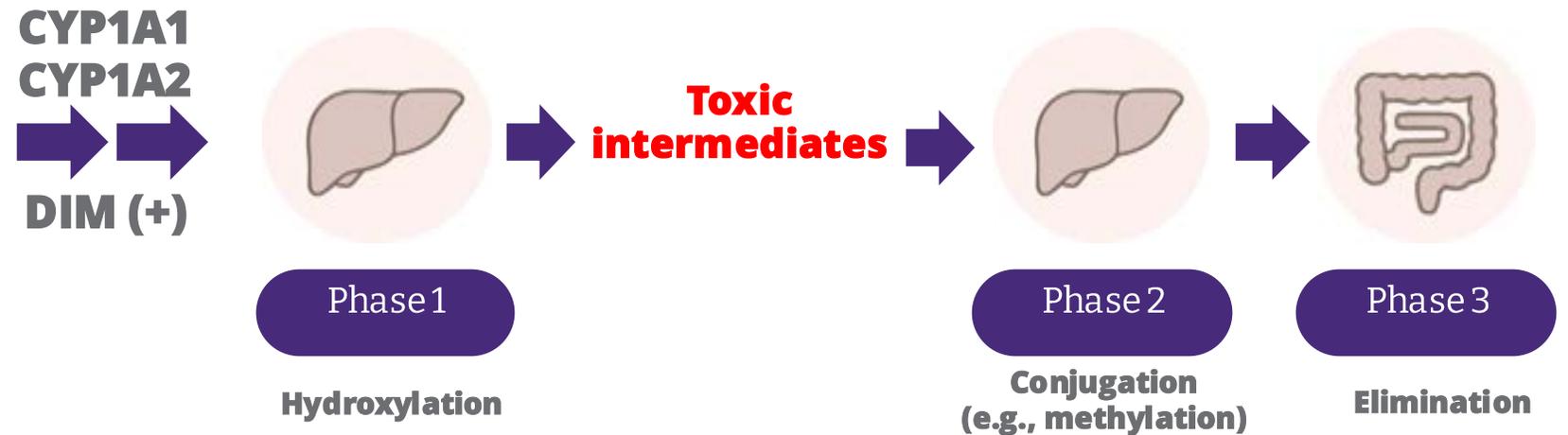
Androutsopoulos VP et al. BMC Cancer. 2009 Jun 16;9:187

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Polling Question

Game time!

Would you give this 34-year-old female with heavy bleeding DIM?

slido.com #DUTCHFEST4
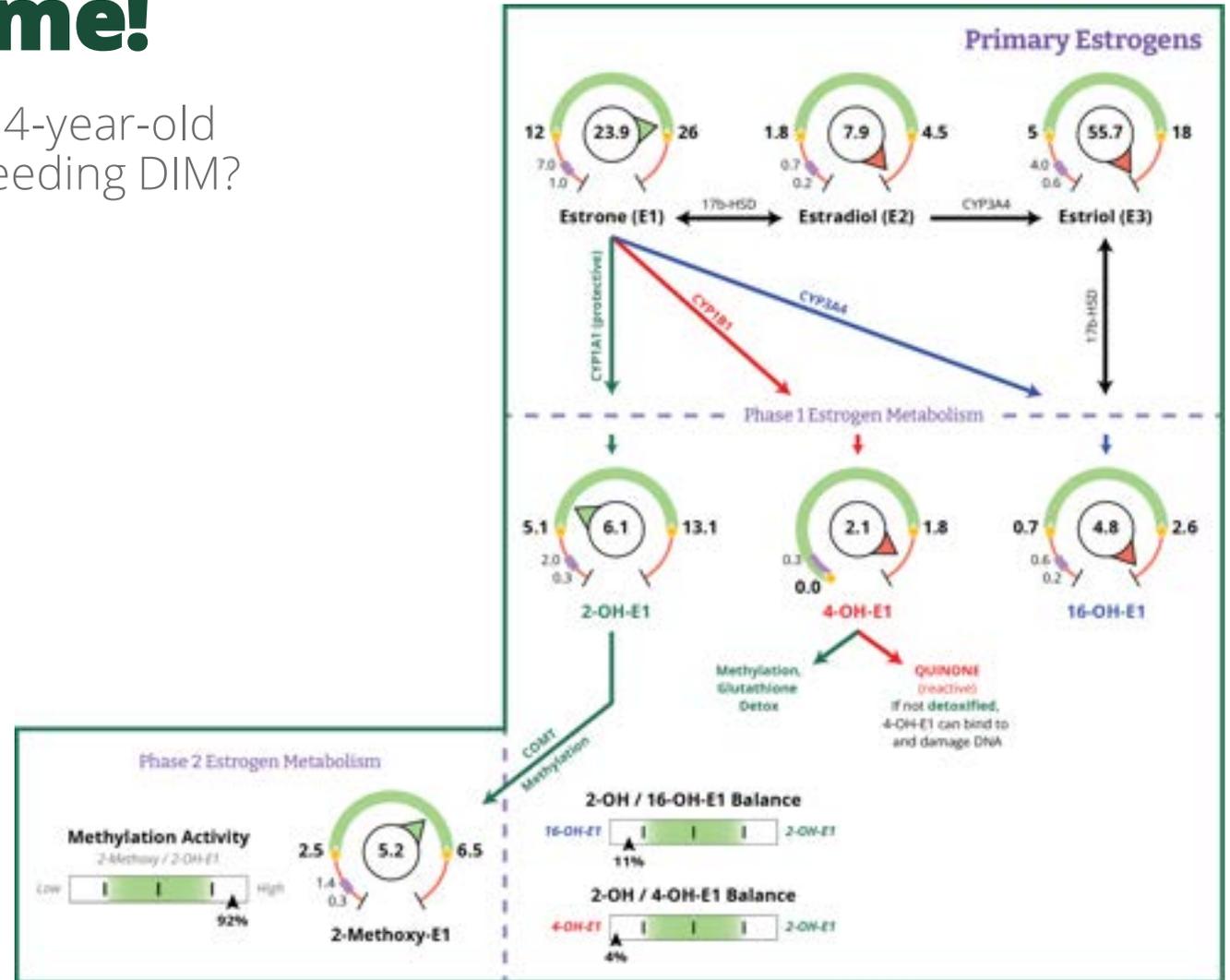
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Question 5: Would you give this 34-year-old female with heavy bleeding DIM?

Polling Question

Game time!

Would you give this 34-year-old female with heavy bleeding DIM?

- What if her methylation activity was low at 4%? What would you do differently?

- What if she had very long irregular cycles, vaginal dryness, and bouts of hot flashes? Would you still give DIM?

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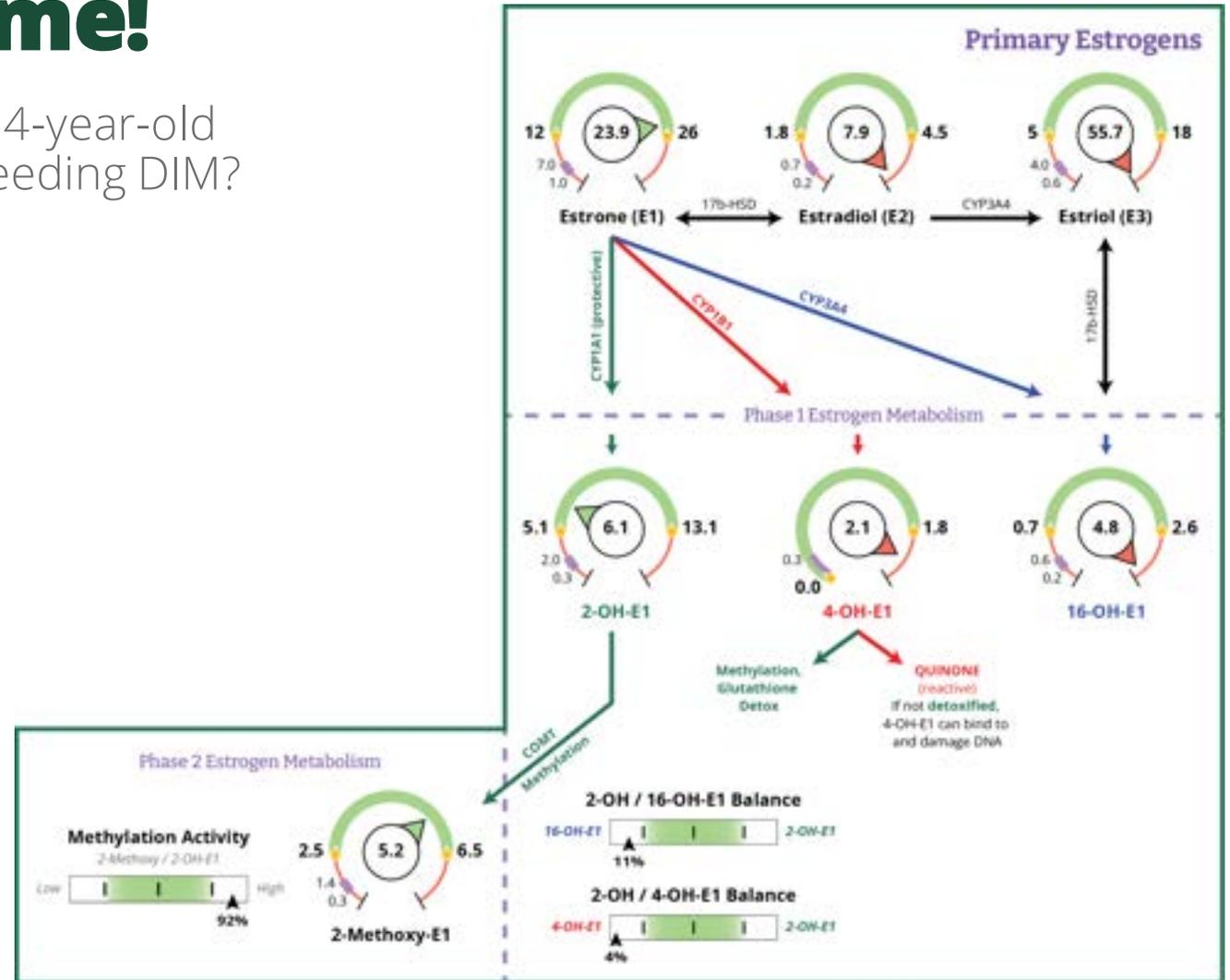
Other ways to promote optimal estrogen detox

- Cruciferous vegetables

- Broccoli sprouts (sulforaphane)

- High dietary fiber foods

- Sulfur rich foods

- Supplements: sulforaphane (glucoraphanin + myrosinase), resveratrol

- Methylation support: B6, B12, folate, magnesium, choline, betaine/TMG, s-adenosyl-L-methionine (SAMe), .

- These foods and supplements can promote optimal estrogen detox and improve symptoms more gently than DIM, possibly without lowering estrogens.

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Polling Question

slido.com
#DUTCHFEST4

Game time!

Would you say this 37-year-old woman has slow, normal, or fast estrogen clearance?

