**HRT and the Menopause**

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0.01 **Chair:** Good evening everyone. I'd like to welcome you to this webinar which is part of a Menopause Series that we are putting together. This is the first one and there's going to be a number following. The next one in the series is on Genitourinary Problems and that's on March 23rd and we'll be sending you out some more details about that.

As usual in the feedback if you could fill in any other issues that you want raised generally with CPD, but as we're developing this menopause series, anything specifically about menopause and we can see if we can incorporate those.

So today is all about HRT and the Menopause and I’m really pleased to introduce a super expert to teach us - a Faculty Trainer, Dr Jane Clarke-Williams. I’m going to hand you over to Jane.

0.56 **Speaker:** Hi. Thank you very much for joining us this evening. At least we can all stay inside and not have to go out in the horrible wet weather. What I’m going to do today is talk about HRT, although obviously I’m sure you all realise there's so much more to menopause care, than just HRT.

So, introducing myself. I was a GP for over 30 years, and I’ve done what we used to call clinical assistantships. I have just recently moved to Wales, having done my practice in the Portsmouth area. I’ve been developing specialist interest over the years in female health and I’m a medical specialist and trainer. This means that I’ve done the British menopause course and done quite a lot of teaching. I used to teach at Southampton University and in the practice as well. I’m currently working in the sector of reproductive health in the clinic at the Cardiff Royal Infirmary. I also do a private menopause clinic.

2.23 **Speaker:** What is the menopause?

The menopause is something that a lot of people refer to. When actually it's a single day that can only be determined retrospectively, because the menopause is when you've had no periods for at least a year. In this country the average age is 51. Now don't forget that there are people that aren't having periods because they've got contraception, they've got the Mirena coil or the implant, and for these people obviously that definition of when's your last period doesn’t actually make sense. People with polycystic ovary syndrome again may have no periods, and obviously surgery and hysterectomy.

Most people though will talk about the menopause as being their symptoms, when they’re changing from having plenty oestrogens having a declining level and ultimately very little. And remember that the average length of symptoms is seven years. So that means that some people have no symptoms at all, and others can have them for 20 or more years. So, as I said the menopause, or what people talk about as the menopause, is a very good opportunity for health promotion. And as women go into their 50s it's an ideal time to try and set them up for a healthy life in their post-reproductive years, remembering that that is about a third of most women's lives. And if we can advise them on smoking and weight all the usual things, alcohol, exercise, these sorts of things are probably best done opportunistically by the nurse when the lady is there for other things. And the obvious time is her routine smear test.

4.56 **Speaker:** So, what are what are the symptoms? This is the list of symptoms that most people think about when we're talking about perimenopausal symptoms. The hot flushes and bleeding changes are very common. The one that often people come to see me about is the poor sleep and that anxiety and people talk about you know head fog and things. So, there are mental symptoms and physical symptoms. And reduced libido is something that a lot of people do mention.

So, the NICE Guidance. This was published in December 2015 and actually the latest review was the end of 2019 and it was a very good guidance. I know we're sent lots of guidance and unless you have lots of time on your hands and as GPs none of us do, and it's impossible to read them all. But this is really good guidance because it looked at all the previous studies and the metanalyses that have been done. So, it was clarifying when to think about HRT prescriptions. It did correct some misinformation and also very importantly and as GPs we know this is important, we individualise the treatment for all patients.

6.45 **Speaker:** So, what were these misconceptions about HRT. The first one (the NICE guidance tried to bust the myth) is that there is no time limit on how long to take it. The menopause is a state of hormone deficiency and the hormones don't comeback so there is no time limit. When we talk about 5 years and 10 years this is just points when research was audited. So, it's the timeline. So, it's not that you must only take it for five years but that's when we've got the figures, because that's when they re-audited their findings. Also, the NICE guidance pointed out that comorbidities do not stop people from being able to take HRT safely and in fact those people with comorbidities may actually benefit more in terms of quality of life from HRT than the fit and healthy people. So, it's very important again you know to think of each person as an individual and try and think things through logically. Not all forms of HRT increase breast cancer risk and certainly the one that I would always think of is vaginal oestrogen which obviously is my particular specialist area, and therefore that's what springs to mind. But breast cancer is such an emotive subject and it's the first thing to people's minds when we're talking about HRT. So, it's very important to have that side of things clear in our minds. And the myth that there are non-hormonal treatments that work as well. Unfortunately, the deficiency state is corrected by replacing the deficiency. For example, in osteoporosis we know that although they are working on some new bone treatments, basically oestrogen is the only thing that can actually build bone as well as preserve it. So, the most important thing is - individualise the care and if we have any one is about a patient then always seek advice. I think we are very tempted as GPs when it comes to HRT what's a little bit odd is that whereas with eyes or a funny heart murmur would always say and oh, I’ll get the cardiologist to check or if you've got a funny thing that you look at like a fungus or something strange with the eyes, we say right we're going to send you to a specialist. And yet when people talk about menopausal symptoms quite a lot of people are quite tempted to say oh you don't want HRT, when really, it’s another specialist area and if you doubt and the patient would like more information about it just, give them the sources to find that.

10.13 **Speaker:** So, there are ten key points to draw out of the NICE guidance.

