

Radio Interview - Esther Crawley & FITNET Trial – 05-Nov-2016

Transcript of Radio Interview between Dr Phil Hammond and Professor Esther Crawley, on BBC Radio Bristol, 5th November 2016, from 09:00am

<http://www.bbc.co.uk/programmes/p04cd54b>

This segment begins at 09:10am (minutes 10.30 to 33.05 on the recording).

PH = Phil Hammond, EC = Esther Crawley

[10.30 PH] Now we're going to talk about Chronic Fatigue Syndrome (ME) now. I'm delighted to welcome Professor Esther Crawley, who I should declare (not a conflict of interest), I should declare that I work in her unit, so we both work treating young people with Chronic Fatigue Syndrome.

You announced a new trial, that you're recruiting people into at the moment, Esther - but before we get onto that, we probably have more questions into the show than I've ever had, on Chronic Fatigue syndrome. Why do you think it attracts such a level of interest, why are people so passionate about it ?

[10.58 EC] I think that the thing about ME (chronic fatigue syndrome) is that it's really importance. It's important for two reasons – it's very common, so probably about 1% of teenagers are missing at least a day a week of school with this illness, probably about 2% are affected, and it's very very disabling, the children miss a lot of school, parents have to stop work, siblings are affected, it uses up a lot of health resources, so it's a very very important illness, but we know very little about it. So there's a very large number of children and adults with this condition, who are not getting any treatment.

[11.29 PH] We certainly know very little about it; we know enough about it to be able to justify setting up specialist units like the ones we [larrikins?] work in, so what are the things we know about it so far – what is known about chronic fatigue syndrome, in terms of its definition and how you diagnose it ?

[11.42 EC] So Chronic Fatigue Syndrome is defined or is diagnosed in children or in adults who have fatigue that stops them doing things, so it has to be disabling, and it has to last a long time. So in children it has to last at least 3 months, in adults 4 months. And then there's a range of other symptoms that are very common in the condition – so one of the one's that's most helpful for diagnosis is something called Post Exertional Malaise; so what that means is that after you do something, you feel much worse afterwards – and that's very helpful in differentiating and helping us know (for example) that it's not depression.

[12.14 PH] So some children who do physical activity can be wiped out for several days afterwards, sometimes longer, they can be 'crashing'.

[12:20 EC] That's right. Other problems can be headaches; memory and concentration problems are almost universal in this condition; there's a particular sleep pattern, where for both adults and children, which is that [12.32] it's very difficult to get off to sleep, and very very difficult to wake up in the morning; teenagers with this condition always sleep too much. So that's the diagnosis.

[12.40 EC] What else we know about it, we know that it's heritable (so it runs in families), interestingly it's more heritable in children than in adults; we know that in most cases it's triggered by something, usually in children a virus or a bacterial infection; and we know that although about 30% of children / teenagers develop problems with low mood and anxiety (no surprising given how awful it is), most teenagers do not have problems with mood.

[13.06 PH] So it's a physical condition that is likely to have a biological basis ?

[13.10 EC] Yeah yeah, that's what we think.

[13.11 PH] So why aren't we putting all our research money into finding that biological basis, rather than trying behavioural changes in terms of sleep and activity – or do you think there won't be a single biological basis, do you think chronic fatigue syndrome will turn out to be 20 different diseases ?

[13.24 EC] Ahh now Phil you see, you've asked me several questions all at once, so let's go for the why-it biological basis first ...

[13.28 PH] Do you think it has a biological basis, and if you do, surely we should be putting all our research money into finding the biological basis of it ?

[13.34 EC] Yeah, an illness that is genetically inheritable, triggered by an infection, and has the symptoms that I see in the clinic, definitely has a biological basis; and we absolutely must find out about the biology. In my mind, the first thing that we need to do is to understand the [13.45] differences between different types of chronic fatigue syndrome - this is not one illness, this is going to be several different illnesses – and the way to do that in the study we've got planned, is we need to look at the genes and all of the biology in thousands and thousands of adults and children – and that's a very important study that we've been trying to do for several years and we'll be trying to do again next year.

[14.07 EC] The issue is that at the moment, there are hundreds of thousands of children and adults with this condition; understanding the biology is not going to change the treatment for 5 or even 10 years' time, and children and adults need treatment right now. So we have to do both things; we have to understand the biology and do research into the biology, and we also have to develop better treatments for children with chronic fatigue syndrome.

[14.30 PH] So I've got a good question here – [I'm not going to read out the name of the person because I don't want to identify the particular patient] – it says “my daughter was diagnosed by Dr Hammond” [EC: that's you] “after 8 years of unasked questions from my local health trust, she had an infection at birth in hospital, she's now age 14. Whilst any publicity about this illness can be positive, how can Cognitive Behaviour Therapy solve an illness that is not psychological ?” We've had lots of similar questions about that, what's your response ?

[14.52 EC] So, Cognitive Behavioural Therapy is there to help people change important things, for example sleep and exercise. Now, in our clinic what we do is we help teenagers to wake up at the same time every morning, and restrict their sleep. That's a very potent biological stimulus. Once you change your sleep, you change a lot of biology, you change the way your brain produces steroid, you change something called the hypothalamic pituitary axis, there's loads of stuff you change.

[15.26 EC] So, if we had a pill we would give it, but a lot of this treatment is as potent as giving a pill. The same is true with exercise, exercise [is a] very potent biological stimulus. Patients with this condition do loads one day, and not very much the next, and we believe that that is, that stimulates a

lot of the symptoms and stimulates the biology; so we try and help children do the same thing every day; and again, that's seems to be a very potent biological thing that we're doing.