Would you expect her to experience symptoms of estrogen excess?
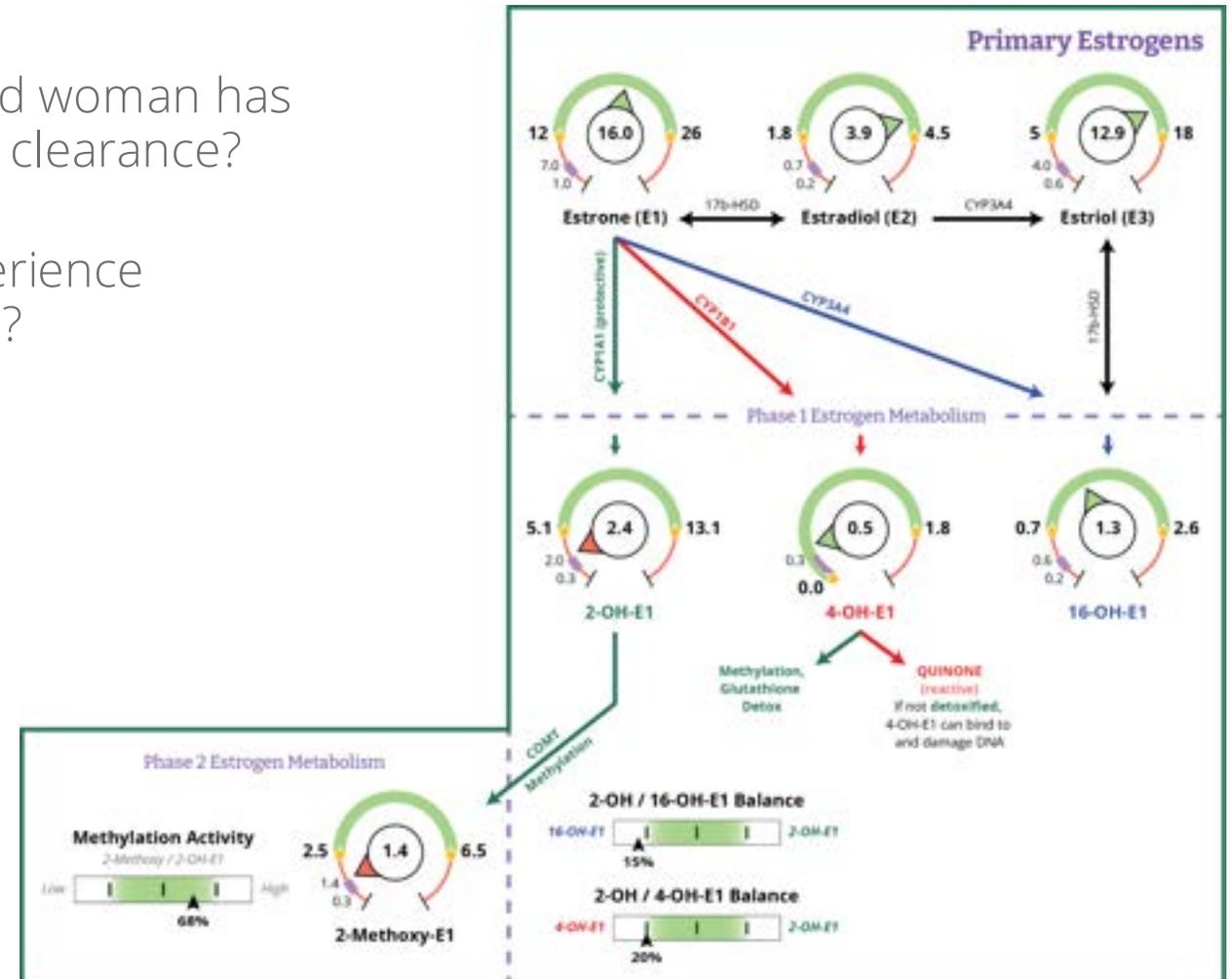
Question 6: Would you say this 37-year-old woman has slow, normal, or fast estrogen clearance?

Would you expect her to experience symptoms of estrogen excess?

Polling Question

Game time!

Would you say this 37-year-old woman has slow, normal, or fast estrogen clearance?

Would you expect her to experience symptoms of estrogen excess?

- She may be at an increased risk of estrogen excess symptoms, but other factors must be considered, such as progesterone levels, cycle length, etc.

- On her test requisition form she marked "sometimes/mild" for estrogen excess *and* estrogen deficiency, so follow-up questions at her next appointment may be helpful.
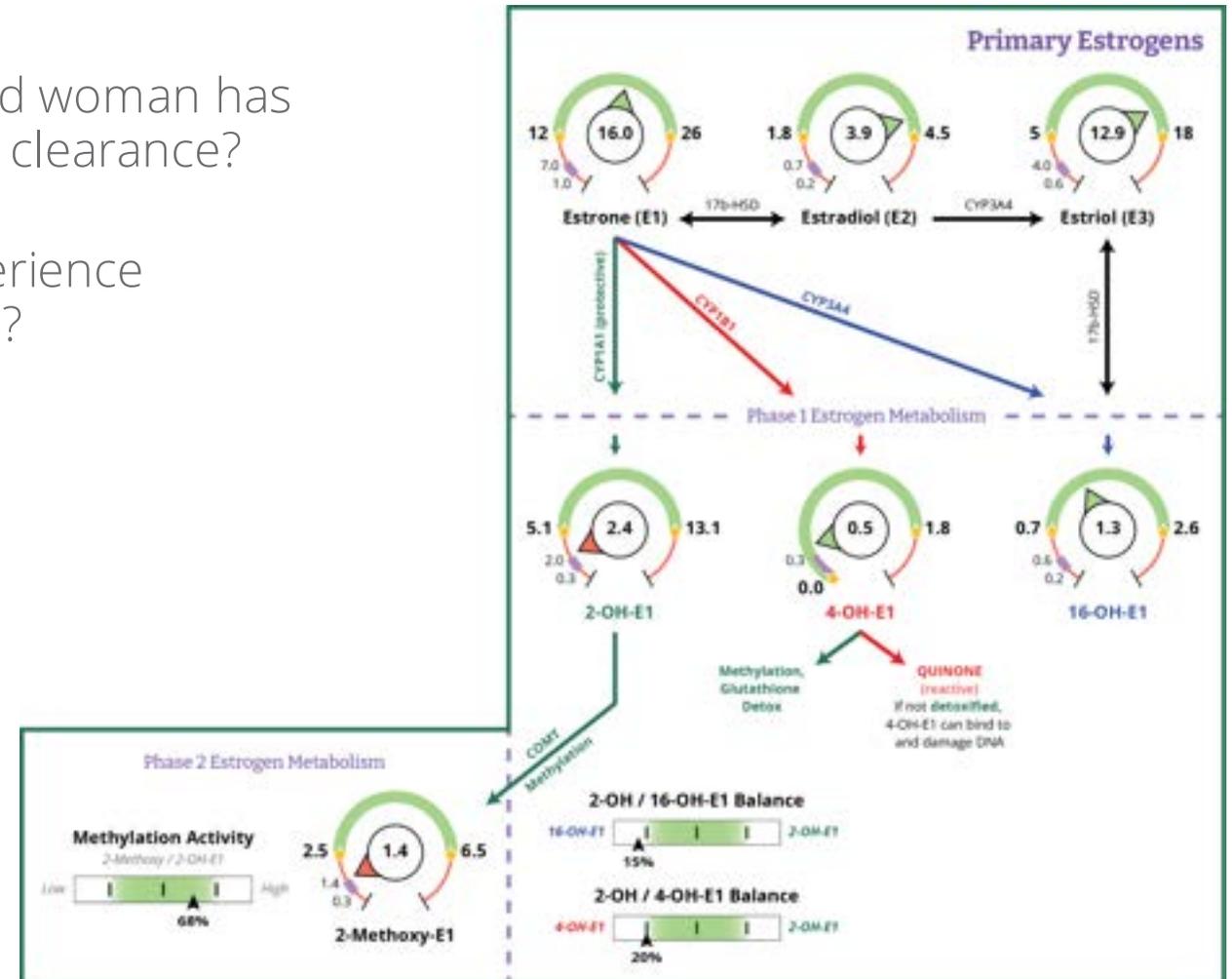
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Polling Question

Game time!

Would you say this 70-year-old woman on TD E2 cream has slow, normal, or fast estrogen clearance?

slido.com
#DUTCHFEST4
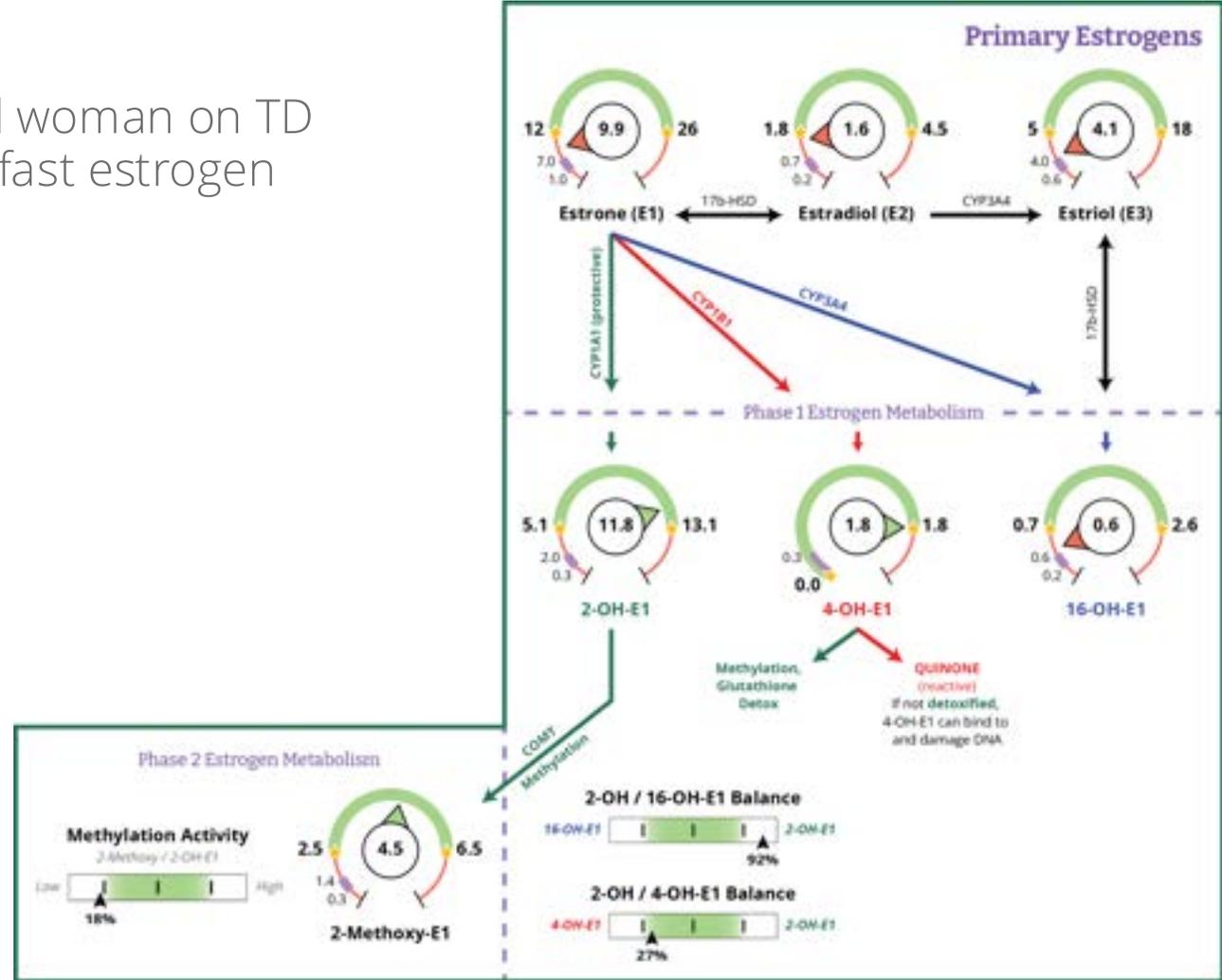
Question 7: Would you say this 70-year-old woman on TD E2 cream has slow, normal, or fast estrogen clearance?

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Polling Question

Game time!

Would you say this 70-year-old woman on TD E2 cream has slow, normal, or fast estrogen clearance?

- As suspected, she is taking DIM (100 mg)

- This aligns with our study in PMP women on TD E2 which found that DIM lowers E1 levels (average E1 went from 8.3 → 6.4).

