DNA blue

Well Woman Genetic Report

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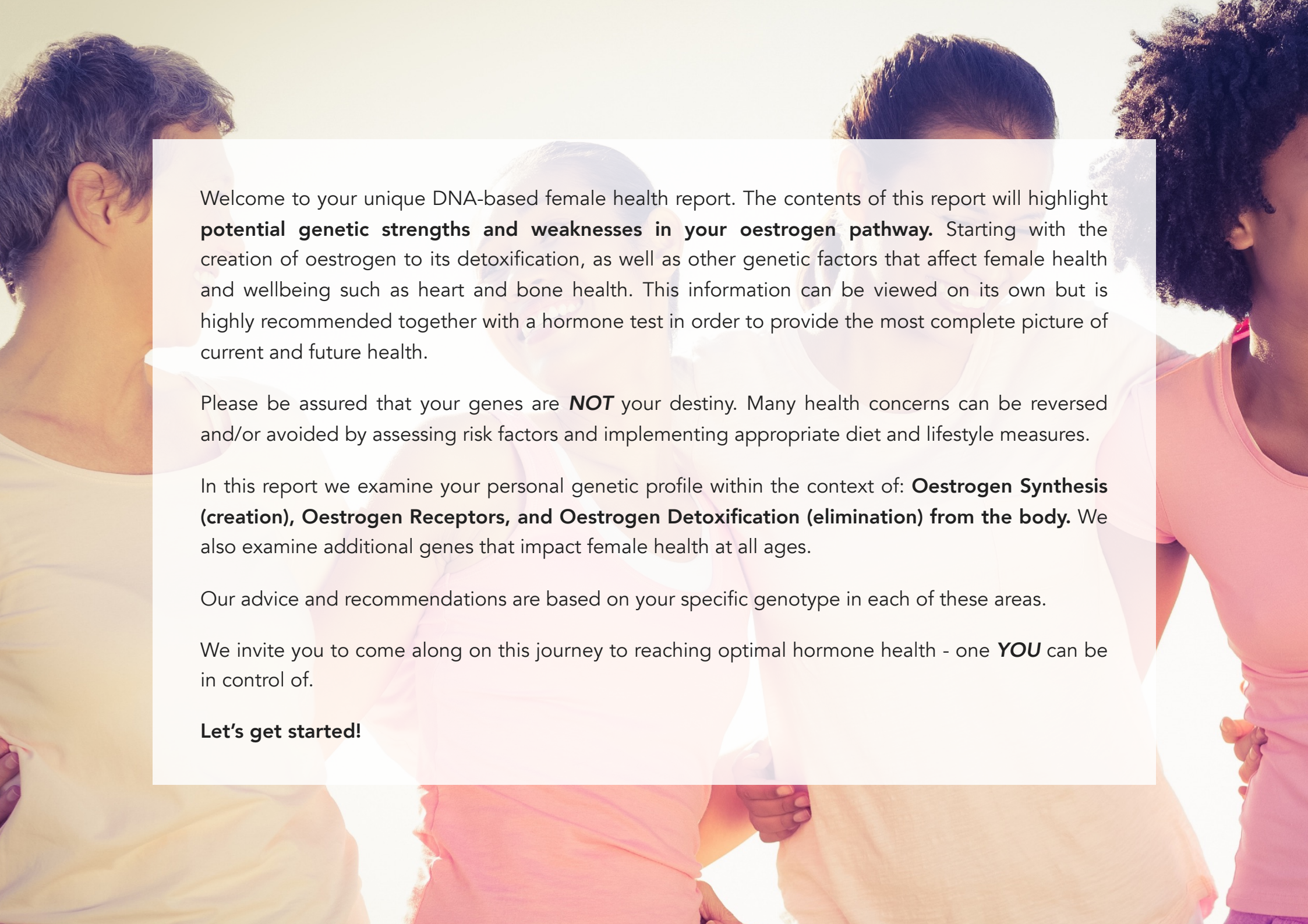


Welcome to your unique DNA-based female health report. The contents of this report will highlight **potential genetic strengths and weaknesses in your oestrogen pathway.** Starting with the creation of oestrogen to its detoxification, as well as other genetic factors that affect female health and wellbeing such as heart and bone health. This information can be viewed on its own but is highly recommended together with a hormone test in order to provide the most complete picture of current and future health.

Please be assured that your genes are ***NOT*** your destiny. Many health concerns can be reversed and/or avoided by assessing risk factors and implementing appropriate diet and lifestyle measures.

In this report we examine your personal genetic profile within the context of: **Oestrogen Synthesis (creation), Oestrogen Receptors, and Oestrogen Detoxification (elimination) from the body.** We also examine additional genes that impact female health at all ages.

Our advice and recommendations are based on your specific genotype in each of these areas.

We invite you to come along on this journey to reaching optimal hormone health - one ***YOU*** can be in control of.

Let's get started!

Understanding your report

What is DNA?

DNA is your body's instruction manual, controlling every single function from when you were only made up of a few cells, until now. It looks like a twisted ladder, made up of two halves.

Each "rung" of the ladder contains two "letters" of DNA code called ***nucleotides*** which bond together in pairs: **A (adenine)** and **T (thymine)** bond together**,** as do **C (cytosine)** and **G (guanine).**

Genes are portions of the ladder containing combinations of the nucleotide code which are "read" as instructions to perform a specific function.

Results

Your results are shown by a combination of the letters **ATCG** along with a traffic light system to indicate if your result is good, neutral or potentially detrimental.

Identical letters (e.g. GG or AA) mean you are either what is called the **wild type** with no genetic variants (SNPs) OR you have **both** genetic variants (from both parents). A combination of letters (e.g. AG) means you have one inherited genetic variant.

- A green result indicates either no variants or a positive variant impact
- An amber result usually indicates one genetic variant present and / or a mildly negative impact
- A red result indicates a negative impact either due to both variants being present or a wild type result that is not as beneficial as the variant

SNPs

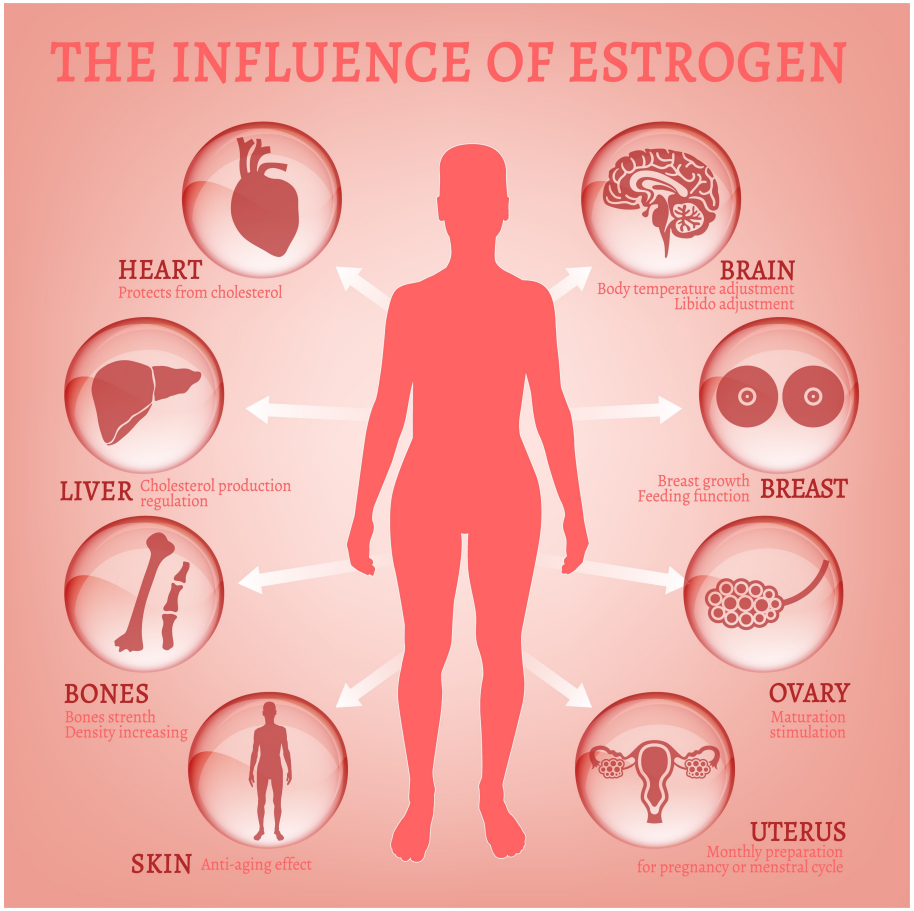
Over time, due to environmental and lifestyle factors, minor changes called **single nucleotide polymorphisms (SNPs)** occur within the DNA code and are passed down from parent to child, from generation to generation. Remember the nucleotides? Well, a C might be replaced by a T, changing the instructions.