* The first one is that we need to have evidence-based information and therefore we can help that woman understand what is available and therefore they can make decisions. We can share the decision making with them, when it comes to treatment options.
* NICE does not want us to take blood tests on anyone over 45. Being a menopause specialist there’s something quite NICE about being a specialist in an area where most of the time the diagnosis is extremely straightforward. And over 45, if a lady comes in with hot flushes and poor sleep or brain fog. All those things you think actually the menopause could be playing a part here. As an aside though, don't forget there are other things. I mean you know checking the thyroid levels and things. There are other things that that patient may have, so the blood test that we don't need is the FSH but obviously if you're trying to diagnose any other condition you know do do those, but not the FSH in the over 45s.
* One thing that NICE brought out is that they said to offer HRT as the first line for menopause related vasomotor symptoms and low mood.
* NICE say - do not routinely offer clonidine or antidepressants.
* And obviously we all need to remember that Fluoxetine and Paroxetine interfere with the action of Tamoxifen. So do not use those in women taking Tamoxifen.
* Offer long-term vaginal oestrogens for urogenital symptoms even if taking HRT and this is very important. As I said earlier this is quite an area of interest for me. Sadly, a hundred percent of people will have the skin changes of their bladder, trigone and vagina from lack of oestrogen. In studies at least 70 to 75 percent of people are affected daily by their symptoms but obviously this is something we don’t tend to talk about or don’t relate all those symptoms to the menopause and lack of oestrogen.
* And also, people on HRT we can discount it you're on the HRT but obviously they might need vagina oestrogens in addition. So, this is safe long term. Even though we know that looking at the little leaflet in with these products they often say only for three months/six months and then review, but we know that if you stop it the symptoms come back because the skin changes are inevitable with lack of oestrogen.
* NICE reminds us to understand appropriate review and when to refer.
* They suggest we use charts. I’m a big fan of charts because at least it’s a basis it to shape our conversation and discussion of options with the lady and the British Menopause Society has some very good charts one of which we’ll come to later.
* And NICE guidance - no arbitrary limits for the length of time they take it.
* When they say we should use blood tests is to confirm the diagnosis of premature ovarian failure. This is extremely important, because lack of oestrogen from the length of time that some of these women are without their oestrogen and actually it causes earlier well earlier death. It has a massive impact on both length of life and quality of life and NICE guidance say that for these ladies unless there's a very good reason not to and really that's only active breast cancer, they should take the HRT at least up to the average age of the menopause which is 51.

15.17 **Speaker:** So as GPs - when are we going to consider HRT, taking those NICE guidelines into account?

As I’ve said every case of premature ovarian failure. So, everybody who has those low levels that are going to impact massively on their bone density, their cardiovascular system, we've said their bladder. It's very important for these people. We need to go in straight away and explain why NICE guidance says that they should all take HRT.

So, disabling hot flushes and poor sleep. I’m sure most of us will consider this with patients presenting in this way.

NICE guidance reminds us that its first line in perimenopausal low mood and anxiety.

Obviously, Sertraline and the SSRIs are really useful, but the first line is HRT.

Remember urogenital symptoms from the perimenopause onwards. Always consider HRT and that systemic or topical and think about HRT when there is risk or presence of osteoporosis.

15.17 **Speaker:** So, the next thing, we've decided which patients we're going to think about giving HRT. We've hopefully given them where to find information. The British Menopause Society site is excellent and that patient arm, which is the women's health concern, really useful advice. And obviously the NHS site. So, our patients can do a bit of research online.

But we're going to think - what are we going to give them?

So, you can give tablets. There is oestrogen only and then there are the ones with oestrogen and progesterone. Ones that are the same dose every day or ones that have the progesterone in an ‘on and off’ sequential preparation. Patches and you apply them once or twice a week. Although we've had awful shortages over the last couple of years from the patches and I think the once weekly ones are not available again yet. But the twice weekly ones are. There’s gel and spray. This is oestrogen only and both used daily. The spray is a new product that's just come out this year. So, the gel and the spray both applied to the thighs. The gel tends to give a slightly more fluctuating dose. Obviously, the patches are slow release. The oral tablets will be a fluctuating dose. The spray is meant to sit in the skin in a sort of a reservoir and therefore the manufacturers tell us (although it’s new product so we'll find out that) gives a very slow and steady level which may be very helpful for some people. The intrauterine systems are progesterone only and although we know for contraception now change every five years, the license for the Mirena is four years. The vaginal tablets, pessaries and creams are oestrogen only and the frequency is as often as you need it. Although very often, we say, build the levels up and then decrease the frequency. But maintain a regular use, otherwise as I’ve said the changes will recur. Then that's the vaginal ring which is just a flexible ring that can be placed into the vagina. Once it's there, no one's going to know that it's there and this is a three monthly. Obviously, someone needs to change it every three months, but it does completely avoid daily administration.

19.47 **Speaker:** So, this is the HRT guide from the British Menopause Society website. Obviously, it's quite small and you probably can't read it all now, and but I’m just really pointing out that the British Menopause Society has very good guides and is easily accessible both for us and the patients.

So, with all these different routes and preparations, what are we going to choose? So why would we go for transdermal – this is patches, gel, spray? If there's increased clotting risk - so these are our smokers, people who've had DVTs in the past, diabetics, people with a BMI over 30. So, this is an awful lot of people who we have to think about. And the reason why we use transdermal preparations it’s because it avoids the first pass effect on the liver and therefore it has no change to your clotting risk. Obviously, people are more prone to clotting. Their risk continues. It doesn't, you know, solve the problem with clotting risk, but the transdermal won't alter your clotting risk and therefore it is safe. The gel tends to be a daily dose and the others are slower release. A lot of our patients do have a BMI over 30 and are pre-diabetic or diabetic and these people we really must remember have an increased clotting risk without adding anything else.

So, if you have a family history of heart disease or you're over 60 and you're suffering with symptoms that you'd like to treat with HRT then I would choose a transdermal route, because we don't want to increase the risk of clots or heart attack or stroke.

If your gut doesn't work then you're not going to absorb any tablets so remember transdermal for those with Coeliac disease, ulcerative colitis, and Crohn's. And this is an area that sometimes we forget but obviously we won't necessarily get the right levels, if we're not giving them a preparation that they can absorb.