- **Keep an eye on that 4-OH!!!**

Menopause
The Journal of The Menopause Society

ORIGINAL STUDIES
The impact of 3,3'-diindolylmethane on estradiol and estrogen metabolism in postmenopausal women using a transdermal estradiol patch
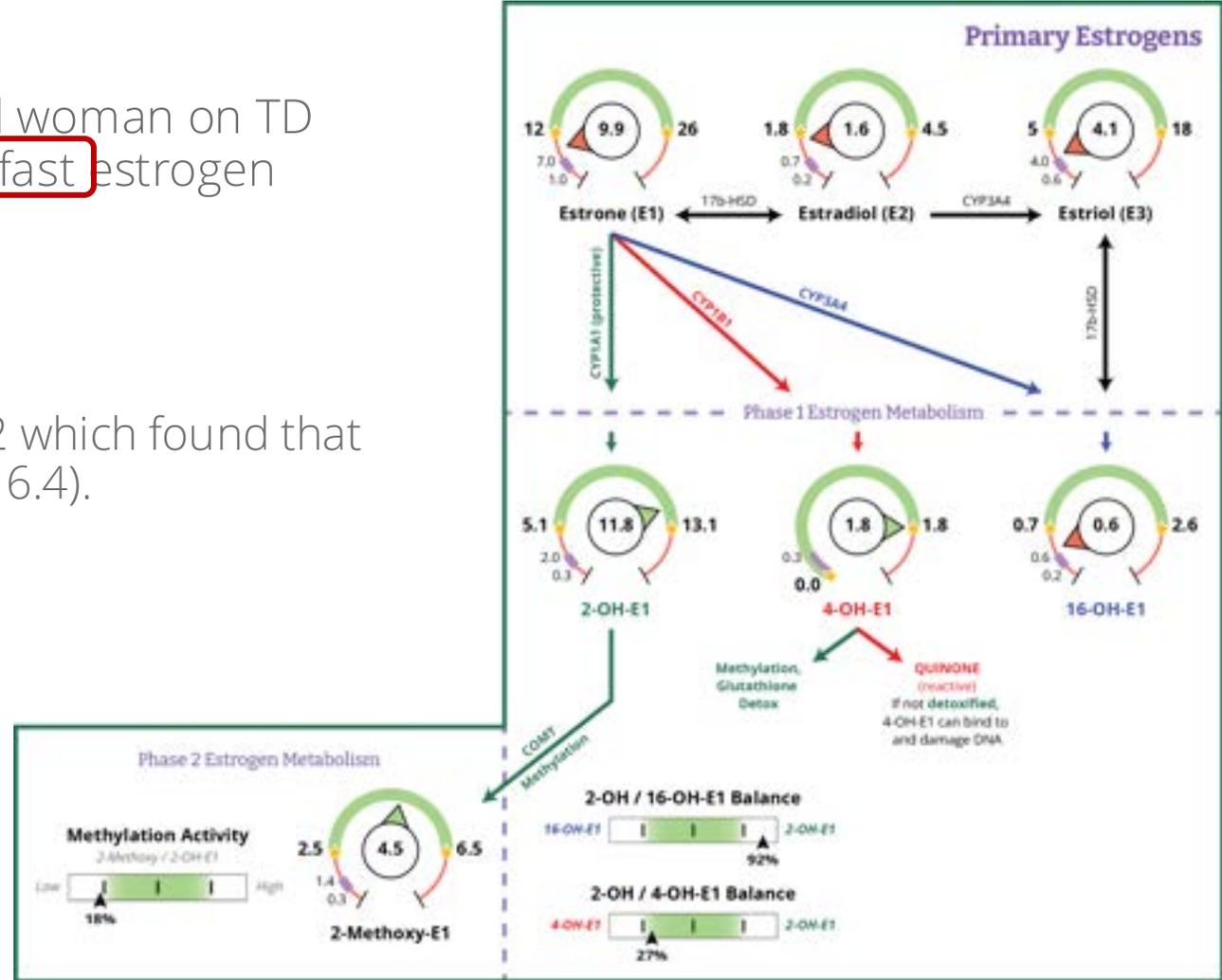
Newman M et al. BMC Complement Med Ther. 2024 Nov 22;24(1):405.

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DUTCH Advanced Insights
Estrogen-Related OATs

4

Organic Acid Tests (OATs)

TEST		RESULT	UNITS	NORMAL RANGE
Nutritional Organic Acids (Urine)				
Vitamin B12 Marker - May be deficient if high				
Methylmalonate (MMA)	Above range	4.9	ug/mg	0 - 2.5
Vitamin B6 Markers - May be deficient if high				
Xanthurenate	Above range	1.23	ug/mg	0.12 - 1.2
Kynurenate	Above range	5.3	ug/mg	0.8 - 4.5
Biotin Marker - May be deficient if high				
b-Hydroxyisovalerate	Within range	7.9	ug/mg	0 - 12.5
Glutathione Marker - May be deficient if low or high				
Pyroglutamate	Within range	50.3	ug/mg	28 - 58
Gut Marker - Potential gut putrefaction or dysbiosis if high				
Indican	High end of range	90.4	ug/mg	0 - 100
Neuro-Related Markers (Urine)				
Dopamine Metabolite				
Homovanillate (HVA)	Within range	4.4	ug/mg	3 - 11
Norepinephrine/Epinephrine Metabolite				
Vanilmandelate (VMA)	Above range	7.3	ug/mg	2.2 - 5.5
Neuroinflammation Marker				
Quinolinate	Above range	13.2	ug/mg	0 - 9.6
Additional Markers (Urine)				
Melatonin - Waking				
6-OH-Melatonin-Sulfate	Below range	1.3	ng/mg	10 - 85
Oxidative Stress / DNA Damage				
8-Hydroxy-2-deoxyguanosine (8-OHdG)	Within range	3.8	ng/mg	0 - 5.2

Page 6

Estrogen Progesterone

The estrogen-related OATs include:
- **Methylmalonate (MMA)**
- **Xanthurenate**
- **Kynurenate**
- **Pyroglutamate**
- **Indican**
- **8-OHdG**

④ Assess whether any of the estrogen-related organic acids are out of range

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- **Methylmalonate (MMA)** - High MMA may indicate B12 deficiency.
- **Xanthurenate and Kynurenate** – High Xanthurenate and/or Kynurenate may indicate B6 deficiency.
- B12 and B6 support optimal methylation.
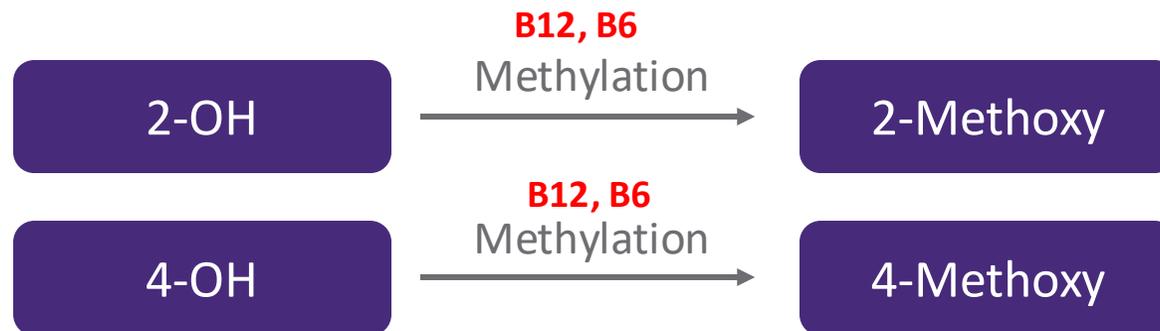
Froese DS, et al. Journal of Inherited Metabolic Disease. 2019;42(4):673-685.

Chen KJ, et al. Asia Pac J Clin Nutr. 2005;14(3):250-255.

- **Pyroglutamate** –

- High Pyroglutamate is associated with glutathione deficiency.

- **Glutathione is a key antioxidant** that helps protect cells from damage.

- If the 2-OH/4-OH balance is below the optimal range (<20%) and/or if 4-OH metabolites are high, consider supporting glutathione if Pyro is high.

- **8-Hydroxy-2-deoxyguanosine (8-OHdG)** –

- High 8-OHdG may indicate a higher **oxidative stress** burden, especially when paired with high 4-OH metabolites or a low 2-OH/4-OH balance. This is because a high oxidative environment can increase the likelihood of 4-OH causing DNA damage.

2-OH / 4-OH-E1 Balance

4-OH-E1 | | | | 2-OH-E1

8%
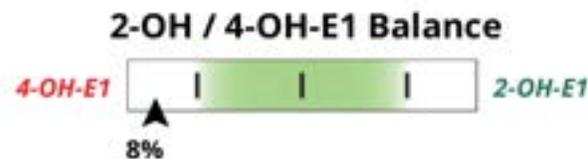
Cavalieri E, et al. Biochim Biophys Acta. 2006;1766(1):63-78.

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- **Indican** – High Indican is a marker of dysbiosis (bacterial imbalance) and intestinal permeability.

- **Dysbiosis may impact (worsen) estrogen detox**.
  - Dysbiosis can increase the likelihood of having high beta-glucuronidase levels.
  - B-glucuronidase is made in the gut by estrobolome, and when in excess, can cause estrogens to be recirculated rather than excreted, increasing estrogen load.

- If paired with high E2 or suboptimal estrogen metabolism, this may contribute to poor estrogen detoxification through the GI tract.
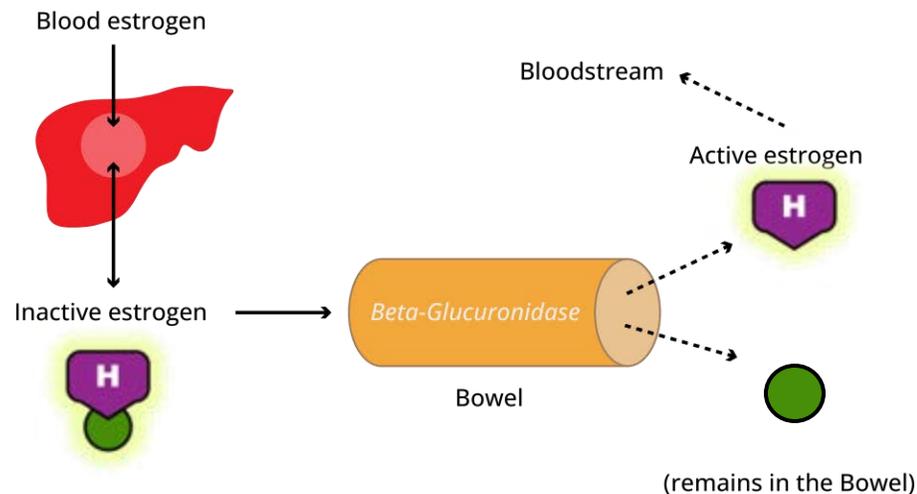
Tahri A, et al. World J Clin Oncol. 2025 Sep 24;16(9):108819.

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- In 2022, we added indican to our report to give insight into gut health.

- Data from Precision Analytical samples in postmenopausal women and in men have shown a small, but statistically **significant association between elevated urinary indican levels (suggesting dysbiosis) and estradiol levels**, reinforcing the assertion that GI dysbiosis is an important factor in circulating estrogen levels.