Some SNPs are positive, making us stronger and more resilient (like being able to digest milk after infancy), some are negative (like being likely to store more fat as a result of past famine or food shortage) and some make no difference at all. SNPs can be passed down from just one parent, or from both, enhancing the effect. SNPs are generally what we are looking for when we test your DNA.

Example of your genetic results table

GENE	RESULT	IMPACT & ADVICE
GENE CODE - Gene Function Explanation of the role the gene plays and what effect genetic variants might have, symptoms, other contributing factors etc.	**GG**	An explanation of your result, how you might be affected along with specific diet and lifestyle advice
GENE CODE - Gene Function Explanation of the role the gene plays and what effect genetic variants might have, symptoms, other contributing factors etc.	**AG**	An explanation of your result, how you might be affected along with specific diet and lifestyle advice
GENE CODE - Gene Function Explanation of the role the gene plays and what effect genetic variants might have, symptoms, other contributing factors etc.	**TT**	An explanation of your result, how you might be affected along with specific diet and lifestyle advice

Oestrogen



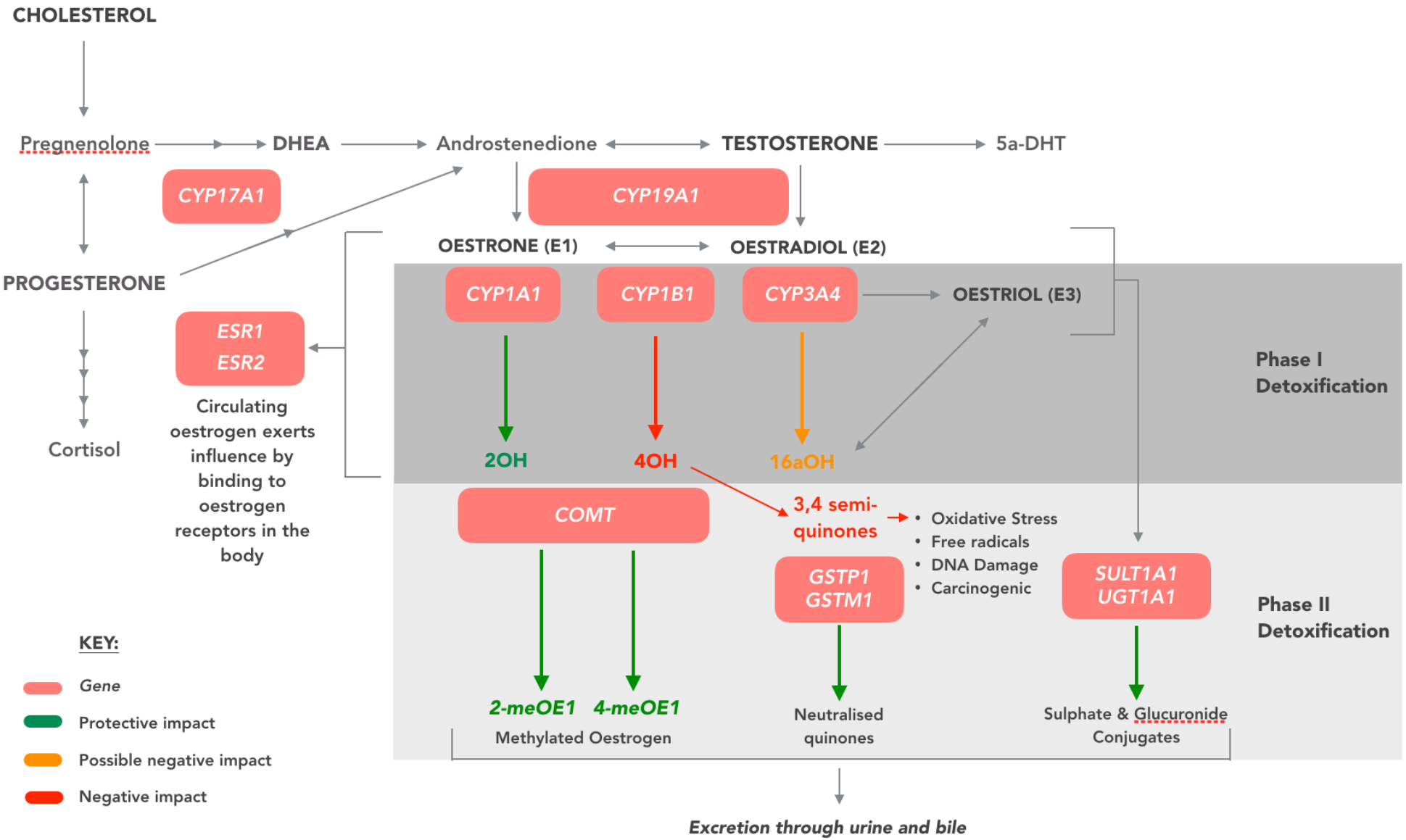
Oestrogen is one of two major female steroidal sex hormones, the other being ***progesterone***. The main source of oestrogen in females prior to menopause is the **ovaries**, after which the main source becomes the **adrenal glands** and **fat tissue**. Oestrogen is also produced by the placenta during pregnancy. Oestrogen levels fluctuate throughout life, naturally increasing during puberty and pregnancy, and falling after menopause. During the menstrual cycle, oestrogen levels peak during ovulation dropping off if pregnancy doesn't occur.

The main roles of oestrogen in the body are to **increase the growth and production of cells**, the **development and regulation** of the **female reproductive system** and **secondary sex characteristics** - breasts, pubic hair etc. Oestrogen is also involved in maintaining **bone density**, plays a role in **blood clotting** and affects skin, hair, mucous membranes and the pelvic muscles.