People with migraines. Migraines as we know are changes of blood flow to the brain and you do carry an increased risk of clotting with migraines with aura, and therefore I would always give a transdermal preparation for these people. Because the migraines are often triggered (and if you talk to them, they often are in a cycle) so with the pill when they're taking the combined pill which obviously, they you would stop if they have the migraines with aura, but it's to do with the fluctuations of hormones. So therefore, a slow release and the patches are the best slow release. Although as I said this spray might prove to be very useful.

23.07 **Speaker:** So, why would we use just an oestrogenic preparation?

Total hysterectomy leaving no endometrium. So, these people can have oestrogen only. Remember though that if the cervix has been left there may still be some endometrium. And the people that we worry about those with endometriosis. If they have persistent areas of endometriosis and as we know these can be so small that no one would know. Even if they've had surgery, little areas might be left. Then you just have to think whether to use oestrogen only or whether to balance it with progesterone. Some people, to check this out sometimes, give them a progesterone challenge to see if they bleed. So, people who've got a cervix stump left after a subtotal hysterectomy - you may give them a block of progesterone and then see if there's bleeding. If there is bleeding, then you are going to need progesterone to prevent hypoplasia of that endometrium.

And ladies who've had their Mirena coil fitted within four years can also have oestrogen only. The license remember is four years for HRT use, although we know the faculty supports are using it for five years. But it's good practice to explain when we're using things off license to our patients. The thing to remember though is a lot of ladies, I mean if you fit the Mirena coil at 54/51 or whatever, an awful lot of ladies will say ‘I love the Mirena coil. I never want it changed. I never want it fitted again.’ And so, with these ladies you must remember that when their coil has been in the five years if they don't want to change and if you’ve not had any periods and you are 56 or whatever, most people would say perhaps not change - add in a progesterone at that point. So, it's very important that with these ladies we either change the Mirena so we give them another four to five years of endometrial protection, or we add the progesterone in at that point.

25.44 **Speaker:** So, when are we not having continuous but going to go for the sequential?

These are the preparations that have oestrogen nearly all the time and then progesterone in blocks. And this means you get a withdrawal bleed. So, the license. Within one or two years of the last period, giving people back their oestrogen and progesterone, can cause a little bit of build-up in the endometrium and the problem is if they get nuisance bleeding. So, you choose sequential when they've not long had their periods, because these people can be very troubled by spotting and funny bleeding. And if they are on a continuous combined preparation, because that period was quite a long time ago, if they get breakthrough bleeding, which is very common (Don't forget, when you start HRT a lot of people get bleeding on and off this is not post-menopausal bleeding per se) if that breakthrough bleeding is troublesome and not settling, then some people might choose to go to a sequential where yes you bleed but you know when you're going to bleed which for some people is easier to manage. So, don't forget sequential doesn't give you continuous progesterone cover and what can happen is that if you leave a lady on her sequential only taking progesterone for half the time, if you leave her on for more than a few years, she may not have sufficient endometrial protection and therefore you may run the risk of hypoplasia. And also, periods - one of the best things about going through the menopause is that you know you don't have periods anymore. So, for these people then after couple of years, up to certainly after four years, you'd want to change them onto continuous combined. But of course, funny bleeding - Mirena is always going to be the gold standard. The Mirena coil sorts out your contraception, sorts out your bleeding, means you really don't have to think about the bleeding or contraception, the endometrial hypoplasia. It's all sorted. And therefore, you can really focus on getting the oestrogen level at the correct dose for this lady whether it’s a tablet or a patch, slow release, daily release etc and therefore the Mirena is the answer for most people.

I’m working the CRI at the moment and I’m fitting goodness knows how many coils a day and therefore I think a lot of us when you're used to using them, you can be extremely positive about them. But a lot of ladies come to me and say that at the minute they are not sure about the coil. People say ‘Oh, you don't have to have it?’ Of course, they don't have to but give them the correct information.

29.58 **Speaker:** So which oestrogen are you going to use?

Remember that the estradiol we now have in our HRTs is identical to human oestrogen. It is the human oestrogen. Yes, it's been made synthetically in the lab, but it is human oestrogen. So, the transdermal one does not affect clotting risk. Some people go on about the bioidentical ones that they can get from private clinics - not my private clinic - but these are mixtures and really it doesn't make sense. If you know what the deficiency is, and you replace it with exactly the same thing, that does make more sense. So, the British Menopause Society would not recommend. And Premarin, which we use for years, that does seem to have more adverse effects than the estradiol. And by adverse effects I mean metabolic effects on lipids and things like that, clotting and what have you. So, we tend to recommend estradiol which is just human oestrogen.

So Ethinylestradiol. This is what's in contraceptive pills or most contraceptive pills. It is potent synthetic oestrogen, and it is more likely to cause clotting. Some of the young women who have premature ovarian insufficiency quite like to be on the pill, because they feel that that’s the same as all their friends. Don’t forget there are a couple of the contraceptive pills that have estradiol in. Qlaira is one of them and these might well be worth thinking about especially as, I don't know whether you know, but Qlaira is also licensed for heavy menstrual bleeding. So, they can be very useful as well.

31.09 **Speaker:** So, the other part of the HRT. Which progesterone are we going to go for?