Estradiol (E2)

Progesterone
Serum Equivalent*, ng/mL
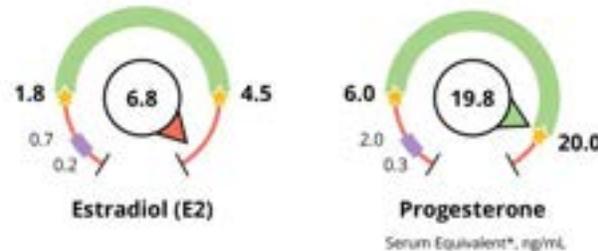
Gut Marker - Potential gut putrefaction or dysbiosis if high				
Indican	High end of range	93.0	ug/mg	0 - 100

37-year-old female
Tender breasts, Mood swings
Severe Anxiety

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Example: 33-year-old female

- Fertility issues, Endometriosis, High estrogen

Methylation Activity
2-Methoxy / 2-OH-E1

Low ▮ High

25%

2-OH / 16-OH-E1 Balance

16-OH-E1 ▮ *2-OH-E1*

5%

2-OH / 4-OH-E1 Balance

4-OH-E1 ▮ *2-OH-E1*

4%

Organic Acid Tests (OATs)

TEST		RESULT	UNITS	NORMAL RANGE
Nutritional Organic Acids (Urine)				
Vitamin B12 Marker - May be deficient if high				
Methylmalonate (MMA)	Within range	1.8	ug/mg	0 - 2.5
Vitamin B6 Markers - May be deficient if high				
Xanthurenate	Above range	2.2	ug/mg	0.12 - 1.2
Kynurenate	Above range	5.2	ug/mg	0.8 - 4.5
Biotin Marker - May be deficient if high				
b-Hydroxyisovalerate	Within range	7.8	ug/mg	0 - 12.5
Glutathione Marker - May be deficient if low or high				
Pyroglutamate	Above range	64.2	ug/mg	28 - 58
Gut Marker - Potential gut putrefaction or dysbiosis if high				
Indican	Above range	106.2	ug/mg	0 - 100
Neuro-Related Markers (Urine)				
Dopamine Metabolite				
Homovanillate (HVA)	Within range	6.1	ug/mg	3 - 11
Norepinephrine/Epinephrine Metabolite				
Vanilmandelate (VMA)	Within range	3.8	ug/mg	2.2 - 5.5
Neuroinflammation Marker				
Quinolinate	High end of range	9.5	ug/mg	0 - 9.6
Additional Markers (Urine)				
Melatonin - Waking				
6-OH-Melatonin-Sulfate	Within range	39.3	ng/mg	10 - 85
Oxidative Stress / DNA Damage				
8-Hydroxy-2-deoxyguanosine (8-OHdG)	Within range	2.7	ng/mg	0 - 5.2

High estrogen levels can induce a B6 deficiency. Low B6 may be impacting her ability to methylate

Low glutathione is especially important due to her 4OH preference

High indican could cause recirculation of estrogens (from gut to blood) worsening high estrogen's impact on endometriosis

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Think about it!

Game time!

In this 33-year-old female with high estrogen and high indican, what would be your next steps?

Methylation Activity
2-Methoxy / 2-OH-E1

Low [ ] High

25%

2-OH / 16-OH-E1 Balance

16-OH-E1 [ ] 2-OH-E1

5%

2-OH / 4-OH-E1 Balance

4-OH-E1 [ ] 2-OH-E1

4%

Organic Acid Tests (OATs)

TEST		RESULT	UNITS	NORMAL RANGE
Nutritional Organic Acids (Urine)				
Vitamin B12 Marker - May be deficient if high				
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Neuro-Related Markers (Urine)				
Dopamine Metabolite				
Homovanillate (HVA)	Within range	6.1	ug/mg	3 - 11
Norepinephrine/Epinephrine Metabolite				
Vanilmandelate (VMA)	Within range	3.8	ug/mg	2.2 - 5.5
Neuroinflammation Marker				
Quinolinate	High end of range	9.5	ug/mg	0 - 9.6
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Melatonin - Waking				
6-OH-Melatonin-Sulfate	Within range	39.3	ng/mg	10 - 85
Oxidative Stress / DNA Damage				
8-Hydroxy-2-deoxyguanosine (8-OHdG)	Within range	2.7	ng/mg	0 - 5.2

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Think about it!

- You might consider a stool test to look at gut health and beta-glucuronidase levels.

- You may consider looking at page 45 of the DUTCH Treatment Guide to learn more about the indican marker, and page 31 to learn more about general phase 3 support and ways to lower beta-glucuronidase levels.

Phase 3 Detoxification

In addition to treating the underlying cause, other ways to support phase 3 detoxification in females and males include:

General phase 3 Support

- **Correct digestive issues:**
  - Hypochlorhydria - hydrochloric acid, apple cider vinegar, bitters
  - Low bile acid – bile acids, choline, taurine, glycine, Collinsonia root – see "Liver Support" on **page 55** for more information.
  - Pancreatic insufficiency - digestive enzymes, bitters
- **Ensure adequate bowel movements with:**
  - Adequate fiber
  - Adequate hydration
  - Movement/Exercise
  - Magnesium, vitamin C
  - Stress reduction, deep breathing
- **Nourish the gut lining:**
  - Deglycyrrhizinated licorice (DGL)
  - Glutamine
  - Okra
  - Slippery elm
- **Support a healthy microbiome/estrobolome:**
  - Optimize diet (Mediterranean, etc.)
  - Recolonize with probiotics and prebiotics
  - See "Lower β-Glucuronidase Enzymatic Activity" on this page
  - Support progesterone if low as it nourishes Bifidobacterium and L. reuteri, decreases gut permeability, offers enteric neuroprotection, and is anti-inflammatory - see Low Progesterone in Females" on **page 8**
  - Treat any current gut infections

Lower β-Glucuronidase Enzymatic Activity

(to lower enterohepatic circulation of 16-OH-E1)

- Avoid antibiotic use when possible
- Avoid high fat and protein diets
- Calcium-d-glucarate
- Dietary fiber
- Low-calorie and vegetarian diets
- Milk thistle
- Prebiotics and probiotics

If Indican is High

- If the Indican organic acid marker on the DUTCH Test is elevated, consider stool testing for further work-up.

Page 31 of the DUTCH Treatment Guide

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Estrogen-Related OATs Treatments

The treatment you choose depends on the cause, but also the symptoms, treatment goals, and patient preferences.

The DUTCH Treatment Guide: **Estrogen-Related OATs**

| Methylmalonate (MMA) *Page 44* | Xanthurenate Kynurenate *Page 44* | Pyroglutamate *Page 45* |

| Indican *Page 45* | 8-OHdG *Page 47* |

◯ OATs Support

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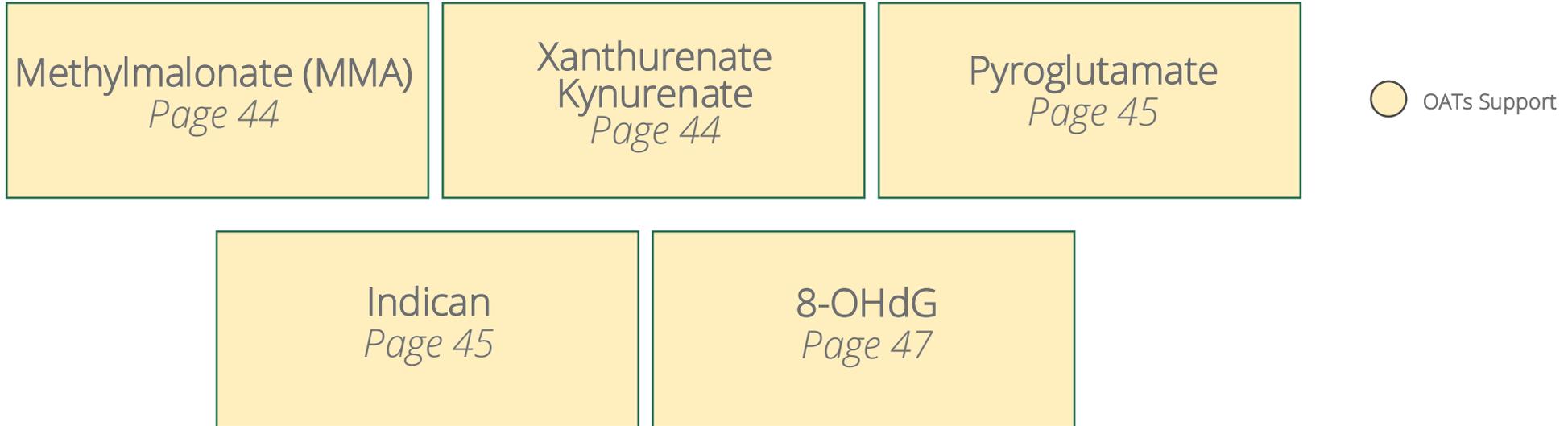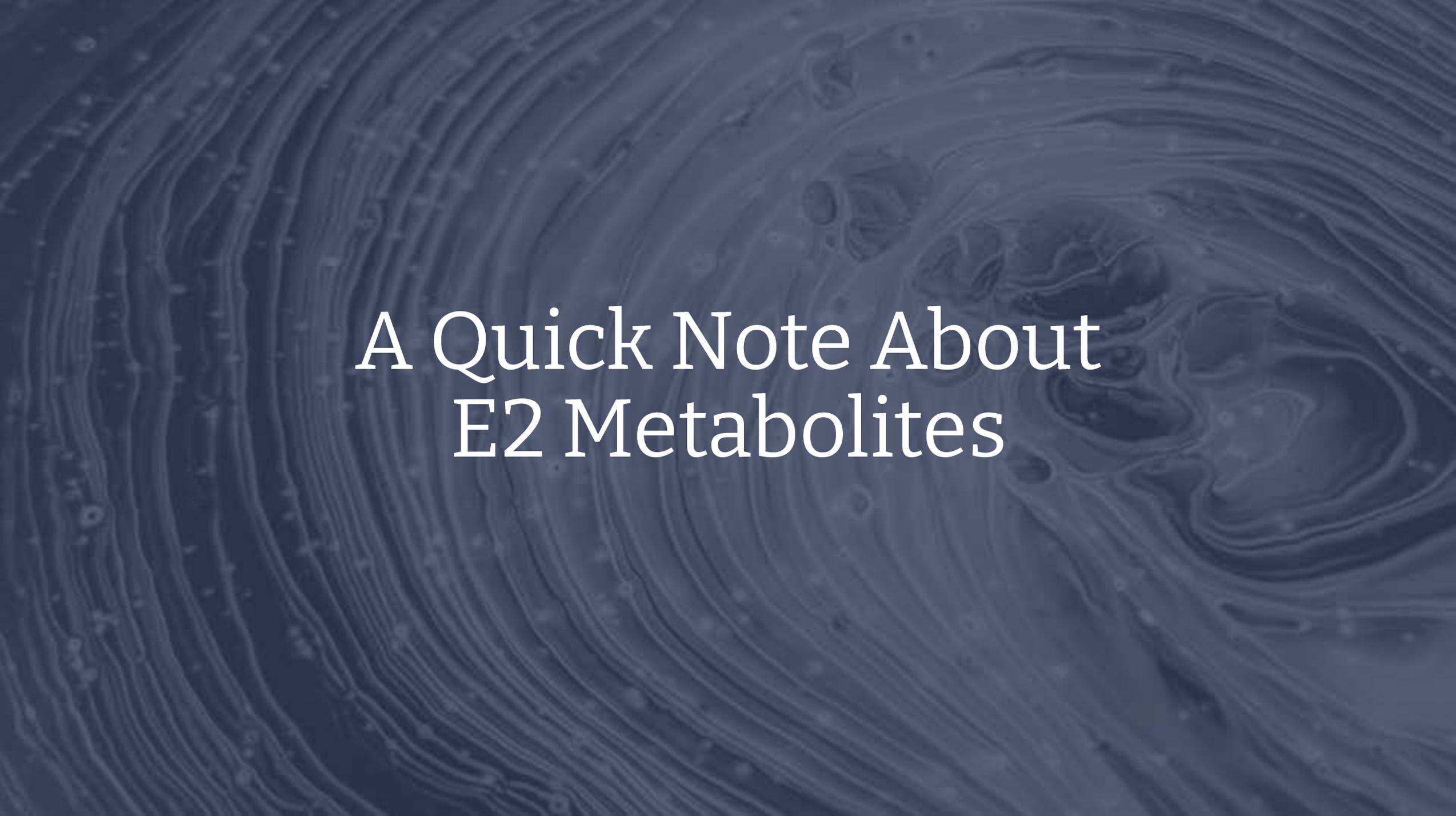
A Quick Note About E2 Metabolites

E2 Metabolites: 2-OH-E2 and 4-OH-E2

- E1 metabolites are shown visually on page 2 (rather than E2 metabolites) because they are **more abundant** and demonstrate **higher reproducibility**.

- **E2 metabolites (2-OH-E1 and 4-OH-E2)** are measured, and their results are listed on page 3 of the report.
  - These serve as a secondary indicator of phase 1 detoxification.