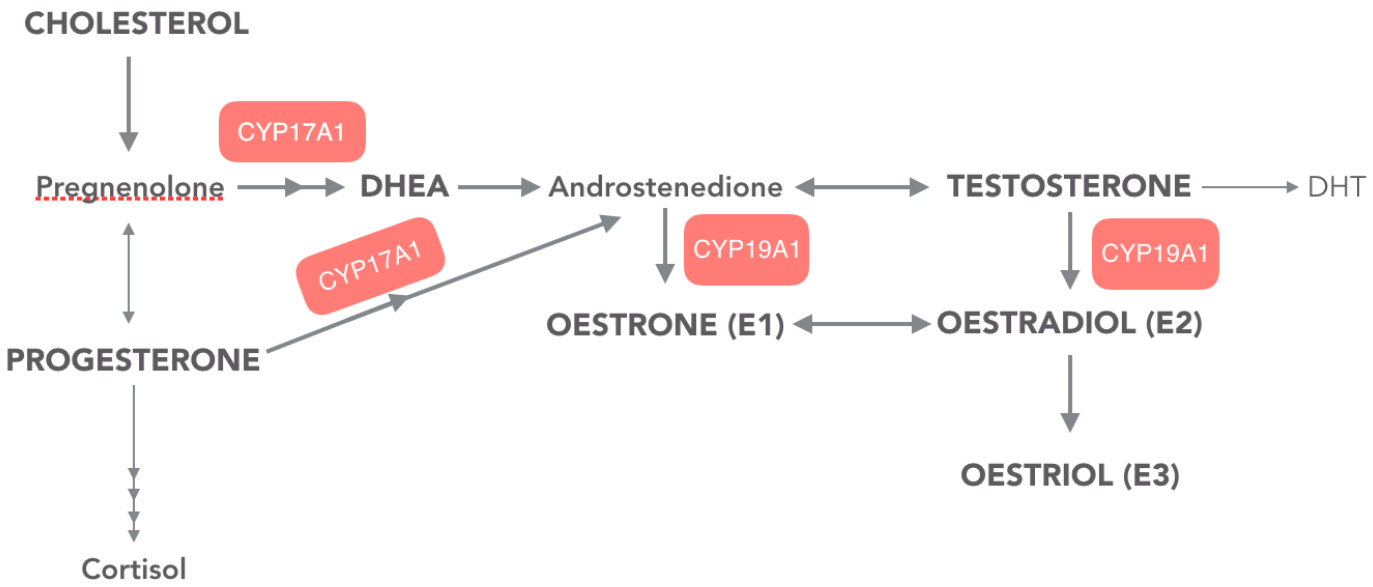
The body produces 3 different types of oestrogen:

- **E1 - Oestrone:** medium strength, predominant after menopause (adrenal glands)
- **E2 - Oestradiol:** strong, predominant during childbearing age (ovaries & adrenal glands)
- **E3 - Oestriol:** weak, predominant during pregnancy (placenta & liver)

Oestrogen Metabolism



Oestrogen Synthesis (production)



E1 and **E2** are produced from the androgens: **androstenedione** and **testosterone** respectively. Although androgens are typically considered male hormones, they play an important part in female physiology since all oestrogens are made from androgens. **E3** is produced from E2 according to the body's needs.

The ***CYP17A1*** enzyme initiates the first step in oestrogen production by converting **pregnenolone** and **progesterone** into oestrogen precursors, including **DHEA**. The ***CYP19A1*** enzyme is responsible for controlling the rate at which androstenedione and testosterone are converted to oestrogen.

*The enzymes **CYP17A1** and **CYP19A1** play a role in driving either low or high oestrogen levels. This is important clinical information since these enzymes are influenced by genetics, diet and lifestyle. Check **page 9** below to see whether your oestrogen production might be too fast or too slow and what you can do about it.*

GENE	RESULT	IMPACT & ADVICE
CYP17A1 - Oestrogen Precursors CYP17A1 belongs to the cytochrome P450 (CYP450) superfamily of enzymes responsible for the production, activation and detoxification of a large number of substances in the body including pharmaceutical drugs, hormones (e.g. oestrogen and testosterone), corticoids and lipids. CYP17A1 is found in many tissues, including the adrenal glands, gonads, ovaries, heart, kidneys and fat tissue. In the oestrogen pathway, CYP17A1 is responsible for the conversion of pregnenolone and progesterone into oestrogen precursors including DHEA. Variants in this gene have been associated with increased enzyme activity leading to higher production of oestrogen precursors and also with post-menopausal depression and anxiety.	**AA**	The A result is associated with normal (not increased) CYP17A1 activity leading to normal production of oestrogen precursors (androgens). CYP17A1 activity is increased by chronic stress, alcohol and excess adipose (fat) tissue regardless of genotype. Ensure regular physical activity, drink alcohol in moderation and practise stress management techniques such as meditation and/ or yoga to maintain normal CYP17A1 activity.
CYP19A1 - Conversion of Oestrogen Precursors to Oestrogen CYP19A1 is another member of the CYP450 superfamily of enzymes mainly found in the gonads, brain, adipose (fat) tissue, placenta, blood vessels, skin and bones. It is also found in endometrial tissue and uterine fibroids. This enzyme regulates the final step in the production of oestrogen, converting androgens to oestrogen. Variants in the CYP19A1 gene are linked to both increased and decreased enzyme activity and may influence the circulating oestrogen:testosterone ratio.	**AG**	The A result is not associated with lower natural oestrogen levels. This may be considered negative since high oestrogen can be harmful over time and can cause unpleasant symptoms such as PMS, heavy menstrual bleeding, weight gain, mood disorders, worsening of menopausal symptoms and is linked to certain cancers. CYP19A1 activity is increased by diet and lifestyle factors such as excess body fat, high insulin levels, inflammation and stress. Maintaining a healthy weight, balancing blood sugar, reducing inflammation and stress will help maintain hormonal balance. DIM (a substance generated from eating cruciferous vegetables such as broccoli and cauliflower), green tea and zinc have been shown to naturally reduce CYP19A1 activity.

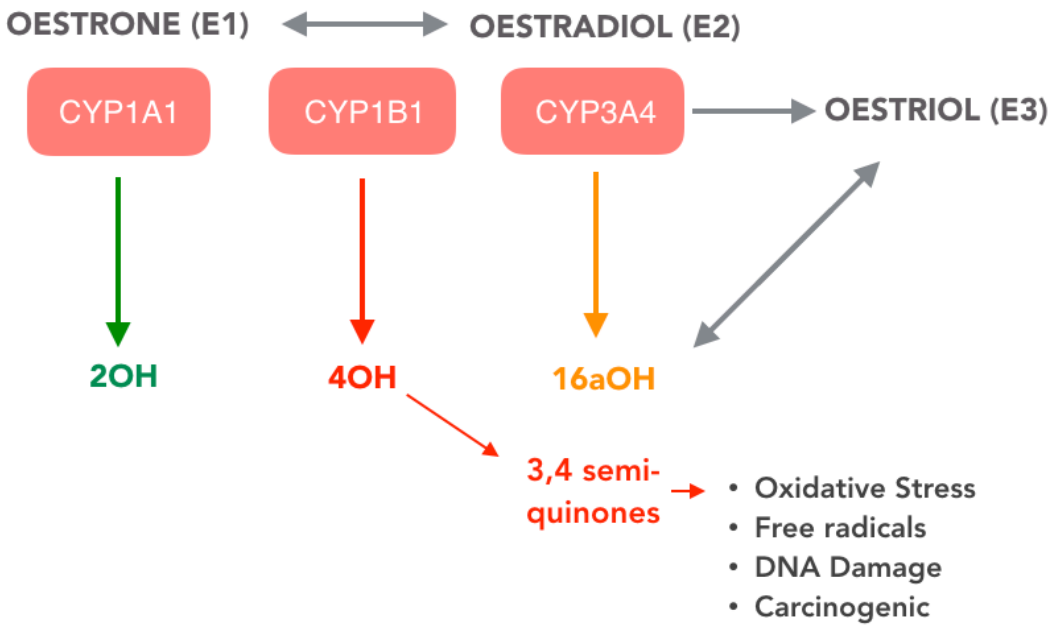
Oestrogen:
Phase I Detoxification

Circulating oestrogen then passes through one of three phase I detoxification pathways:

- ***CYP1A1:*** produces **2OH oestrogen** which is 'weak' in action and thought to be neutral or even beneficial in the body. This is the most favourable pathway in terms of oestrogen metabolism.