We’ve had so many shortages haven't we over the last year a couple of years, which very thankfully all seem to be resolving. And so, a lot of us have had to think more closely about what progesterone we use. So, the micronised progesterone which comes in capsules and the dydrogesterone which is only in combination with oestrogen, in the products Femoston. These are the closest to human progesterone and with recent studies it does look like they do have less effect on breast cancer risk, they are lipid-friendly, and studies would suggest that when taking these progesterones, your lipid profile improves, and they do seem to have less effect on clotting risk. So, these are good options. Obviously, it's a bit of a problem for the dydrogesterone, that it's only in Femoston and therefore is only available with an oral oestrogen which obviously we don’t want to use in these ladies with their large BMIs or all the other things we've mentioned. But, because of the shortage of everything else we've now used micronised progesterone a lot. I would mention that in the leaflet with the micronised progesterone, it says to take them and have days off or whatever. You'll find that the leaflet is not helpful. I tend to say use it every day or in a sequential regime and always take the micronised progesterone at night because it improves sleep. It's quite sedating, so this is really good news for some of the people with terrible sleep problems.

So Norethisterone and medroxyprogesterone are synthetic and androgen progesterones. They do increase clotting risk, breast cancer risk and have an adverse effect on lipid profile.

And don't forget (I haven't got shares in Mirena) - it hasn't had its breast cancer risk evaluated.

33.36 **Speaker:** So micronised progesterone more likely to leave patients with breakthrough bleeding and also, it's more expensive and certainly in England when you try and prescribe it, it does say it's an amber. So that means under specialist advice. Although obviously with all the shortages we're all using it much more. But it's really good in so many ways. And yet it has less good control on bleeding.

Norethisterone and medroxyprogesterone acetate very good control of bleeding but then we've said they're less good on the lipids and clotting and the breast cancer risk. The only one transdermal progesterone at the moment is the norethisterone in the combined patches. And that dydrogesterone as I said it’s only available in the combined oral Femoston, which is a real shame because it'd be so handy to have that option as well.

And of course, Mirena is the best endometrial protection and offers contraception and has very few systemic side effects. It's just a very good choice.

35.00 **Speaker:** So, when are we going to start these people?

People come at all different lengths of time because a lot of people think just wanted to do the menopause naturally, whatever that means. But a lot of people will just live with the symptoms until they get to a point where they are just desperate, and this can be at any age. So, we do see people in their 60s. I know some of those have taken them and then stopped them because the GP said ‘Oh you've been on it for more than five years. You've got to stop it or whatever’. But starting HRT, it is of most benefit before the age of 60 or within a few years of the menopause. The window of opportunity that we talk about is a few years around the menopause which is the last day obviously of your periods. But it suggests that it has a protective effect against ischemic heart disease. The problem then is that if you stop before the age of 60 it appears that you then have a little blip of a temporary increase in your risk of ischemic heart disease. If you continue to and don't stop until you’re after 60, this doesn't seem to happen. And Cochrane analysis and WHI seem to suggest there is no increased risk in cardiovascular disease events or all-cause mortality if you start it more than 10 years after the menopause. And this can have an effect on the breast cancer risk, of course.

So, when we're going to review these patients. We've started them on the HRT. It's a good idea to touch base at three months. With COVID times of course this can be over the phone but it's quite nice at some point I think to meet all these ladies. You do need to check their weight, because we really want to know what that BMI is and their height and not everyone will tell you. And also, people's BMIs as we know can go up as well as down. And therefore, it is important if we're starting them on oral preparation and then we then think - oh no, they've developed pre-diabetes, or they've put on weight, or they've been diagnosed with Crohn's disease etc. We need to review this patient to check that circumstances haven't changed. So, three months just to check, how are you? Has the bleeding settled? Because as I’ve said when you first start it irregular bleeding, whether it's sequential or continuous combined, is possible. And then once a year.

37.49 **Speaker:** So, we talked about starting, we've talked about review. What about stopping?

As I said, there is no arbitrary time limit says we need to review every year to ask - Is it still safe? Is it still relevant? Have your circumstances changed for the preparation?

The stopping side of things - you need to discuss it with the lady. So, we've already said that there’s possibly this temporary increase in cardiovascular disease if you stop it before you're 60. So, some people worry about continuing it thinking ‘Gosh, am I going to get a heart disease and therefore I want to stop it before I’m 60?’ And obviously evidence from studies would suggest that that’s not a good reason to stop it because in fact the opposite may happen. Whether you stop it suddenly or phase it out makes absolutely no difference to whether the symptoms will return. But if you stop it suddenly the symptoms, if they're going to come back, might come suddenly, which is unpleasant. If you phase it out at least you may have a gentler check whether the symptoms are going to come back. Of course, if they come back, then there’s no harm in restarting it. So, can you always consider vaginal treatment, and this is ongoing. So, when anyone talks to me about stopping their HRT, or really, I’ll talk about it even if they’ve come in about a sore finger! If they're on the HRT don't forget that even if they stop the tablets or patches because they’re not going through ‘the change’ which is where your levels are dropping and that’s what gives you the systemic symptoms, always talk about vaginal treatment because I mean when we go to old people's homes they do tend to smell a bit of urine and this is because of lack oestrogen in the vagina causing all those problems within the bladder and the bladder trigone and the urethra. So, you know I do think we need to talk about everyone. Don’t stop HRT without at least giving the patient the choice and the information required.

40.18 **Speaker:** Okay, so we're all going to worry about breast cancer, aren't we? If you pick up the Daily Mail you have a new scare story about almost everything. Anyway, if you've had breast cancer or you have breast cancer, this is considered a contraindication to systemic HRT. If a lady is so desperate that they will do anything, then that would be a lady you'd ask the oncologist, and you would involve a menopause specialist. So, remember vaginal oestrogens (I know I bang on about them all the time, don't I?) but they do not affect your risk of diagnosis or recurrence of breast cancer. But obviously with tamoxifen users, yes tamoxifen binds so strongly to those receptors in the breasts, that vaginal oestrogens can be considered. Again, I’d check with your local menopause specialist and the oncologist should always be involved. But in fact, as a specialist, I’m quite happy to use vaginal oestrogens for a short time because they can be very helpful for people with really bad symptoms.