- For example, in this 40-year-old female, the elevated 2-OH-E2 confirms her strong 2-OH preference.
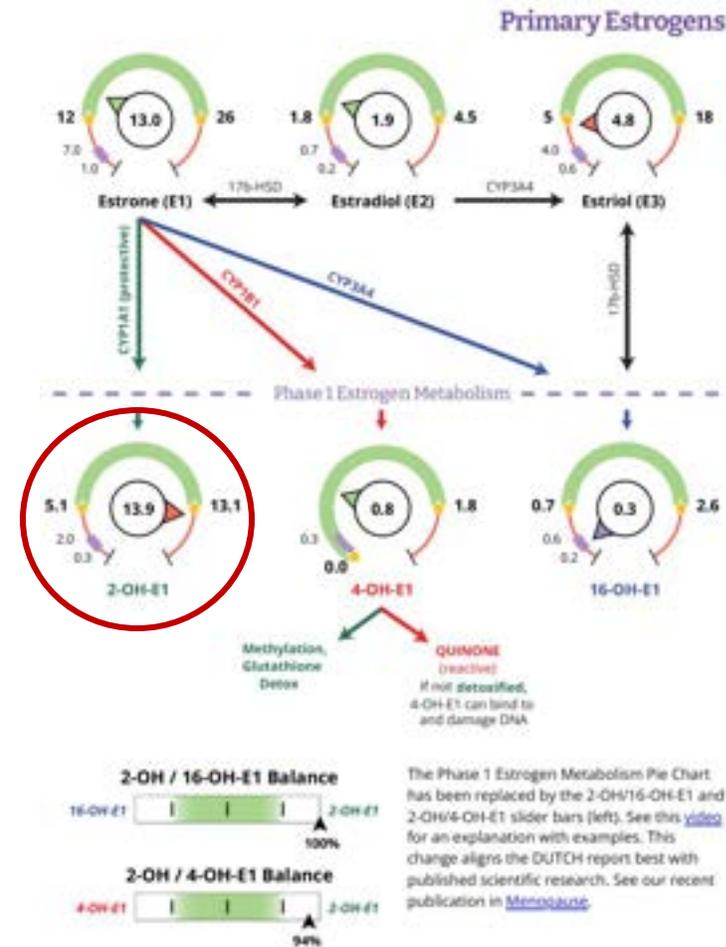
2-OH-E2	Above luteal range	4.59	ng/mg	0 - 3.1	0 - 0.52
4-OH-E2	Within luteal range	0.35	ng/mg	0 - 0.52	0 - 0.12

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Putting it All Together!

DUTCH Advanced Insights: Putting it all together!

- **24-year-old female** diagnosed with Premature Ovarian Insufficiency (POI). Complains of fatigue, low libido, and stressful roommate situation (doesn't like to be home). BMI 21.3.
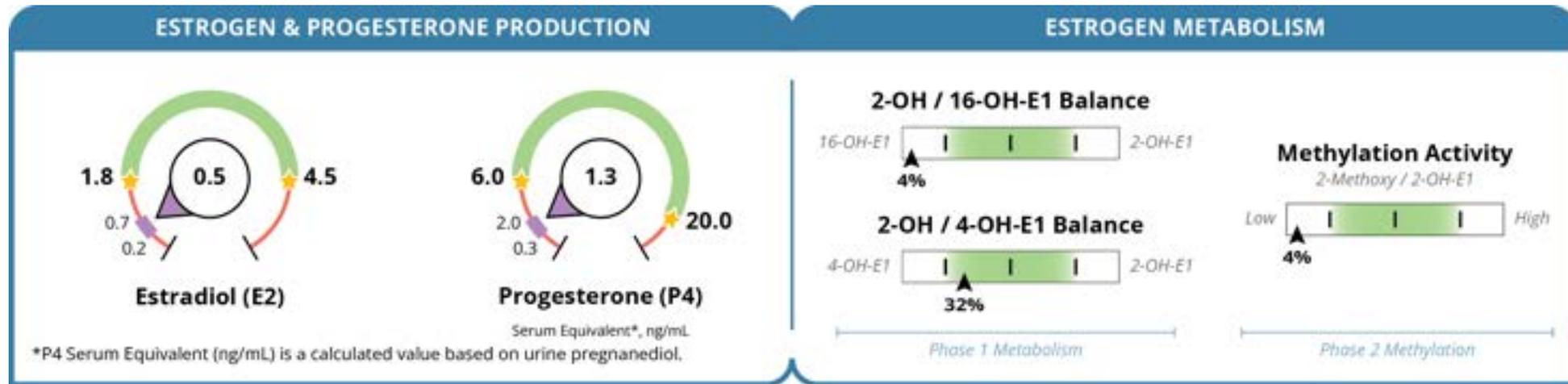
DUTCH Advanced Insights: Putting it all together!

- 24-year-old female diagnosed with POI.

- **What could be contributing to low E2?**

   Clue: Inducers of this enzyme include St. John's wort, pesticides, caffeine, smoking, PAHs, moderate alcohol consumption, and obesity.

Total Estrogen 11.2 ng/mg
(luteal reference range 35-70)

- **24-year-old female** diagnosed with Premature Ovarian Insufficiency (POI). Complains of fatigue, low libido, and stressful roommate situation (doesn't like to be home). BMI 21.3.

Organic Acid Tests (OATs)

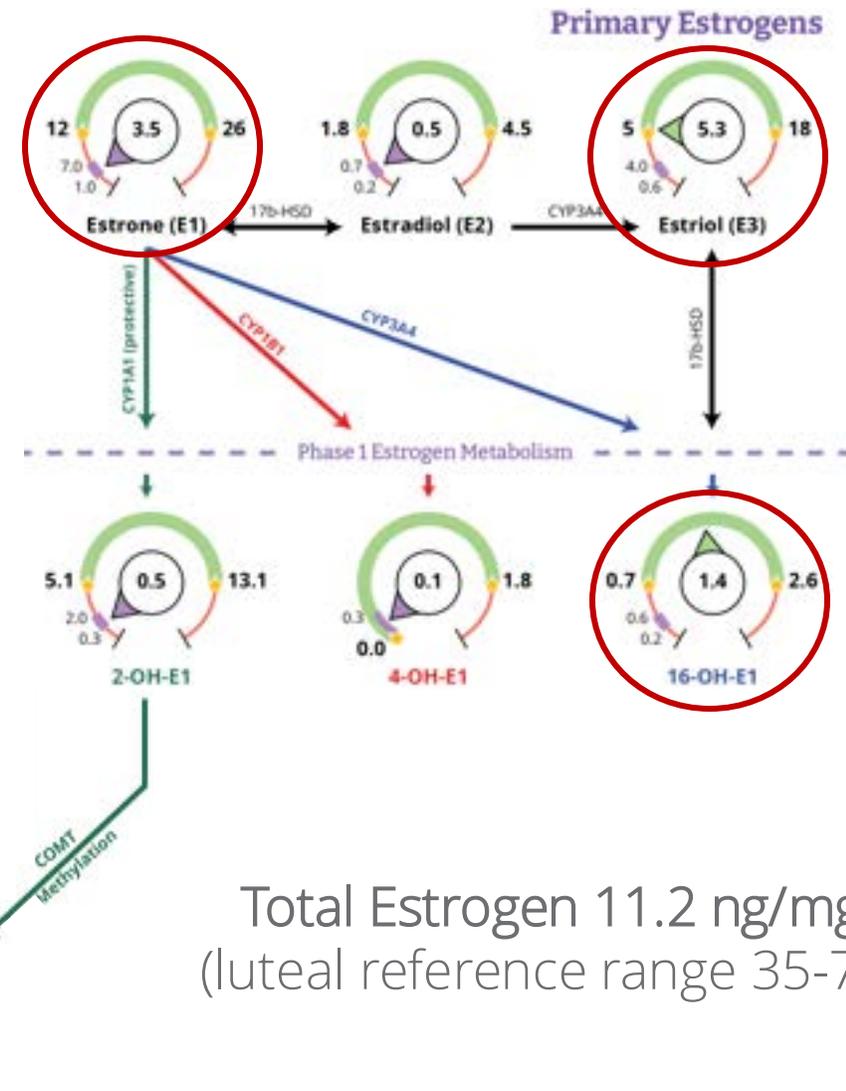| TEST		RESULT	UNITS	NORMAL RANGE
Nutritional Organic Acids (Urine)				
Vitamin B12 Marker - May be deficient if high				
Methylmalonate (MMA)	Above range	3.2	ug/mg	0 - 2.5
Vitamin B6 Markers - May be deficient if high				
Xanthurenate	Within range	0.26	ug/mg	0.12 - 1.2
Kynurenate	Above range	5.4	ug/mg	0.8 - 4.5
Biotin Marker - May be deficient if high				
b-Hydroxyisovalerate	Within range	4.8	ug/mg	0 - 12.5
Glutathione Marker - May be deficient if low or high				
Pyroglutamate	Within range	35.5	ug/mg	28 - 58
Gut Marker - Potential gut putrefaction or dysbiosis if high				
Indican	Within range	58.7	ug/mg	0 - 100
Neuro-Related Markers (Urine)				
Dopamine Metabolite				
Homovanillate (HVA)	Within range	5.0	ug/mg	3 - 11
Norepinephrine/Epinephrine Metabolite				
Vanilmandelate (VMA)	Within range	3.2	ug/mg	2.2 - 5.5
Neuroinflammation Marker				
Quinolinate	High end of range	9.1	ug/mg	0 - 9.6
Additional Markers (Urine)				
Melatonin - Waking				
6-OH-Melatonin-Sulfate	Within range	40.1	ng/mg	10 - 85
Oxidative Stress / DNA Damage				
8-Hydroxy-2-deoxyguanosine (8-OHdG)	Within range	2.1	ng/mg	0 - 5.2

- **What B vitamins might you recommend she supplement to improve her methylation activity?**
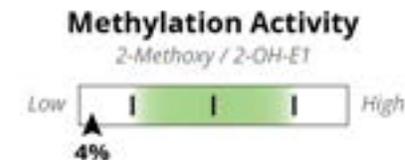
Methylation Activity
2-Methoxy / 2-OH-E1

Low _____ High

4%

DUTCH Advanced Insights: Putting it all together!

- **29-year-old female** diagnosed with PCOS. Complains of irregular cycles, high stress, facial hair, and breast tenderness. BMI 29.3.
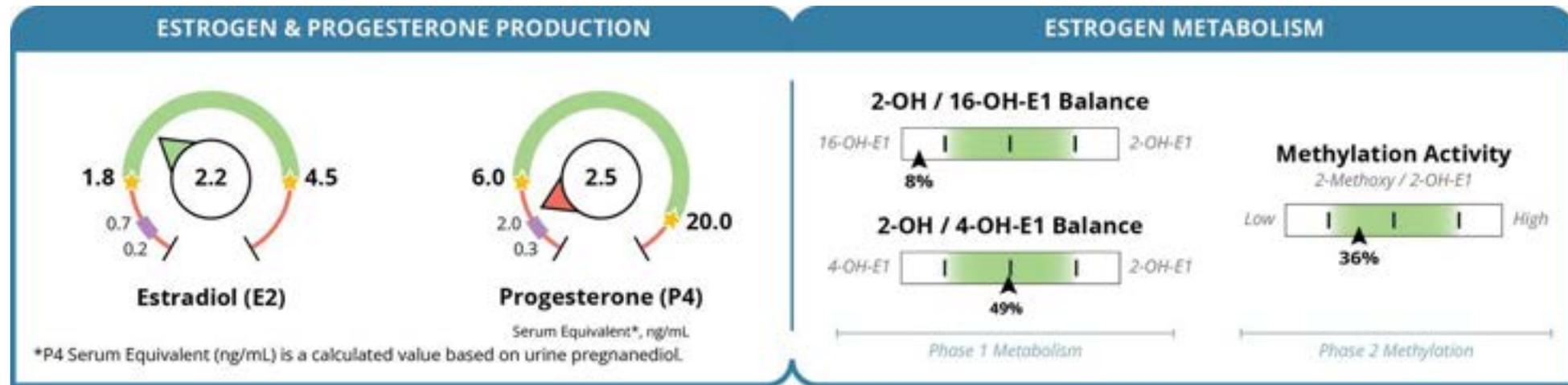
DUTCH Advanced Insights: Putting it all together!