- ***CYP1B1:*** produces **4OH oestrogen,** generating harmful free radicals in the process. 4OH oestrogen has stronger oestrogenic properties than 2OH oestrogen and has been associated with undesirable oestrogen-linked conditions and DNA damage. This is the least favourable pathway of oestrogen metabolism.

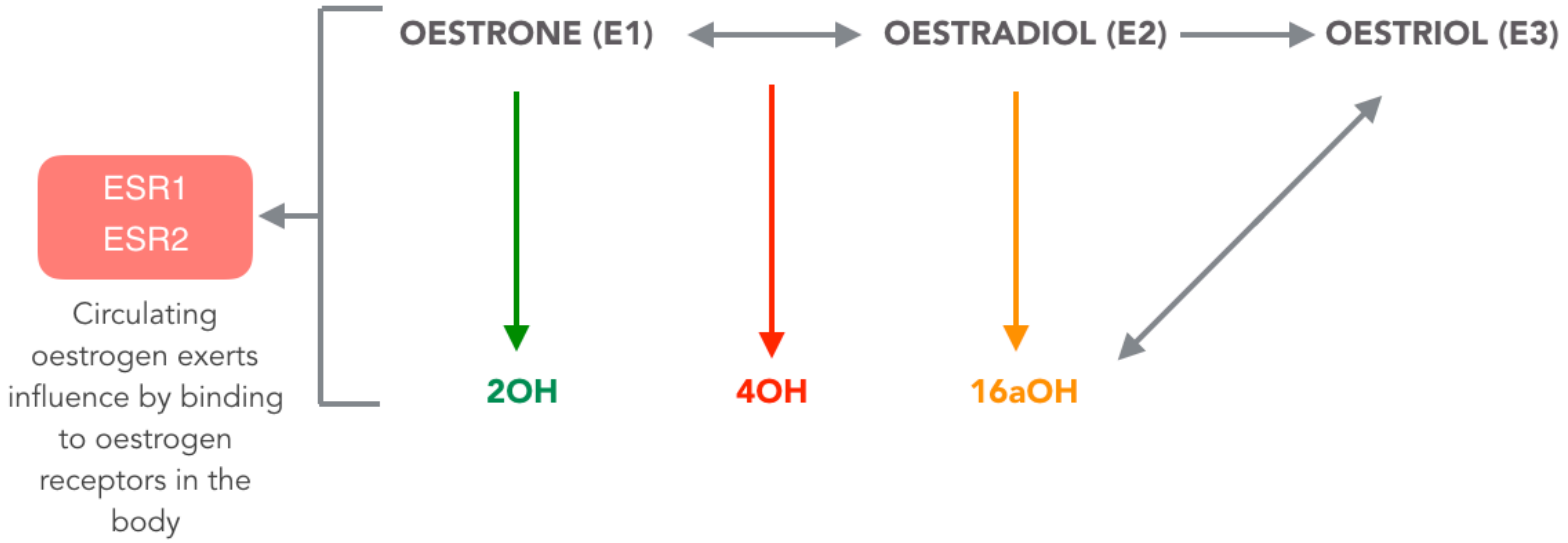
- ***CYP3A4:*** produces **16OH oestrogen**, thought to be stronger than 2OH and potentially harmful, although further research needs to be done. As a result, this is though to be a less favourable pathway.



*Knowing which **phase I pathway/s** your body favours is important since it indicates the forms of oestrogen likely to be dominant in your circulation. Check **page 11** to see which pathway/s your body favours and which diet & lifestyle measures you should implement or avoid in order to maintain a healthy balance.*

GENE	RESULT	IMPACT & ADVICE
CYP1B1 - Production of 4OH Oestrogen CYP1B1 is another primary phase I detoxification gene (and member of the CYP450 superfamily) involved in oestrogen metabolism, particularly the production of 4OH oestrogen, a potent form of oestrogen that can be harmful in the body. 4OH oestrogen binds strongly to oestrogen receptors, and is therefore more potently and longer acting. Variants in this gene are associated with increased activity which creates the harmful free radical quinones, and increased circulating 4OH oestrogen. CYP1B1 activity is further increased by high oestrogen levels.	**CG**	The CG genotype is linked to moderately increased CYP1B1 activity and production of 4OH oestrogen. This is unfavourable since 4OH is highly oestrogenic and increased CYP1B1 activity has also been shown to produce harmful free radicals which can damage DNA. Diet and lifestyle factors such as smoking, stress and eating charred foods increase CYP1B1 activity further and should be avoided as much as possible. Support phase II detoxification pathways (see pages 14-17 below) and increase antioxidants to manage free radical damage. Grapefruit has been shown to powerfully reduce CYP1B1 activity. Consult your doctor if you are on medication since grapefruit is known to interact strongly with certain medications.
CYP3A4 - Production of 16aOH Oestrogen CYP3A4 is a phase I detoxification gene (and member of the CYP450 superfamily) involved in oestrogen metabolism, particularly the production of 16aOH oestrogen, which is thought to be potentially harmful in the body. A large number of medications are metabolised through the CYP3A4 pathway such as codeine, acetaminophen (paracetamol), diazepam, the oral contraceptive pill (OCP) and statins. CYP3A4 also converts E2 to E3. Variants in this gene are associated with increased activity, undesirable for oestrogen metabolism, and affecting drug metabolism.	**TT**	The T result is associated with normal (not increased) CYP3A4 activity. This is positive since 16aOH oestrogen has been linked to oestrogen excess conditions. CYP3A4 activity can increase due to diet and lifestyle factors such as obesity, excess alcohol consumption, stress, certain medications and toxic chemical exposure. Regular physical activity, moderate alcohol consumption and increased antioxidant intake are beneficial. Grapefruit is a potent inhibitor of this pathway. Consult your doctor if you are on medication, however, since you may be affected by consuming grapefruit.

Oestrogen Receptors



Once produced, oestrogen moves through the blood and exerts its influence in the body by binding to oestrogen receptors (ERs). ERs are important since they are also known to bind to DNA and control gene expression.

There are two types of oestrogen receptors encoded by two separate genes:

- **ER alpha (ESR1):** found in highest concentration in the endometrium, ovaries and hypothalamus (in the brain). ESR1 increases the action of the attached oestrogen
- **ER beta (ESR2):** found in highest concentration in the ovaries, kidneys, brain, bone, heart, lungs, intestinal mucosa and endothelial cells. ESR2 weakens the action of the attached oestrogen