But as you probably know much better than me, aromatase inhibitors, the way they work is that when we’re postmenopausal we still produce some testosterone. Our oestrogen levels have fallen because the ovaries are no longer producing it, but we do have testosterone and some of that testosterone the aromatase converts some into the oestrogen. So, the aromatase inhibitors the way they are working on these ladies where their ovaries are no longer producing oestrogen, then the aromatase inhibitors stop that conversion of some of your testosterone to oestrogen. Therefore, if you give them any sort of systemic oestrogen, they don't stop that. So, don’t forget don't give any oestrogen to people on aromatase inhibitors. In discussion with the oncologist sometimes these ladies have swapped onto tamoxifen and then we can perhaps consider carefully about vaginal oestrogens.

42.56 **Speaker:** Does systemic HRT increase breast cancer risk?

So, oestrogen only - there was that recent meta-analysis wasn't it that suggested that oestrogen only may have some effect on breast cancer risk. But then the next meta-analysis seems to show that it has little or no effect. So, oestrogen only HRT is much safer, as far as you know if you’re thinking about breast cancer risk. So, those ladies that have had their hysterectomy, don't have the endometriosis, don't have any endometrium left - these ladies can consider the oestrogen only HRT, being happy that it’s not going to have an effect on increasing that breast cancer risk.

So, the combined HRT it does carry a small increased risk of breast cancer and it is time dependent so if you are on it for five years or ten years, yes it does have a greater effect on your breast cancer risk than if you're on it for a shorter time. We know that all the research would suggest that dydrogesterone and micronised progesterone has a smaller impact on breast cancer risk. But we're talking an extra you know six or so per thousand ladies and therefore you've got to get it all in proportion.

So, life-style factors and we need to remember that obesity does more than double your risk of breast cancer. Fat is estrogenic so being having a lot of fat means more oestrogen around and therefore that has a much bigger effect on people than taking HRT. So, remember that when you're looking at risk these risks aren’t additive. If you’re an obese smoker and who does no exercise and things, unfortunately you are going to be more at risk anyway. So paradoxically the people where the risk has more impact on that overall risk of going to be those ladies with a very low background risk. Don't forget if you have a very, very high risk of breast cancer, adding in a 0.6 extra risk is of little consequence. So, a high-risk person has to make their decisions about HRT on their personal risk if it's very high. HRT is not going to have any significant impact on their risk because they are already high.

45.57 **Speaker:** The Women's Health Concern which is the patient information part of British Menopause Society has this really good little picture which obviously NICE guidance says - why not use pictorial information? So, as you can see this is just giving you an image. It's not completely accurate but it just gives an essence of it. So, a lot of people sadly will get breast cancer whether they’re on HRT or not. And far more people, even if you're on HRT, far more people would have got breast cancer whether that on HRT or not. But it does have an increased risk and that’s no two ways. In the past we have always used the data that showed that there was a slightly decreased risk of breast cancer in ladies who are on oestrogen only. That meta-analysis that was reported not that long ago suggested that this was not as true as we had thought. But in fact, breast cancer specialists are saying that part of the problem is, or not problem but the part of the explanation of this is, if you have cells in your breast that are hormone sensitive with the potential for malignant change then keeping on oestrogen and progesterone which is the normal balance, can keep those cells multiplying when lack of oestrogen would have suppressed them. But they think that oestrogen only HRT has a suppressing effect and therefore the reason that it looked like there were less is that those cancers, because they were suppressed by oestrogen only, may appear later. And those that have the progesterone, because they keep on having the hormonal influence, may actually show earlier.

48.09 **Speaker:** So, if you're on the pill obviously breast cancer risk is much the same as HRT. If you drink two units of alcohol per day it has a greater increase on your risk, than having your HRT. If ladies come to you and say I’m worried about taking HRT because of breast cancer risk and they're having more than two units of alcohol a day, you could say to them look if you are really worried by the symptoms why not cut down on the amount of alcohol you drink and then you will maintain the same risk. Smokers again - but this is what we said before. If you're obese, if your BMI is more than 30, you've more than doubled your risk and so those ladies who are very large, smoking, drinking the alcohol they can take HRT because they're not going to change their risk, they have already changed their risk. Obviously, you need to explain to them that they have increased their risk of breast cancer. Taking HRT is going to have an insignificant effect on increasing their risk. They've already done that with their weight. Obviously losing weight, stopping the alcohol, and taking more exercise would be really helpful to all of us.

49.37 **Speaker:** So, what about other cancers? We've talked about breast cancer a lot. So, there was some question - does it have an effect on ovarian cancer and some studies thought that a couple of the types did. The survival rates of epithelial ovarian cancer were not affected by HRT. We know that it doesn't affect recurrence in early endometrial cancer. But obviously if you have endometrium left as we've said before and you only take oestrogen you can increase the risk. So, if ladies who had endometrial cancer and had awful symptoms and wanted treatment you would give them progesterone and oestrogen. On the Welsh site there is a good chart that details risks with HRT.

50.44 **Speaker:** So, the summary of what we've talked about so far.

The perimenopause is an ideal time for intervention. So, whether you're considering HRT or not, this is a really good time to talk to people. You can have a massive impact on them if you're talking about you know the calcium-rich diet and the weight-bearing exercise. People worry about breast cancer risk and then if you have a fractured neck of femur one year survival rate is awful isn't it. So, it's a really good time.