- **29-year-old female** diagnosed with PCOS. Complains of irregular cycles, high stress, facial hair, and breast tenderness. BMI 29.3.

- **How does her high E1 change your treatment plan?**
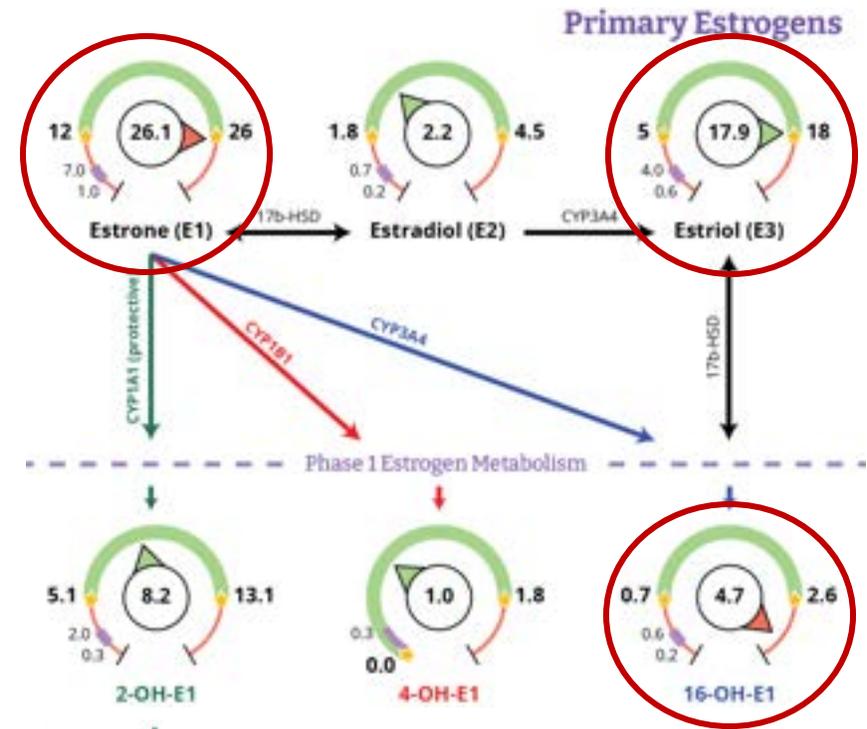

Total Estrogen 64.95 ng/mg
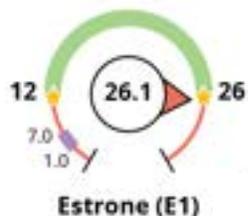(luteal reference range 35-70)

- **29-year-old female** diagnosed with PCOS. Complains of irregular cycles, high stress, facial hair, and breast tenderness. BMI 29.3.

- **Why is her low glutathione more concerning with a low 2/4 balance?**

2-OH / 4-OH-E1 Balance

4-OH-E1 ▮▮▮ 2-OH-E1

17%

- **How might her high indican relate to her high estrogen (E1)?**

12 — 26.1 — 26
7.0
1.0

Estrone (E1)

Organic Acid Tests (OATs)

TEST		RESULT	UNITS	NORMAL RANGE
Nutritional Organic Acids (Urine)				
Vitamin B12 Marker - May be deficient if high				
Methylmalonate (MMA)	Within range	1.3	ug/mg	0 - 2.5
Vitamin B6 Markers - May be deficient if high				
Xanthurenate	Within range	0.37	ug/mg	0.12 - 1.2
Kynurenate	Within range	2.0	ug/mg	0.8 - 4.5
Biotin Marker - May be deficient if high				
b-Hydroxyisovalerate	Within range	8.3	ug/mg	0 - 12.5
Glutathione Marker - May be deficient if low or high				
Pyroglutamate	Above range	67.2	ug/mg	28 - 58
Gut Marker - Potential gut putrefaction or dysbiosis if high				
Indican	Above range	102.3	ug/mg	0 - 100
Neuro-Related Markers (Urine)				
Dopamine Metabolite				
Homovanillate (HVA)	Within range	4.0	ug/mg	3 - 11
Norepinephrine/Epinephrine Metabolite				
Vanilmandelate (VMA)	Within range	3.9	ug/mg	2.2 - 5.5
Neuroinflammation Marker				
Quinolinate	Above range	15.1	ug/mg	0 - 9.6
Additional Markers (Urine)				
Melatonin - Waking				
6-OH-Melatonin-Sulfate	Within range	62.9	ng/mg	10 - 85
Oxidative Stress / DNA Damage				
8-Hydroxy-2-deoxyguanosine (8-OHdG)	Within range	2.1	ng/mg	0 - 5.2

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DUTCH Advanced Insights: Putting it all together!

- **39-year-old female** with suspected endometriosis. Complains of dysmenorrhea, heavy bleeding, and frequent night wakings. BMI 26.6.
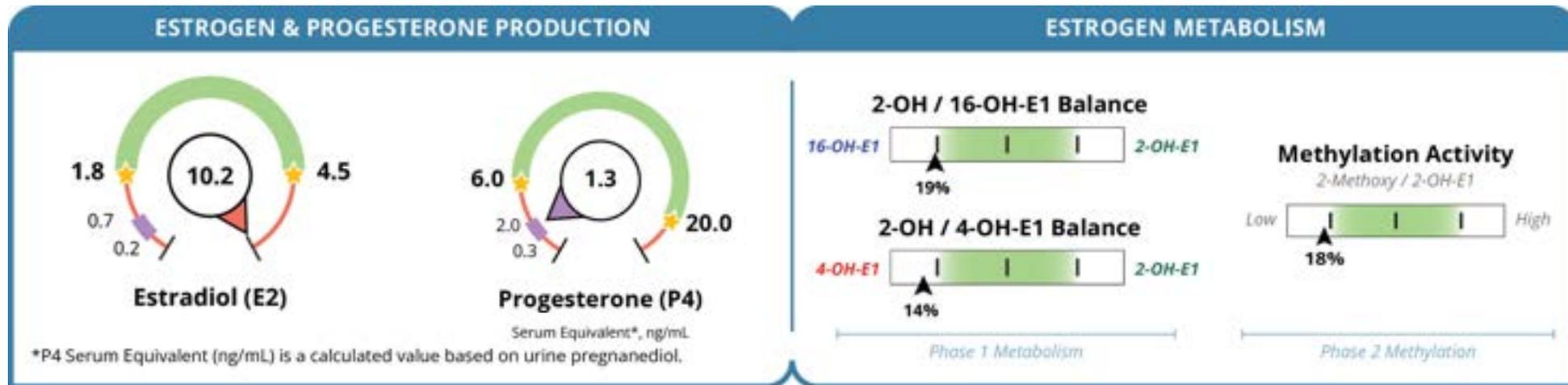
- **39-year-old female** with suspected endometriosis. Complains of dysmenorrhea, heavy bleeding, and frequent night wakings. BMI 26.6.

- **If she is anovulatory (*and her progesterone is always in the PMP range*), is it likely that her progesterone beta metabolism preference is contributing to her night wakings?**

Progesterone (P4)

600 · 116 · 2000
200
60

b-Pregnanediol

5b · 5a

200 · 34 · 740
50
15

a-Pregnanediol

5a-Metabolism (P4)
a-Pregnanediol / b-Pregnanediol

Low (5b) | I   I   I | High (5a)

25%

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DUTCH Advanced Insights: Putting it all together!

- **39-year-old female** with suspected endometriosis.

- Her **4-OH-E2** (*on page 3*) is **above range** at 0.61 ng/mg, however, her 4-OH-E1 is within range. Are you concerned about increased breast cancer risk?

2-OH / 4-OH-E1 Balance

4-OH-E1 | | | | 2-OH-E1

14%

- Would you give DIM in this case?

Methylation Activity

2-Methoxy / 2-OH-E1

Low | | | | High

18%

Primary Estrogens

Estrone (E1) — Estradiol (E2) — Estriol (E3)

Phase 1 Estrogen Metabolism

2-OH-E1 | 4-OH-E1 | 16-OH-E1

2-Methoxy-E1

Total Estrogen 76.15 ng/mg
(luteal reference range 35-70)
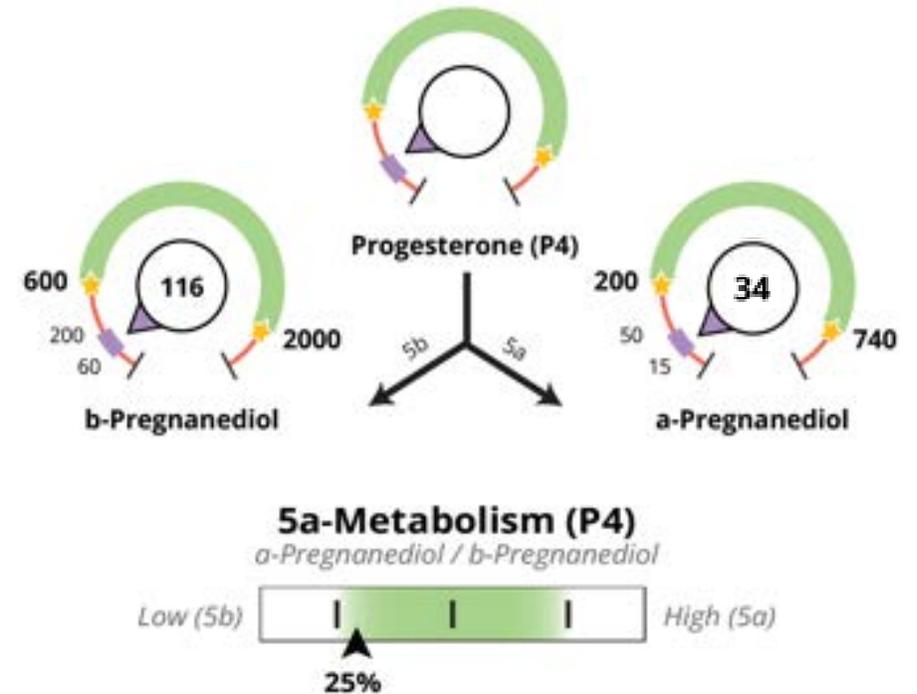
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DUTCH Advanced Insights: Putting it all together!
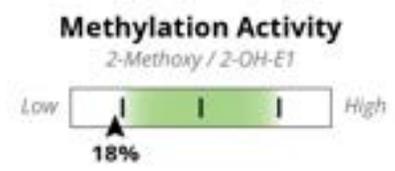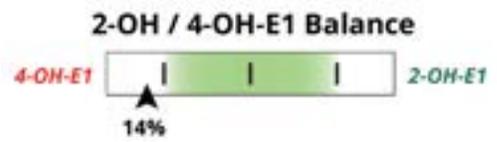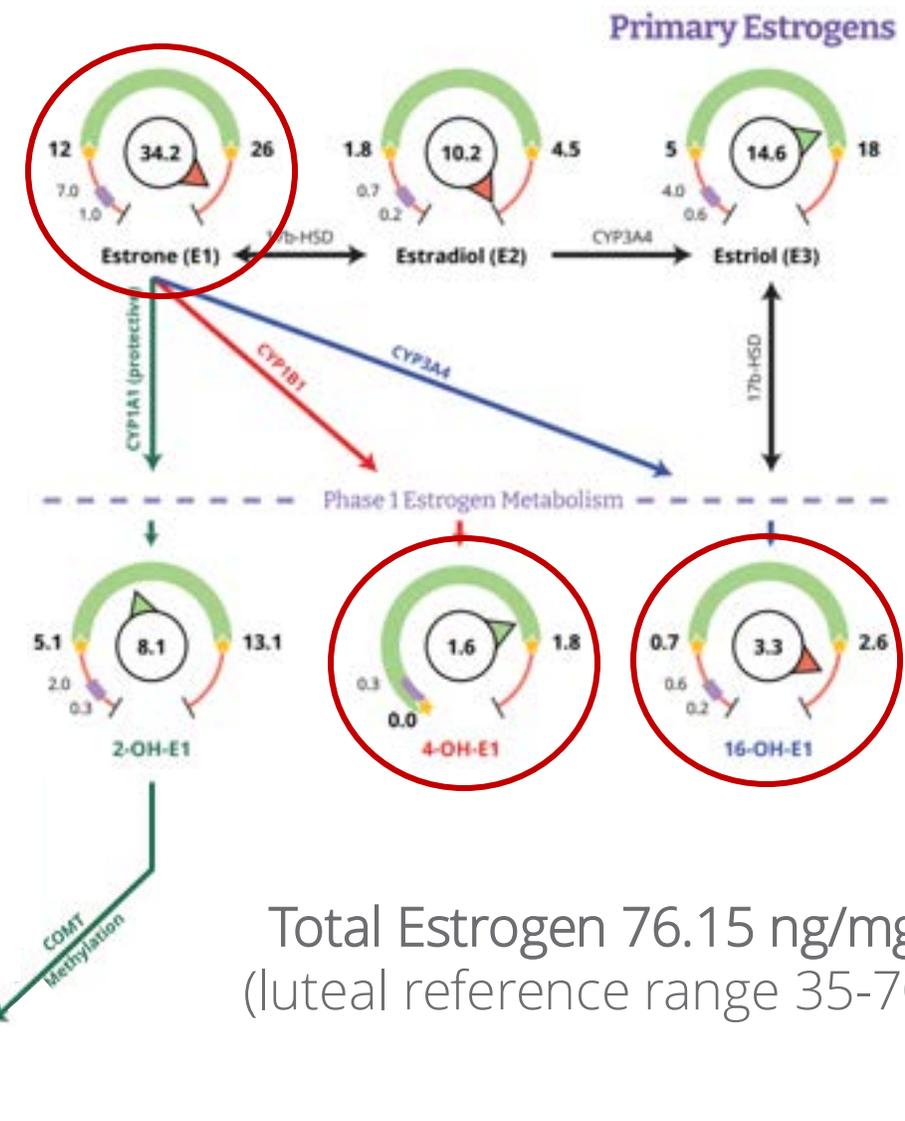
- **39-year-old female** with suspected endometriosis. Complains of dysmenorrhea, heavy bleeding, and frequent night wakings. BMI 26.6.