GENE	RESULT	IMPACT & ADVICE
ESR1 - Oestrogen Receptor 1 (alpha) The ESR1 gene regulates oestrogen receptor alpha activity which is involved in hormone binding and activation, and also regulates gene transcription. ESR1 is thought to enhance the effect of the oestrogen (natural or synthetic) that attaches to it. This is necessary for oestrogen to perform its functions in the body but can be negative if high amounts of very strong forms of oestrogen (e.g. E2 and 4OH) are dominant in circulation. Variants in ESR1 are associated with enhanced receptor activity. Here we look at two variants (Pvull and Xball) known to affect ESR1 activity.	**CC**	The CC genotype is associated with increased ESR1 activity and likelihood of higher oestrogen activity in the body where oestrogen receptors are present. It is particularly important that you maintain balanced oestrogen levels and encourage CYP1A1 activity (over CYP1B1 and CYP3A4) to ensure that 'healthy' 2OH is dominant in circulation over 'stronger' 4OH and 16aOH. Optimising phase II elimination of oestrogen will help to support healthy oestrogen levels (see pages 14-17). Consuming cruciferous vegetables has been shown to naturally reduce ER activity.
	GG	The GG genotype is associated with increased ESR1 activity. This genotype increases risk of oestrogen-linked conditions (especially endometriosis), particularly if 4OH and 16OH oestrogen are dominant in circulation. Care should be taken to reduce circulating oestrogen by encouraging CYP1A1 activity (or reducing CYP1B1 and CYP3A4) to ensure that "weaker" 2OH oestrogen is dominant in circulation (see advice on pages 10 & 11), and improving phase II detoxification pathways (see advice on pages 14 - 17). Consuming cruciferous vegetables has been shown to naturally reduce ER activity.
ESR2 - Oestrogen Receptor 2 (beta) The ESR2 gene regulates oestrogen receptor beta activity which is involved in hormone binding and activation, and also regulating gene transcription. ESR2 is thought in some cases to reduce the effect of the oestrogen (natural and synthetic) that binds to it. It has been observed that tumour tissue shows an increase in ESR1 and decrease in ESR2. Since oestrogen is also protective against heart disease, ESR2 has been linked to cardiovascular health, particularly in conjunction with hormone therapy such as the oral contraceptive pill (OCP) and hormone replacement therapy (HRT) which can increase risk.	**TC**	The TC genotype is associated with moderately reduced risk of cardiovascular disease (CVD), lower circulating triglycerides (fat) and increased "good" HDL-cholesterol in post-menopausal women. Oestrogen-progesterone hormone replacement (HRT) was found to further decrease risk of CVD in menopausal and post-menopausal women. CVD risk is highly affected by diet and lifestyle factors such as being overweight, low exercise and a diet high in refined sugar and unhealthy fats which will increase your risk. Maintain a healthy weight by exercising regularly and watch intake of unhealthy fats (margarine, vegetable oils and refined, processed foods).

Oestrogen:
Phase II Detoxification

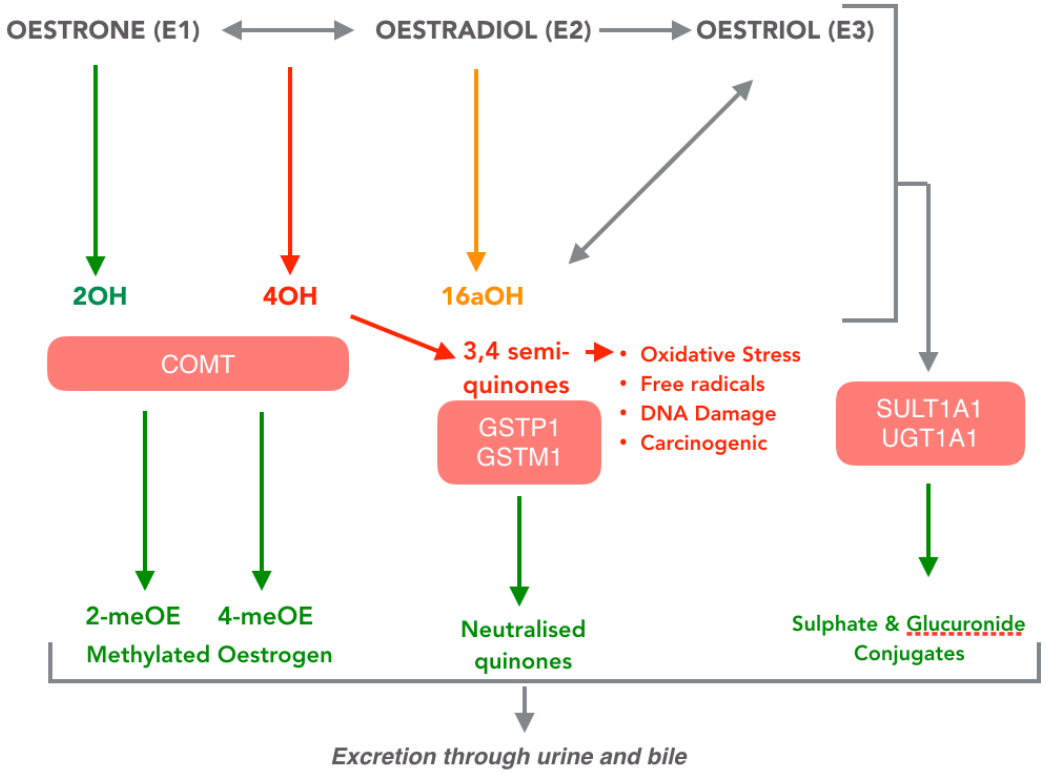
After phase I, oestrogen metabolites pass through phase II detoxification where they are neutralised and prepared for excretion via 4 main pathways:

- **COMT (Methylation):** the ***COMT*** enzyme turns 2OH and 4OH into the neutral compounds, 2-meOH and 4-meOH respectively via a process called methylation. Methylation is a major mechanism for preventing the potentially harmful effects of oestrogen in the body.

- **GSTs (Glutathione Transferases):** the ***GSTs*** are vital phase II detoxification enzymes responsible for providing protection against toxins by neutralising free radicals in the body with the help of the powerful antioxidant, **glutathione**.

- **SULT (Sulphation):** oestrogen metabolites are also deactivated via sulphotransferase enzymes

- **UGT (Glucuronidation):** the **UGT** enzymes render oestrogen more water-soluble and ready for excretion via the bile to the small intestine



*Knowing which of your **phase II pathways** need extra support is important. Learn to optimise these pathways through diet & lifestyle measures to ensure healthy elimination of oestrogen (and other nasties like toxins & medication). Check **pages 15 - 17**.*

GENE	RESULT	IMPACT & ADVICE
COMT - Oestrogen Methylation COMT is an important phase II detoxification enzyme responsible for inactivating many compounds including dopamine, adrenalin and oestrogen via methylation. COMT methylates 2OH and 4OH oestrogen to 2-me and 4-me oestrogen respectively, making them inactive and ready for excretion. Variants in COMT lead to reduced enzyme function and slower inactivation of oestrogen (and other compounds) via this pathway. High oestrogen levels reduce COMT activity.	**AG**	The AG genotype is associated with reduced COMT activity and less efficient inactivation and clearance of oestrogen (and other compounds) via methylation. This could lead to a tendency to high oestrogen levels. Review your MTHFR results on the next page to see if you are also a 'poor methylator' which slows down COMT activity further. A diet rich in B vitamins and 'clean' protein will help to improve methylation ability. Magnesium and ellagic acid (red berries) support healthy COMT. Optimising other phase II pathways will reduce the burden on COMT. On the other hand, this genotype may be beneficial post-menopause, due to increased oestrogen levels.
GSTM1 - Neutralising Free Radicals GSTM1 is one of the GST superfamily of enzymes. It is present in virtually all tissue but is most highly active in the liver, kidneys and intestines. It is responsible for neutralising compounds such as free radicals, environmental toxins, carcinogens and pharmaceutical drugs via the powerful antioxidant, glutathione. Since free radicals damage DNA, it is also involved in preventing cellular and DNA mutations. Variants in this gene are very common with approximately 50% of the population having only one or no copies of the gene at all, increasing susceptibility to environmental toxins and free radical damage.	**AG**	Likely to have one copy of the GSTM1 gene. This could lead to a reduced ability to neutralise free radicals. Diet and lifestyle factors like smoking, high alcohol intake, consumption of grilled meats and exposure to chemicals in detergents or cosmetics should be avoided as much as possible to reduce toxic load. This is particularly important if you have the high activity CYP1B1 genotype (see page 11 above). Cruciferous vegetables, glutathione, antioxidants and 'clean' protein help to support this pathway.
GSTP1 - Neutralising Free Radicals GSTP1 is another member of the GST superfamily of enzymes highly expressed in the liver, kidneys, oesophagus, thyroid and intestines. Its main role is protection of cells against toxins and carcinogens such as pollution, heavy metals, cigarette smoke, pesticides and UV exposure via the powerful antioxidant, glutathione.	**AG**	The GA genotype is associated with moderately impaired GSTP1 activity and reduced ability to neutralise free radicals. High levels of oxidative stress due to smoking, alcohol consumption, stress and excessive exercise; and low glutathione levels will slow GST activity further. Reducing stress and inflammation and increasing antioxidants, particularly glutathione, is recommended to fight free radical damage. Support this pathway by eating plenty of cruciferous vegetables and 'clean' protein (see page 27).