With every single lady we have an opportunity to have a big impact on their lives and well-being and decrease our workload later. All women should have access. So, I really think that we need to be able to give them information to make their own minds up. There is a lot of information out there and if you can recommend good sites and good sources of information to your patients. The British Menopause Society have produced lots of little videos and they’re on YouTube. So, there are lots of places. I think it's very important as GPs - please try and keep an open mind about your patients’ decision about HRT. Because I think so many people do just say – ‘Oh you don't want to do that’ and I think that we're missing a trick because actually we could save ourselves work later on.

So, the safety of HRT does depend on how old you are, how long you take it for and making sure that you've got an appropriate choice of preparation for that particular lady.

But basically, if you're under 60 and you don’t have any health concerns then you shouldn't really be worried about the safety profile. You still need the information to make a sensible choice about whether you're going to consider it or not, but it's really a very safe thing to do as long as you are sensible but use that information

53.00 **Speaker:** So, thank you so much for listening. I hope that that's been useful and obviously I’m very happy to take any comments or questions, but I do hope that you found that relevant and useful.

53.17 **Chair:** Thank you Jane. That was really interesting. There are lots of questions. Some of them have been answered as you've continued, but we'll go through them.

If a lady who had the menopause at the age of 50, presents the GP as a delayed presentation at the age of 60 what you do?

53.33 **Speaker:** Well, I think that as I said these ladies, I feel very sorry for them because there seems to be quite a lot of pressure on people to get through the menopause. You know, keep going. Don't take this terrible stuff. And it leaves a lot of people really desperate. Being 60 is not a problem. You consider their risks and it's like the heart disease risk. With a 60-year-old, I’d always go for transdermal, and you'd also again advise them on the relative risk. So no, being 60 is no contraindication to starting HRT. But an appropriate preparation and do let her know the risks and then she can make her mind up.

54.27 **Chair:** Thank you. There are some questions about the gel and the spray. So, what are the brand names you would use of the gel and the spray?

54.33 **Speaker:** The gel is the EstroGel. It's used widely on the continent and we've used a lot of it with all these shortages. The problem there is the leaflet doesn't necessarily state how to take it in the way that would want. So, because we all know that you want the lowest preparation for the lowest time, that does the trick etc. But it's EstroGel.

Now the spray is literally a brand-new product. I can't remember the name but if you googled oestrogen, you’ll find it because it was presented at the latest British Menopause Society. It's just coming out, so it may not be in the BNF. It’ll probably be on the new instructional MIMS. But yes, if you looked up oestrogen on any of the BMS or any of those sites, you'd find it.

55.44 **Chair:** Do you know how to use the spray?

54.45 **Speaker:** It comes with a sort of - it looks a bit like a baby's bottle in a way with a little trumpet end, and you spray it directly onto the skin and it builds up a reservoir in your skin so it's just a spray onto the skin of your thigh.

55.05 **Chair:** Thank you. So, can we prescribe topical oestrogens in a young, non-menopausal woman with vaginal dryness?

54.45 **Speaker:** So yes. Obviously love talking about vaginal lesions, as you can probably tell. There are quite a few times when people can get vaginal dryness. The Depo-Provera users can be in a low oestrogen state. Breast feeding - again people could be hypo-estrogenic and get symptoms down below. People who have real soreness vulvitis /vulvodynia - it might well be trying worth trying oestrogen gel on them. I mean we use it in young, pre-pubescent children who have labial fusion and things. So yes, oestrogen gel can be used outside the post reproductive years in appropriate places. So, I reckon if they've tried everything it’s definitely worth a try.

57.10 **Chair:** Would transdermal preparations be safe in patients who've had a DVT or PE due to anti-phosphate?

57.17 **Speaker:** So, it won’t alter that personal risk, but these people are at high risk aren't they if you had your multiple PEs or whatever, you are the high-risk person. And so therefore you'd need to explain to them. I think if they were under the doctor, you'd wait until it had been at least six months from any clotting process. If they're under the haematologist, I would always discuss it with them. But basically, if you've had a DVT in the past, and a lot of these people it’s because they had a traffic accident or surgery or whatever, and so yes you can use transdermal on those people. But I think that if they are under a consultant I would always liaise.

58.08 **Chair:** Do you have a preference between EstroGel or Sandrena?

58.13 **Speaker:** EstroGel is quite easy because it's a pump. However, we are all different; different products suit different people and I think therefore we're lucky that we’ve got a choice. Just be aware of the preparations and if it's a preparation that’s appropriate. You can ask the preference of the patient. You’re probably actually going to be more influenced by how much they cost and your pharmacy advisor - what's going to be on your pharmacological list. So, no there's no preference between the Sandrena and the EstroGel except it's just what's on your formulary and what does the patient like.

59.00 **Chair:** The next question: How would you manage a lady who presents 10 years after she stopped her HRT with continuing bothersome symptoms?

59.11 **Speaker:** I’d definitely approach it with sympathy. What we need to hone in on, is which particular symptoms is she complaining about. I mean poor lady, if she was on her HRT her doctor said you know you're 55 you've got to stop it and all the symptoms came back and they’ve been persistent. You've got to obviously check that this person isn’t you know hypothyroid or got anything else going on. So, I would definitely make sure that you’re not missing a new problem. But if it's just that they were told to stop and they've suffered ever since, I would always think of a very low-dose transdermal product. But obviously you just need to double check. If it's sexual problems, then I would think about the vaginal route for that lady. Check the symptoms, check them on other diagnoses that you're missing, but yes then think about a transdermal.

1.00.24 **Chair:** There's a question about changing from sequential to continuous combined at age. So, someone's 45 maybe not sequential, would you change them to continuous combined at 47/48 or would you have to wait?