- B12 may improve her methylation activity.

Methylation Activity

2-Methoxy / 2-OH-E1

Low [ ] High

18%

- **How might increasing her methylation activity improve her symptoms?**

Organic Acid Tests (OATs)

TEST		RESULT	UNITS	NORMAL RANGE
Nutritional Organic Acids (Urine)				
Vitamin B12 Marker - May be deficient if high				
Methylmalonate (MMA)	Above range	2.7	ug/mg	0 - 2.5
Vitamin B6 Markers - May be deficient if high				
Xanthurenate	Within range	0.33	ug/mg	0.12 - 1.2
Kynurenate	Within range	1.3	ug/mg	0.8 - 4.5
Biotin Marker - May be deficient if high				
b-Hydroxyisovalerate	Within range	9.4	ug/mg	0 - 12.5
Glutathione Marker - May be deficient if low or high				
Pyroglutamate	Within range	35.9	ug/mg	28 - 58
Gut Marker - Potential gut putrefaction or dysbiosis if high				
Indican	Within range	44.8	ug/mg	0 - 100
Neuro-Related Markers (Urine)				
Dopamine Metabolite				
Homovanillate (HVA)	Within range	5.5	ug/mg	3 - 11
Norepinephrine/Epinephrine Metabolite				
Vanilmandelate (VMA)	Within range	2.9	ug/mg	2.2 - 5.5
Neuroinflammation Marker				
Quinolinate	Within range	8.7	ug/mg	0 - 9.6
Additional Markers (Urine)				
Melatonin - Waking				
6-OH-Melatonin-Sulfate	Below range	1.5	ng/mg	10 - 85
Oxidative Stress / DNA Damage				
8-Hydroxy-2-deoxyguanosine (8-OHdG)	Within range	0.9	ng/mg	0 - 5.2

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DUTCH Advanced Insights: Putting it all together!

- **55-year-old PMP female** on 15 mg prednisone for the past month. She has not been able to taper below 15 mg without her ulcerative colitis flaring up. Complains of hair loss, hot flashes, irritability, and sleep issues. BMI 28.1.
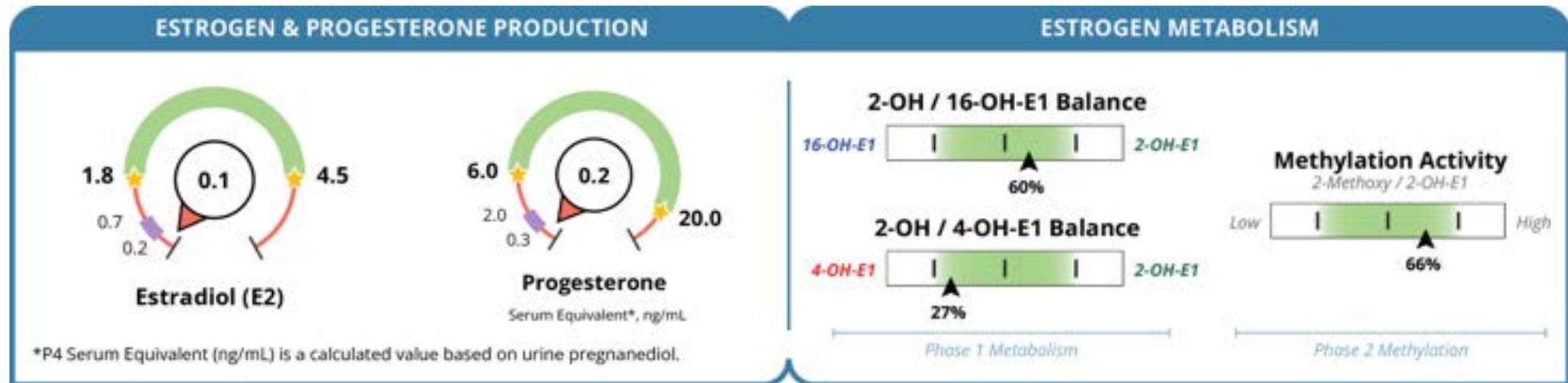
DUTCH Advanced Insights: Putting it all together!

- **55-year-old PMP female** on 15 mg prednisone for the past month. Complains of hair loss, hot flashes, irritability, and sleep issues. BMI 28.1.

- **Would you treat her low-end 2/4 balance given that her estrogen is so low?**

Primary Estrogens

Estrone (E1) — Estradiol (E2) — Estriol (E3)

Phase 1 Estrogen Metabolism

2-OH-E1 — 4-OH-E1 — 16-OH-E1

2-Methoxy-E1

2-OH / 4-OH-E1 Balance

4-OH-E1 — 2-OH-E1

27%

Methylation Activity
2-Methoxy / 2-OH-E1

Low — High

66%

Total Estrogen 1.63 ng/mg
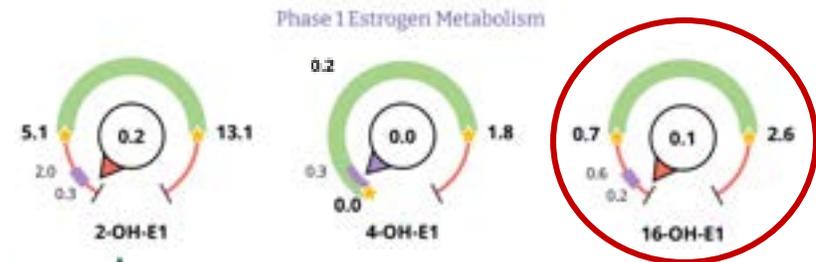(PMP reference range 3.5-15)

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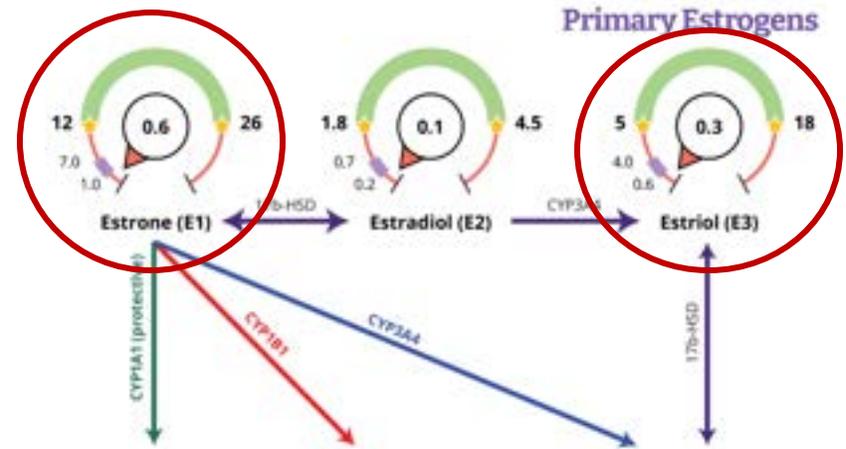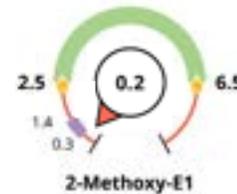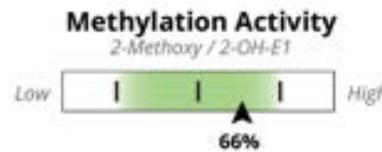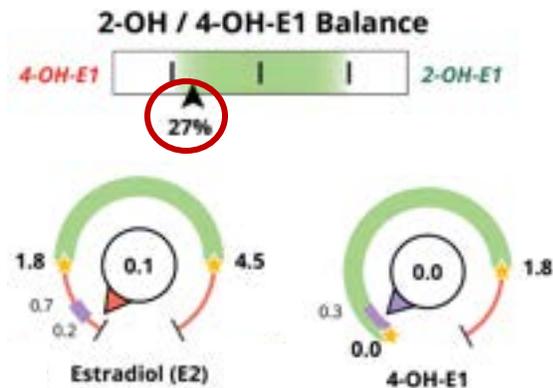# DUTCH Advanced Insights: Putting it all together!

- **55-year-old PMP female** on 15 mg prednisone for the past month. She has not been able to taper below 15 mg without her ulcerative colitis flaring up. Complains of hair loss, hot flashes, irritability, and sleep issues. BMI 28.1

True or False?