GENE	RESULT	IMPACT & ADVICE
MTHFR - Methylation & Oestrogen Detoxification The MTHFR gene is responsible for converting folate (vitamin B9) into its active form. Active folate is an important component of methylation, a biochemical reaction involved in many processes in the body including detoxification, DNA synthesis and repair (vital for healthy cell division), gene expression, foetal development, and the metabolism of neurotransmitters, especially dopamine and serotonin. Variants in MTHFR lead to low activity and therefore low production of active folate. Here we look at two variants on the MTHFR gene (A1298C and C677T) known to impact function.	**TG**	The G result is associated with reduced activity leading to low production of active folate (methylfolate), an important component of the methylation cycle. Healthy methylation is important for the deactivation and elimination of oestrogen and is highly affected by diet and lifestyle factors as well as genetics. You may be at increased risk of mood disorders, and have a reduced ability to eliminate oestrogen. B vitamins, magnesium and low alcohol is recommended to support healthy methylation. Avoid folic acid (synthetic folate) which reduces the availability of methylfolate further!
	GG	The T result (A1298C) is associated with healthy enzyme activity and production of active folate (methylfolate), an important component of the methylation cycle. Healthy methylation is important for the deactivation and elimination of oestrogen from the body and is highly affected by diet and lifestyle factors as well as genetics. B vitamins, magnesium and low alcohol intake is recommended to support healthy methylation.
SULT1A1 - Sulphation SULT1A1 is highly expressed in the liver, small intestine, kidney, uterus, adrenal glands and breast tissue. It is one of the enzymes involved in deactivating oestrogen and other hormones, neurotransmitters and medications in the body. Variants in SULT1A1 cause reduced activity and therefore reduced deactivation of substrates - including oestrogen.	**TC**	The T result is associated with intermediate sulphation (deactivation) of oestrogen and its metabolites. A diet rich in sulphur-containing foods such as garlic, onion, Brussels sprouts, broccoli and kale, will help to support this pathway. Focus on optimising other phase II pathways (methylation and glucuronidation) to reduce the burden on this pathway.

GENE	RESULT	IMPACT & ADVICE
UGT1A1 - Glucuronidation UGT1A1 encodes an enzyme expressed largely in the liver, kidneys, gut, prostate, ovaries and breast tissue. It is responsible for the inactivation of molecules such as oestrogen and other steroid hormones, thyroxine and common drugs such as morphine and acetaminophen (paracetamol), and bilirubin, preparing them for excretion via urine and bile. Variants in UGT1A1 can cause slow glucuronidation. Intestinal dysbiosis (unhealthy gut bacteria balance) can cause compounds conjugated (inactivated) by UGT enzymes to become unconjugated (reactivated) and re-released into circulation. This is due to the bacterial production of an enzyme called beta-glucuronidase. In the case of oestrogen this means that bound oestrogen (ready for excretion) can become unbound and re-released into circulation leading to high oestrogen levels.	**TG**	The G result is associated with slower UGT1A1 enzyme activity and poor glucuronidation of oestrogen and other compounds. Intestinal dysbiosis will impede this pathway further. Consider probiotic support if you suspect or have confirmed dysbiosis, or if you have been on antibiotics. Foods that support glucuronidation include apples, oranges and cruciferous vegetables - all of which naturally contain calcium-D-glucarate, a compound shown to inhibit beta-glucuronidase released by gut bacteria, and watercress.
UGT1A6 - Glucuronidation UGT1A6 encodes an enzyme responsible for the inactivation of molecules such as oestrogen and other steroid hormones, thyroxine and common drugs such as morphine and acetaminophen (paracetamol), and bilirubin, preparing them for excretion via urine and bile. Variants in UGT1A6 can cause slow glucuronidation. Intestinal dysbiosis (unhealthy gut bacteria balance) can cause compounds conjugated (inactivated) by UGT enzymes to become unconjugated (reactivated) and re-released into circulation. This is due to the bacterial production of an enzyme called beta-glucuronidase. In the case of oestrogen this means that bound oestrogen (ready for excretion) can become unbound and re-released into circulation leading to high oestrogen levels.	**AG**	The G result is associated with reduced UGT1A6 activity and reduced inactivation and elimination of oestrogen, thyroxine and other substances detoxified by this pathway. It is also linked to increased risk of gallstones. Intestinal dysbiosis will disrupt the effectiveness of this pathway further. Consider pre and probiotic support if you suspect or have confirmed dysbiosis, or have been on antibiotics. Foods that support this pathway include apples, oranges and cruciferous vegetables - all of which naturally contain calcium-D-glucarate, a compound shown to inhibit beta-glucuronidase released by gut bacteria, and watercress.

Other Important Factors Affected by Genetics

Heart Health

Blood Clotting

Normal blood clotting (coagulation) is an important process that prevents excessive bleeding after an injury. Platelets and proteins in your blood work together and thicken to stop excessive bleeding by forming a clot over the injury. Clots are usually dissolved naturally after the injury has healed. Sometimes, however, clots form inside blood vessels without any obvious injury causing narrowing of the blood vessel (atherosclerosis) and can become dangerous. Once a clot has formed it can travel to other parts of the body and can cause deep vein thrombosis (DVT), heart attack, pulmonary embolism (clot in the lung) and stroke. Risk factors such as obesity, age, smoking, certain medications and genetics affect your clotting ability. Oestrogen increases clotting factors in the blood. Pregnancy, the oral contraceptive pill and HRT all increase oestrogen levels and therefore risk. Human factor V (F5) is one of several substances that aid normal blood clotting. People with an inherited condition, F*actor V Leiden*, have an increased tendency to develop blood clots. Women are particularly at risk of increased blood clotting due to higher oestrogen levels than men.

*Have you inherited **Factor V Leiden** increasing your risk of abnormal blood clotting? Check **page 22** to see your status.*

Cholesterol

Despite its bad reputation, cholesterol plays many vital roles in the body. It is essential for healthy cell membranes, the transport of fats between cells, cell signalling, nerve conduction and serves as the precursor to steroid hormones (androgens, oestrogen and testosterone), bile acid (important for digestion) and vitamin D. Cholesterol is produced mostly in the liver and is carried through the bloodstream by various lipoproteins. Low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) cholesterol are dubbed "bad" because of their role in fatty build-ups in arteries (atherosclerosis), high-density lipoprotein (HDL) is dubbed "good" because it helps carry LDL away from the arteries back to the liver to be broken down and removed from circulation. Some cholesterol is also obtained through the diet.