1.00.33 **Speaker:** I think that for these yes, I’d change them because a lot of people get fed up with bleeding. If they were truly you know perimenopausal, then it may well be that after two years or whatever that they won't bleed. I think some people just want the continuous combined just through choice. So, I would consider them. Very often if they are taking the sequential and they’re missing the odd bleed, if each time they have the bleed they're having a heavy bleed straight away, I would advise them to have the Mirena coil. But if they’re just having a scanty bleed and they’re missing, then it sounds like they should swap. Remember the people who need contraception those that take the progesterone only pill may have had no periods from when they started the progesterone pill. If you explained to the lady who's been on the progesterone only pill that the bleeding pattern is going to be the same as that or maybe none at all or maybe a bit hit and miss, then I think it's worth a try.

I wouldn't leave someone on the sequential forever, you know. You will find some people that have been on it for a very long time and you just say - it would be sensible to swap. But those ladies who have premature ovarian failure, then they often like a bleed because they feel more like their peers.

1.02.13 **Chair:** There's one about blood pressure. How do you use HRT if someone's got high blood pressure, or do you stop it if they became hypertensive on it?

1.02.21 **Speaker:** I think you'd want the transdermal preparation for these people. HRT doesn't have much impact on your blood pressure. The combined pill is a high dose synthetic preparation being given to people who have plenty of oestrogen already and this is can have a big impact on that blood pressure, so we've got to be aware of that. HRT is partially replacing a natural part of our makeup and therefore it has a lot less effect. The reason we like to check the blood pressure is that you would treat the blood pressure and sort that out as a separate issue to the HRT. I would treat the blood pressure as a separate issue but obviously if you thought ‘why isn't it coming down?’ you could think about it. But I’d always go for transdermal.

1.03.24 **Chair:** I think Jo's question has been asked really. It’s about starting it at the age of 50 or 60 but someone's upped the stakes a little bit what about if they're 70 - would you still continue?

1.02.21 **Speaker:** If a person has been on HRT all those years, I’d prefer them to be on a transdermal. Most menopause specialists would say that if you're taking HRT you have decreased your risk of heart disease and stroke. So, it's actually your osteoporosis. You know you're at a lower level than anyone anyway so if you just carry on taking it not at risk. I would explain to the patient that getting older in itself is going to increase their risks of heart disease and stroke and things. If someone's on it very long term it may be that you can slowly decrease the levels. When you're taking HRT in your 40s or 50s, I’d start them on the two milligrams and some people may need quite high doses early on. But if you're 70 you'd want the minimum - you might only want half your 25-microgram patch. So, explain to the patient that there are risks. These are made by them getting older, not by the HRT. If people are aware of the risk factors which you’ve explained to them carefully, then if they're terribly symptomatic as long as you've ruled out that there isn't an alternative cause for their hot flashes or whatever, then I would say yes you can. But obviously you'd be very cautious you go for the absolute minimum dose. Again, what symptoms are bothering them? And if it's the vaginal dryness or the water works, perhaps think about localised treatment. But you can start it later on but very cautiously in a tiny dose.

1.05.46 **Chair:** There's a question on progesterone. It causes the endometrium to thicken, so how does it protect against endometrial hyperplasia?

1.05.55 **Speaker:** Progesterone is the one that sort of maintains the endometria. It sort of stabilises I suppose. As we know the Mirena releases progesterone. It thins the lining of the womb and changes mucus at the neck of the womb. The progesterone only pill thins the light in the womb. And so that's how it stabilises it. And that's why the Mirena coil is so brilliant for hyperplasia and is used for the very elderly who have endometrial cancer even. We might treat it with a Merina coil alone or Medroxyprogesterone. So yes, it does have a stabilising effect.

1.06.43 **Chair:** Okay there's a couple more questions. We’ll see if we can fit them in the next few minutes. So, if the patient's been in amenorrhoeic for a couple of years and on Depo-Provera and then they have perimenopausal symptoms, would you go straight to continuous combined or sequential?

1.06.59 **Speaker:** So here we're talking about license, aren't we? If I was on the progesterone only pill if I still need contraception, I’d carry on with my progesterone only pill and if I’d been amenorrhoeic, I would just add in a continuous combined. It just makes sense. Or the implant if they've had it if they're used to that or if they have a slightly irregular bleeding pattern and they ‘re used to that pattern, then I’d just say yes keep going. But then if the bleeding became a nuisance, you'd consider the Mirena coil or go back to sequential. But I said we shouldn’t give someone sequential on top of their progesterone only pill. That doesn't make sense to me.

1.07.47 **Chair:** Oestrogen only is the lowest breast cancer risk, so can we pitch Mirena and oestrogen as similar risk profiles?

1.07.55 **Speaker:** There’s no evidence. There's no study being done on the risk profile, so I wouldn't assume that the Mirena with oestrogen only HRT has a lower risk. It sort of makes sense but there’s no evidence. So, I can't really say either way.

1.08.19 **Chair:** There's a question about guidelines. They mention active or recent arterial thromboembolic disease as a contraindication. So, what they want to know is how recent is recent, and how active is active?

1.08.29 **Speaker:** Well, I think if you if you've got a DVT I’d certainly leave it six months after they've had their treatment. But if a lady is on HRT and has a heart attack and then a lot of cardiologists would just continue the HRT. But as I said, if you have an embolic event you talk to the haematologist and most would say can you leave it for six months.

1.09.05 **Chair:** I've got about six or seven questions left in about three minutes, so we'll speed up now. So, if this lady has a hysterectomy done due to medication resistant endometriosis is it wise to give her a trial of HRT with progesterone and if there's no bleeding for the first few months safe to carry on with just oestrogen?