4-OH metabolites are likely causing DNA damage that is resulting in high 8-OHdG.
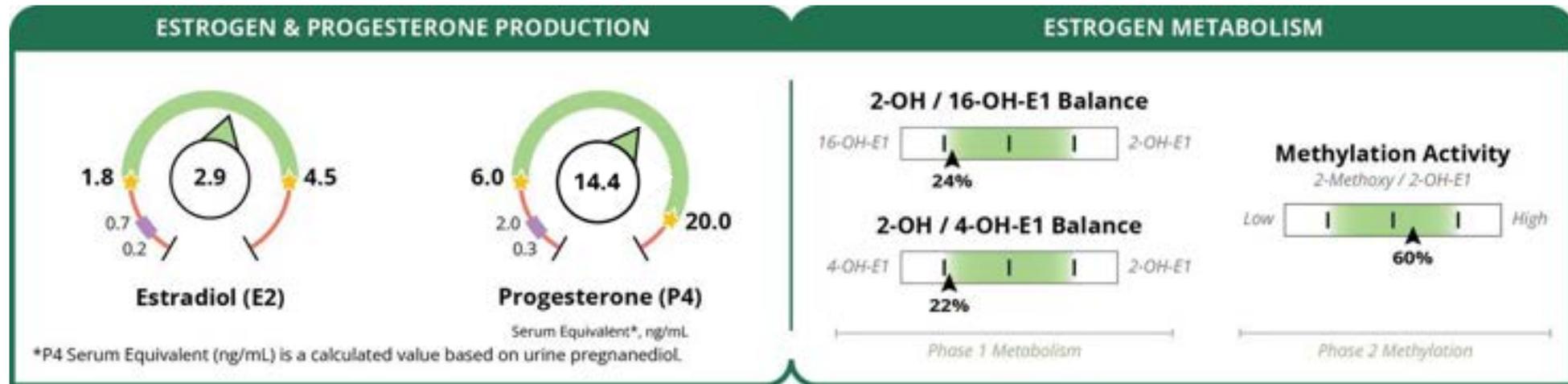

2-OH / 4-OH-E1 Balance

4-OH-E1 ———— 2-OH-E1

27%

1.8   0.1   4.5
0.7
0.2
Estradiol (E2)

0.0   1.8
0.3
0.0
4-OH-E1

Organic Acid Tests (OATs)

TEST		RESULT	UNITS	NORMAL RANGE
Nutritional Organic Acids (Urine)				
Vitamin B12 Marker - May be deficient if high				
Methylmalonate (MMA)	Within range	1.6	ug/mg	0 - 2.5
Vitamin B6 Markers - May be deficient if high				
Xanthurenate	Within range	0.60	ug/mg	0.12 - 1.2
Kynurenate	Within range	1.5	ug/mg	0.8 - 4.5
Biotin Marker - May be deficient if high				
b-Hydroxyisovalerate	Above range	16.5	ug/mg	0 - 12.5
Glutathione Marker - May be deficient if low or high				
Pyroglutamate	Within range	50.3	ug/mg	28 - 58
Gut Marker - Potential gut putrefaction or dysbiosis if high				
Indican	Within range	58.0	ug/mg	0 - 100
Neuro-Related Markers (Urine)				
Dopamine Metabolite				
Homovanillate (HVA)	Within range	5.9	ug/mg	3 - 11
Norepinephrine/Epinephrine Metabolite				
Vanilmandelate (VMA)	Within range	4.7	ug/mg	2.2 - 5.5
Neuroinflammation Marker				
Quinolinate	Within range	3.0	ug/mg	0 - 9.6
Additional Markers (Urine)				
Melatonin - Waking				
6-OH-Melatonin-Sulfate	Below range	9.3	ng/mg	10 - 85
Oxidative Stress / DNA Damage				
8-Hydroxy-2-deoxyguanosine (8-OHdG)	Above range	6.5	ng/mg	0 - 5.2

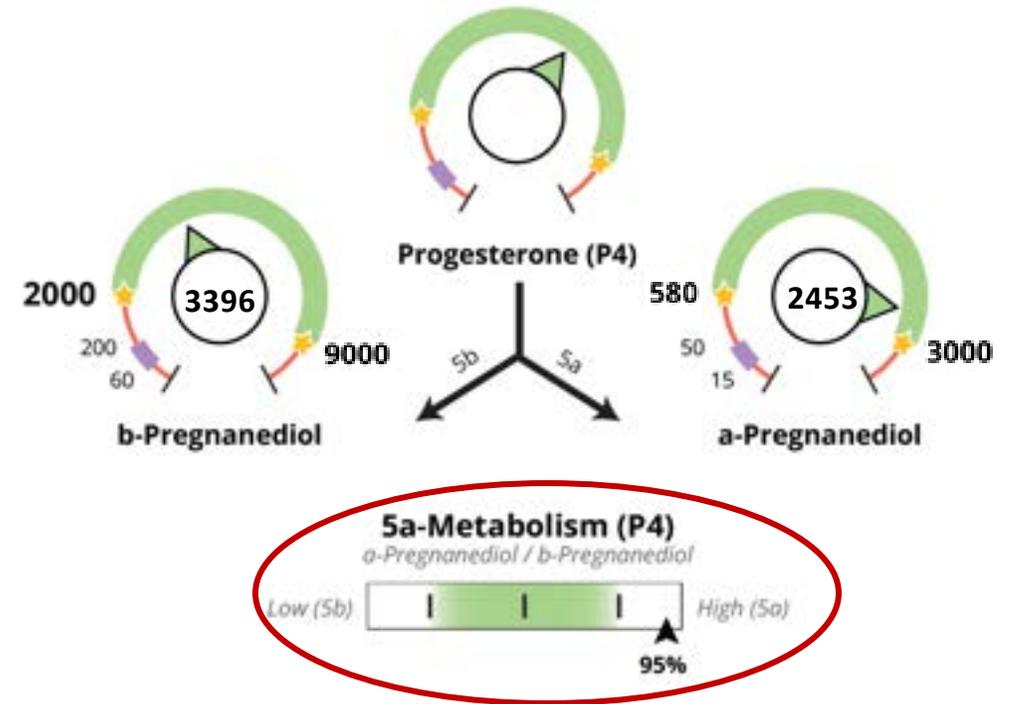8-OHdG is elevated signifying oxidative stress is causing DNA damage.

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DUTCH Advanced Insights: Putting it all together!

- **58-year-old PMP female** on 100 mg OMP, 0.075 E2 patch, 5 mg transdermal T cream, and 1.0 mg vaginal E3. Complains of acne, occasional bothersome hot flashes, and weight loss resistance. BMI 30.1.

ESTROGEN & PROGESTERONE PRODUCTION

Estradiol (E2): 1.8 — 2.9 — 4.5; 0.7 / 0.2

Progesterone (P4): 6.0 — 14.4 — 20.0; 2.0 / 0.3

Serum Equivalent*, ng/mL

*P4 Serum Equivalent (ng/mL) is a calculated value based on urine pregnanediol.

ESTROGEN METABOLISM

2-OH / 16-OH-E1 Balance — 16-OH-E1 ... 2-OH-E1 — 24%

2-OH / 4-OH-E1 Balance — 4-OH-E1 ... 2-OH-E1 — 22%

Methylation Activity — 2-Methoxy / 2-OH-E1 — Low ... High — 60%

Phase 1 Metabolism | Phase 2 Methylation

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- **58-year-old PMP female** on 100 mg OMP, 0.075 E2 patch, 5 mg transdermal T cream, and 1.0 mg vaginal E3. Complains of acne, occasional bothersome hot flashes, and weight loss resistance. BMI 30.1.

- **Since she makes so much a-pregnanediol, could you safely lower her OMP dose?**
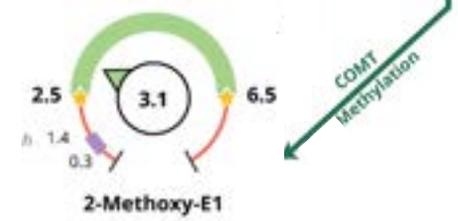
- **58-year-old PMP female** on 100 mg OMP, 0.075 E2 patch, 5 mg transdermal T cream, and 1.0 mg vaginal E3. Complains of acne, occasional bothersome hot flashes, and weight loss resistance. BMI 30.1.

- **Is her 1.0 mg vaginal E3 significantly increasing the estrogenic activity in her body?**

Primary Estrogens

Total Estrogen 72.75 ng/mg
(luteal reference range 35-70)

Total Estrogen is less clinically relevant to due high (weak) E3 affecting the total!

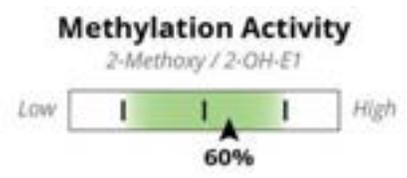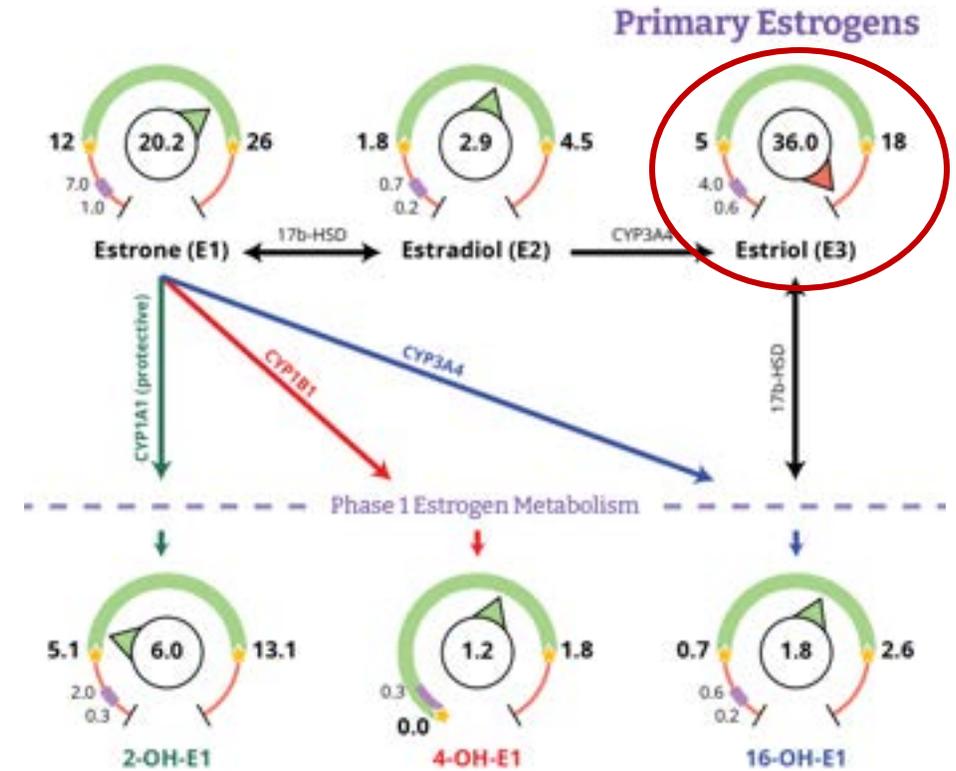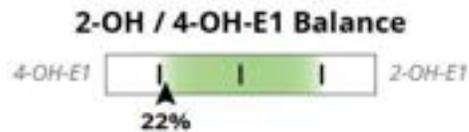dutch®

DUTCH Advanced Insights: Putting it all together!

- **58-year-old PMP female** on 100 mg OMP, 0.075 E2 patch, 5 mg transdermal T cream, and 1.0 mg vaginal E3. Complains of acne, occasional bothersome hot flashes, and weight loss resistance. BMI 30.1.

- High 8-OHdG and low glutathione are more concerning due to her poor 2/4 balance

2-OH / 4-OH-E1 Balance

4-OH-E1 [   ] 2-OH-E1

22%

- **Looking at her OATs, what might be affecting her inability to lose weight?**

Organic Acid Tests (OATs)

TEST		RESULT	UNITS	NORMAL RANGE
Nutritional Organic Acids (Urine)				
Vitamin B12 Marker - May be deficient if high				
Methylmalonate (MMA)	Within range	1.4	ug/mg	0 - 2.5
Vitamin B6 Markers - May be deficient if high				
Xanthurenate	Within range	0.54	ug/mg	0.12 - 1.2
Kynurenate	Above range	5.2	ug/mg	0.8 - 4.5
Biotin Marker - May be deficient if high				
b-Hydroxyisovalerate	Within range	4.8	ug/mg	0 - 12.5
Glutathione Marker - May be deficient if low or high				
Pyroglutamate	High end of range	57.7	ug/mg	28 - 58
Gut Marker - Potential gut putrefaction or dysbiosis if high				
Indican	Within range	65.6	ug/mg	0 - 100
Neuro-Related Markers (Urine)				
Dopamine Metabolite				
Homovanillate (HVA)	Within range	5.0	ug/mg	3 - 11
Norepinephrine/Epinephrine Metabolite				
Vanilmandelate (VMA)	Within range	5.1	ug/mg	2.2 - 5.5
Neuroinflammation Marker				
Quinolinate	Above range	9.9	ug/mg	0 - 9.6
Additional Markers (Urine)				
Melatonin - Waking				
6-OH-Melatonin-Sulfate	Within range	43.5	ng/mg	10 - 85
Oxidative Stress / DNA Damage				
8-Hydroxy-2-deoxyguanosine (8-OHdG)	High end of range	4.9	ng/mg	0 - 5.2

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Thank You!

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