Triglycerides are the most common type of fat in the body, they store excess energy from your diet and are carried by VLDL. Ideally, you want to have lots of circulating HDL, and less LDL and triglycerides. Total cholesterol is the overall amount of circulating cholesterol in your bloodstream (HDL, LDL, VLDL /triglycerides).

Apolipoprotein E (APOE) is one such lipoprotein responsible for removing "bad" cholesterol from circulation.

*Variants in **APOE** decrease your ability to remove "bad" cholesterol, increasing your risk of cardiovascular disease. Check your status on **page 21**.*

Heart Health

Nitric Oxide

Your arteries produce nitric oxide (NO) to help them to relax and to increase oxygen and blood flow. When plaque builds up in your arteries (atherosclerosis), your capacity to produce NO reduces causing arterial stiffness and contributing to reduced oxygen and blood flow. The best way to increase NO is through exercise. When you put demand on your body during exercise, your muscles need more oxygen which is supplied by the blood. As the heart pumps with more pressure, the lining in your arteries releases NO into the blood, relaxing and widening the vessels. As we age, our blood vessels and NO system become less efficient due to free radical damage (see page 23 for more information on free radicals), inactivity, and poor diet, causing our veins and arteries to deteriorate. Another way to increase NO is through diet, most notably by consuming foods rich in the amino acid, L-arginine, found in foods such as nuts and seeds, good quality animal meat and quinoa. The ***NOS3*** gene is responsible for producing the enzyme, ***nitric oxide synthase (NOS)***, which in turn is responsible for making nitric oxide in the blood vessels.

*Variants in **NOS3** can lead to low NO production which is linked with cardiovascular disease. Check your NOS3 status on **page 22**.*

GENE	RESULT	IMPACT & ADVICE
APOE - Cholesterol Levels APOE produces apolipoprotein E, a protein that binds and transports fats in the body. APOE is highly expressed in the liver, kidneys and brain and is responsible for removing cholesterol, particularly "bad" LDL and VLDL cholesterol from the bloodstream. Variants in APOE are associated with increased total cholesterol, particularly LDL and triglycerides (a type of fat) due to decreased clearance. As a result, APOE variants have been linked to high cholesterol, cardiovascular disease and also with cognitive decline. High LDL cholesterol and triglycerides are often a predictor of other conditions such as obesity, high blood pressure, high blood sugar, low thyroid function and stroke. Here we look at two variants (rs429358 & rs7412) in the APOE gene which are known to have an impact on function, particularly when inherited together.	**TT**	The TT genotype for this SNP (rs429358) is not associated with elevated LDL cholesterol and triglyceride levels, and therefore is not linked to increased risk of atherosclerosis. Although genetically robust, poor diet and lifestyle habits such as low exercise, smoking and eating a diet high in refined, processed foods and unhealthy fats (margarine and most vegetable oils), will put you at risk of heart disease. Maintain a healthy weight by exercising regularly, watch your intake of unhealthy fats, processed foods, refined sugar and alcohol. Dietary fibre (from vegetables, beans, fruit and whole grains), and oily fish have been shown to be beneficial in lowering triglycerides.
	CC	The C result for this SNP (rs7412) is associated with increased LDL cholesterol and higher post-meal triglycerides, increasing risk of plaque build-up in the arteries. Your risk increases further in combination with each C result for the rs429358 SNP above. Poor diet and lifestyle choices such as lack of exercise, smoking, high alcohol intake and eating processed foods high in trans and saturated fats, will increase risk regardless of your genotype. It is particularly important that you avoid unhealthy fats such as vegetable oils, margarine and processed foods. Focus on healthy fats found in olive oil, avocados, nuts, seeds and oily fish. Maintain a healthy weight by exercising regularly.

GENE	RESULT	IMPACT & ADVICE
Factor V Leiden (F5) - Blood Clotting This gene encodes human factor V (F5), one of several substances that aid normal blood clotting. F5 is responsible for increased blood clotting. This leads to the potential to form abnormal and potentially harmful blood clots that can lead to deep vein thrombosis (DVT), heart attack, pulmonary embolism (clot in the lung) and stroke. The variant in this gene is the most common reason behind inherited thrombophilia (abnormal blood clotting), accounting for 40-50% of cases, however, not everyone with the variant will experience abnormal blood clots. Women with this variant should discuss with their doctor before taking the oral contraceptive pill, HRT or tamoxifen. This variant also increases risk of preeclampsia in pregnancy.	**CC**	The C result is associated with normal F5 activity and decreased risk of abnormal blood clotting. Diet and lifestyle factors such as smoking, being overweight, low physical activity, a family history of clotting disorders, being on the oral contraceptive pill (OCP) or hormone replacement therapy (HRT), all increase your risk of abnormal blood clotting regardless of genotype. Regular exercise, omega-3, garlic and vitamin E all help to maintain healthy blood consistency and reduce risk of abnormal clotting.
NOS3 - Nitric Oxide Production The NOS3 gene produces the enzyme nitric oxide synthase (NOS) responsible for making nitric oxide (NO). NO protects the health of blood vessels and is involved in vasodilation (opening of the blood vessels). Variants in NOS3 result in low production of NO which is associated with cardiovascular disease, and with erectile dysfunction in men. Recent research shows that antioxidants, including omega-3, have a positive effect on cardiovascular risk by lowering triglycerides and increasing “good” cholesterol.	**GT**	The T result is associated with lower NOS activity leading to reduced production of nitric oxide (NO), which is linked to increased triglycerides and cardiovascular disease. Diet and lifestyle factors such as low exercise and a poor diet high in unhealthy fats and low in antioxidants will increase your risk regardless of your genotype. The best way to ensure and maintain heart health is to participate in regular, moderate exercise, consume an antioxidant-rich diet (variety of fruit, veg, herbs and oily fish), avoid processed foods (high in sugar and unhealthy fats), and minimise stress as much as possible.

Healthy Ageing

Choline

Choline is an important nutrient for healthy cell membranes, brain development, nerve function, muscle movement, and for supporting and maintaining energy, liver function and metabolism. It is also a source of methyl groups for the function of methylation enzymes such as COMT and BHMT which assist in inactivating oestrogen and lowering homocysteine (hcy) respectively. High hcy has been connected to cardiovascular disease, and neurological conditions like Parkinson's, Alzheimer's and depression. Choline can be attained from the diet through foods such as eggs, beef liver, sunflower seeds, pumpkin seeds, almonds and cruciferous vegetables. Choline is also made internally by the body via the *PEMT* gene. Oestrogen increases *PEMT* activity and therefore choline production.

*Variants in **PEMT** reduce choline production, particularly after menopause. Check your status on **page 24.***

Free Radicals

Free radicals are highly unstable molecules that damage your cells, speed up ageing, and play a role in disease. We all produce free radicals as part of normal human metabolism. We also generate, ingest, absorb and inhale them though chemicals and pesticides in our foods, in our water, cosmetics and household cleaning products, cigarette smoke, charred foods, excessive exercise, stress, air pollution and medication.

Antioxidants help to keep free radicals in check. Vitamins A, C and E are all powerful antioxidants derived from food and that help combat free radical damage. This is one of the main reasons that a healthy diet and lifestyle is so important. *Superoxide* is a potent free radical produced in the body that is neutralised with the help of the antioxidant, *superoxide dismutase (SOD).*

*Variants in **SOD2** reduce the production of SOD. increasing need for antioxidants. Check your SOD2 status on **page 24.***

Vitamin D

Dubbed the 'sunshine' vitamin due to the fact that most vitamin D in the body is produced through exposure to sunlight. We also obtain a small amount from the diet. Vitamin D helps to regulate calcium and phosphate which are important for strong and healthy bones and teeth; it mediates the production of dopamine; cell growth and differentiation, and supports a healthy immune system. Low vitamin D has been linked with poor bone health, depression, inflammation, frequent infections and autoimmune disease.