1.09.22 **Speaker:** I think if they've had a hysterectomy we don’t know whether they've got bleeding or not do we? That would be my only concern. If you have the endometrium in your vagina, like your cervix, then you can test whether you're going to bleed. I had a lady - she'd had a severe endometriosis. I’d been giving of HRT for seven/eight years. She then presented with vaginal bleeding and this was because she had a recurrence of her endometriosis in her vaginal stump and that was seven or eight years after being on the oestrogen only. So, I think a lot of people say well perhaps your endometriosis is burnt out but to be honest for people with endometriosis I’d probably just give them patch with a bit of progesterone potentially. I think endometriosis is horrible and therefore if they've had surgical treatment for it you know what just keep everything suppressed.

1.10.22 **Chair:** If someone had endometriosis which was resistant to medication before the age of 45 and then they developed the menopause due to hysterectomy what would we do then?

1.10.38 **Speaker:** Always continuous combined I would have thought. Well, I think if it's resistant, if they've still got some endometriosis continuous combined.

1.10.49 **Chair:** Premature ovarian failure. Using FSH if they're taking Desogestrel or the combined pill. Can you use that?

1.10.59 **Speaker:** Not with the combined pill. You can use the combined pill to treat them, but you need them not to be on oestrogen to check their FSH levels. And remember you'd need two readings of FSH about two to three months apart to check because all our hormones go like this - that’s why we're such even-tempered people us women.

1.11.41 **Chair:** A couple of questions on cancer risks which I think you've dealt with already. What’s the oldest woman you have prescribed HRT for?

1.11.41 **Speaker:** Probably someone in their 70s. Of course, vaginal oestrogens - another whole issue - any age.

1.11.55 **Chair:** If using sequential, what's the minimum time of progesterone block would you recommend?

1.12.00 **Speaker:** I tend to make it easy for the patient and tend to do two weeks on two weeks off. That just makes sense just because it's easy to remember. People say minimum of 12 days but it's much easier just to go for the 14. Just because it's much easier for all of us to plan our lives in easy ways.

1.12.27 **Chair:** The last question now - what's the best combination HRT and contraception if you're not using Mirena?

1.12.33 **Speaker:** Well, I suppose if you're under 50 you might think about the Qlaira because if you’ve got no risk factors and you’re not overweight etc. But if you're not using the Mirena, I think I’d try the ones that have the lower risk like a Femoston-Conti or Femoston Sequin but let's just see. But you can always step up. So, if there's symptoms not controlled, you change the oestrogen. If there's bleeding problems you’re going to change the progesterone. So, you would either increase the dose or go up the scale - the micronised progesterone, dydrogesterone, MPA, norethisterone. So, bleeding you go up the list but obviously you increase their risks of clotting and all that sort of thing but obviously we start trying to start down here. Once you're over 55, people aren't really going to want the Mirena coil. But earlier than that I just think you just explain that if they have troublesome bleeding. If they don't have troublesome bleeding - fab. If they do that's one way to sort it out.

1.13.49 **Chair:** How would you convert from sequential to combined and continuous and how long do you leave breakthrough bleeding before investigating?

1.14.00 **Speaker:** Oh, that's probably another whole series! I think we probably need to tackle bleeding problems with hormones as a separate issue.

But bleeding is very common in the first three months. It's quite common in the next six months. You just have to take a careful history. Is it breakthrough bleeding or isn't it? I think if people want to try on continuous combined, see what the bleeding pattern settles down as. But yes, postmenopausal bleeding is probably another thing we need to talk about.

1.14.30 **Chair:** Is Utrogestan a micronised progesterone and if so, is there a preference whether to prescribe cyclical or continuously? The BNF has a few different regimes.

1.14.45 **Speaker:** Utrogestan and EstroGel have different regimes to what we're using in this country. If you're giving the modernised progesterone you give the same dose. So, if you're doing it two weeks on two weeks off, you're going to give two capsules a night two weeks on and two off. If you're giving it continuous you give one capsule a night for the whole time. And that's the same for all of them. If you're doing the NPA you're going to do 5milligrams every day or 10milligrams half the time. Norethisterone you're going to do 1milligram etc. So that sort of pattern.

1.15.25 **Chair:** Two quick questions. Can we leave the Mirena coil in if it's inserted after the age of 45 for another 10 years, to act as HRT?

1.15.33 **Speaker:** You can leave it in for contraception purposes or bleeding purposes. So if it's fitted after the age of 45 for the other two indications (contraception and heavy menstrual bleeding) you can leave it in and I take it out at 55. The license is four years for HRT. I’d let it go to five years then I’d either change it or I’d explain to the patient do you want your Mirena changed or should we add in the progesterone.

1.16.09 **Chair:** And for the 65 of us still here, the last question: can micronised progesterone be safely used vaginally to protect the endometrium?

1.16.16 **Speaker:** I think the magnetised progesterone capsule - some people do want to pop them up. I’m not sure how well they're absorbed. So, I’m not sure whether they'd give as good endometrial protection. You can get those200 milligram pessaries but they're very expensive. Your pharmacy advisor might get a bit worried by that. But I’m not sure they'd be absorbed very well.

1.16.46 **Chair:** Can you just clarify the Utrogestan regime again. Which is the one that you would use?

1.16.54 **Speaker:** Utrogestan - with the gel I’d start with one pump a day rubbed into the thigh leave it to dry and that's every day. And I’d go then to two pumps if symptoms aren't controlled - again for four to six weeks. You can go up. So, the EstroGel every day but start at one pump rather than start at two pumps unless you're converting maybe if you're converting them from two milligrams of all to then you'd go straight for the two pumps but if they're starting afresh, I’d always start with one pump and build up. But every day. No breaks.

1.17.45 **Chair:** Brilliant. We're done. Thank you very much Jane that was really informative. Thank you everyone for attending. As I said that this is going to be part of a series. We've got one on genitourinary problems next month and then we'll probably have one every month or so until we run out of ideas. Thank you all. Have a nice evening. Thank you very much Jane.