The *VDR* gene regulates the body's receptivity to vitamin D3, the active form of vitamin D in the body.

*Variants in **VDR** decrease receptivity to vitamin D3. Check you status on **page 25.***

GENE	RESULT	IMPACT & ADVICE
PEMT - Choline Requirement The PEMT gene encodes an enzyme responsible for producing choline in the liver via methylation. This is the most significant source of choline other than that absorbed through the diet. Choline is important for healthy cell membranes, brain development, nerve function, muscle movement, and for supporting and maintaining healthy energy, liver function and metabolism. It also provides vital methyl groups for the function of the methylation enzymes COMT and BHMT. Oestrogen raises PEMT activity, increasing the production of choline. As a result, choline requirement increases after menopause. Variants in PEMT are linked with lower choline production, and liver and muscle dysfunction, particularly non- alcoholic fatty liver disease.	**TT**	The T result is associated with reduced PEMT function. Low choline levels increase risk of non-alcoholic fatty liver disease and elevated homocysteine levels which puts you at risk of cardiovascular disease. A diet rich in choline foods (organic, free-range eggs, liver and meat) and green leafy vegetables is necessary to reduce your risk of the above, particularly after menopause when oestrogen levels no longer support the internal production of choline optimally.
SOD2 - Antioxidant (Neutralising Free Radicals) SOD2 produces an enzyme that breaks down a harmful free radical in the body called superoxide. Superoxide is a natural by-product of metabolism and causes damage to cells, premature ageing (wrinkles), inflammation and heightened risk of disease. Variants in SOD2 cause decreased ability to break down superoxide leading to increased free radical damage. SOD2 requires manganese (found in pineapple, almonds, peanuts, walnuts, hazelnuts, pumpkin seeds, chia seeds, sunflower seeds, beans, spinach, green and black tea and brown rice) to function optimally.	**AG**	The GA genotype is associated with intermediate SOD2 enzyme activity and therefore a reduced ability to break down the harmful superoxide free radical. This genotype has also been linked to the development of cirrhosis of the liver in heavy drinkers due to poor protection from oxidative stress (high amounts of free radicals which cause damage to the body). Ensure to eat a varied diet rich in manganese foods (listed left) and antioxidants such as vitamins A, C and E. Avoid smoking, heavy drinking, excessive exercise, environmental and dietary chemicals (opt for organic produce where possible) and sunburn to minimise free radicals in the body.

GENE	RESULT	IMPACT & ADVICE
VDR - Vitamin D The VDR gene is regulates the body's receptivity to vitamin D3, the active form of vitamin D. This vitamin can be acquired from certain foods but is mostly manufactured in the body following exposure to sunlight. Vitamin D serves many important functions in the body: it aids in the absorption of calcium and phosphate - keeping bones and teeth healthy; it mediates the production of dopamine (one of the body's 'feel good' chemicals) this is one of the reasons why lack of sunlight is associated with low mood; it is also crucial for cell growth and differentiation, and supports a healthy immune system. Low vitamin D has been linked with poor bone health, depression, inflammation, frequent infections and autoimmune disease. Over 30% of the population carry variants which may lead to low vitamin D receptivity. Here we look at two variants (BsmI and TaqI) on the VDR gene which are known to affect vitamin D receptivity.	**TC**	The BsmI TC genotype is associated with reduced receptivity to vitamin D. This means that you are likely to need a higher amount of vitamin D to reduce your risk of associated conditions such as fragile bones (particularly post menopause), poor immunity, and low mood. Exposing your skin to sunlight regularly (without tanning or burning) or, if that's not possible, taking a good quality vitamin D supplement - especially during winter months - will help maintain adequate levels. Consume foods rich in vitamin D including fatty fish, beef liver, egg yolk and mushrooms.
	AG	The TaqI GA genotype is associated with reduced vitamin D3 receptor activity. This means that you are likely to need a higher amount of vitamin D to reduce your risk of associated conditions such as fragile bones (particularly post menopause), poor immunity, and low mood. Your risk is increased if you have a T result for the BsmI SNP above. Exposing your skin to sunlight regularly (without tanning or burning) or, if that's not possible, taking a good quality vitamin D supplement - especially during winter months - will help maintain adequate levels. Consume foods rich in vitamin D including fatty fish, beef liver, egg yolk and mushrooms.

Nutrition & Lifestyle Advice

Reduce / Eliminate

Everyday Hormone Disruptors

Chemicals in plastic, household detergents and cosmetics that you come into contact with daily are known to disrupt your hormones. ***Swap plastic bottles and soft plastic food containers for glass,*** *and* ***switch cosmetics and household detergents containing parabens*** *and other harmful chemicals to more* ***natural alternatives where possible.***

Dairy & Non-Organic Meat and Eggs

Animal products such as cheese, milk, yoghurt, meat and eggs naturally contain various steroid hormones including oestrogen, testosterone and progesterone. Organic options contain the same amount of hormones but less harmful chemicals. *Try to* ***reduce your intake of animal products and stick to organic, free-range, grass fed options*** *where possible.*

Dysbiosis & Refined Carbohydrates (sugar)

Imbalanced gut bacteria (dysbiosis) and a diet high in refined carbohydrates reduce the healthy elimination of oestrogen and other hormones. ***Probiotics and dietary fibre*** *will help to* ***eliminate dysbiosis,*** *improve digestion and support detoxification pathways, particularly* ***Glucuronidation. Calcium-D-glucarate*** *found in cruciferous vegetables and citrus has been found to* ***inhibit beta-glucuronidase*** *released by gut bacteria, and encourages phase II detoxification.*

Alcohol, Caffeine and Unfiltered water

Contain toxins that can disrupt hormones and place demand on your liver which can affect detoxification.

Increase

Regular Moderate Exercise

Since adipose (fat) tissue produces hormones, decreasing body fat and maintaining a healthy weight is important for balanced hormone levels and health in general. If you are carrying excess weight, lose it slowly and sensibly, ***stick to an achievable exercise regime to maintain a steady weight.*** *Exercise also helps improve mood, mental clarity and keeps bones and joints strong and healthy.*

Specific Hormone-Friendly Foods

'Clean' protein: nuts, seeds, beans, quinoa, lentils, organic, free-range eggs and meat & wild caught fish
Berries: blackberries, cranberries, raspberries, strawberries & blueberries
Cruciferous vegetables: broccoli, cabbage, kale, turnips, mustard greens, Brussels sprouts, cauliflower, collard greens & kohlrabi
Herbs & spices: maca root, sage, oregano, ginger, turmeric, ashwaganda, milk thistle, coriander, tulsi (holy basil) & chaste berry

Complex Carbohydrates and Healthy Fats

Both help to balance blood sugar and sustain energy for longer reducing the urge to reach for sugary (refined carb) snacks/ foods and caffeine. In moderation, they also help to maintain a healthy body weight.

Complex carbs: oats, buckwheat, quinoa, brown rice, beans, carrots, sweet potato, parsnips, pumpkin, swede, apples, apricot, berries, pears & melon

Healthy fats: extra virgin olive oil (not heated), avocados, coconut oil (fine when heated), nuts and seeds & fatty fish

Herbal teas & Filtered Water

Herbal teas such as chamomile, tulsi, rooibos, peppermint, dandelion, nettle, maca, rhodiola, ginseng; and filtered water help to keep your kidneys and liver working well and support detoxification & hormone balance