[15.51 PH] So you think that Cognitive Behavioural Therapy works by changing people's sleep routines and their activity routines, which has a profound affect on their hormone levels and their biology ?

[16.00 EC] Yeah, and I think that, the thing is that a lot of teenagers, you can give them a lot of information about it, and you can tell them what to do, and they just go and do it, but changing sleep and changing exercise is really hard. So what Cognitive Behavioural Therapy does is to help support teenagers in making those changes.

[16.17 PH] And how good is the evidence at the moment to support Cognitive Behavioural Therapy and Graded Exercise Therapy, which are two therapies particularly offered at the moment to adults (I know you're trialling it in our particular unit). A lot of people have criticised the PACE research data, and now that the researchers have been forced to hand over the data it's been reanalysed and they're suggesting that the outcomes aren't as good as originally claimed in the original trial – and that actually, Cognitive Behavioural Therapy and Graded Exercise Therapy don't work very well.

[16:41 EC] Okay, so again there are several questions, let me see if I can take them one by one.

So the evidence for Cognitive Behavioural Therapy and Graded Exercise Therapy is good, it's good in adults; so there are quite a lot of trials in adults now that show that, if you're an adult with Chronic Fatigue Syndrome, your best chance of getting better is Cognitive Behavioural Therapy and Graded Exercise Therapy. In children, there are about 5 trials that show that Cognitive Behavioural Therapy has a much better outcome for Chronic Fatigue Syndrome.

[17.11 EC] We've reviewed all the world literature for recovery, and if you're a child with Chronic Fatigue Syndrome, whichever method you choose, you have about a two-thirds chance of recovery at 6 months, with treatment, compared to a less than ten percent chance of recovery without treatment. So I'll just say that again, two thirds at six months with treatment, compared to 10% without treatment.

[17.31 EC] So whichever, if you're a child or an adult with this condition, it's really really important; the important message is that you're much more likely to get better, if you get specialist treatment.

[17.44 PH] So do you ...

[17.44 EC] Shall I go on to the PACE Trial ?

[17.44 PH] Yes, because you don't appear to accept the criticisms of the PACE Trial, now that it's been reanalysed. Are you saying, that it's conclusion should stand, or that looking back on it, probably the treatments aren't as effective as we thought ?

[17.55 EC] So, I think we have to be absolutely clear about what they did in the reanalysis. So the PACE trial looked at your chance of getting better with GET (Graded Exercise Therapy), CBT (Cognitive Behavioural Therapy), or Pacing in addition to Specialist Medical Care. So, your chance of improvement. And it showed very convincingly that you're much more likely to improve with those treatments.

[18.17 EC] Now, as a secondary analysis (so that was their main analysis) that was what they always intended to do ...

[18.22 PH] And you're satisfied the trial was properly constructed and fair and valid ?

[18.24 EC] Absolutely, it was a GREAT, great trial. I mean, you know, it's very difficult to do trials in this condition, but they did as good as anybody could have done.

[18.28 EC] Now, the reanalysis was based on recovery, and the reanalysis just looked at recovery. Now, in my research, what I found (and I don't think this will be any surprise to anybody with this condition), is that how you define recovery, depends on who you are. So every child that we asked, on how to define recovery, comes up with a different definition. What the reanalysis did is, first of all they did a reanalysis of recovery based on what the authors originally said they were gonna do, and that reanalysis done by the authors is entirely consistent with their original results.

[18.58 EC] Then the people that did the reanalysis did it again, using a different definition of recovery, that was much much harder to reach – and the trial just wasn't big enough to show a difference, and they didn't show a difference. Now, you know, you can pick and choose how you redefine recovery, and that's all very important research, but the message from the PACE Trial is not contested; the message is, if you want to get better, you're much more likely to get better if you get specialist treatment.

[19.26 PH] Okay. And before we go on to the new trial that you're doing at the moment, I just want to go back to what your thoughts are, that the biological basis of this might be. Because people say in some people there might be raised inflammatory markers, in some people it might be due to the hypothalamo-pituitary axis, it might be due to the microbiome, it might be due to the mitochondria, it might be due to all sorts of things. Have the things that have been looked into in smaller trials – there was a news piece about it, a bit like going into hibernation – now I know these are all small studies, but if you were theorising, if you were given a million pounds to start researching into the biological basis, what are the particular avenues that you think are most likely to be fruitful ?

[19.58 EC] So, I think when we look at this, we're limited by imagination, and (ah) the studies to date are too small, and are what we call 'cross-sectional' studies. So, if I was given a million pounds, I would do what we've planned to do, which is to collect biological samples from thousands and thousands of patients, to subdivide the illness into [20.19] different things. So what I think is probably a group of patients with chronic fatigue syndrome have a raised inflammatory response to infection; I think there's a group of patients who very rapidly disorder their cortisol levels; I think there's going to be a group of patients who may have problems with serotonin. But the truth of the matter is we don't know who those patients are going to be, and we [20.38] need really large, large sample sizes with multiple time points, to work out this very very complicated illness.

And we have to stop doing these really small studies, because I think they're just confusing. They don't end up being what's called 'replicated', so they're not reproduced a second time, and I don't think they're adding, at the moment, to the world literature.

[20.58 PH] So you're committed to keep trying to do a large scale biological trial ...

[21.02 EC] Absolutely, we've been trying to do that ...

[21.03 PH] As well as the other things you're doing about CBT, that's what you want to do ...

[21.05 EC] Yeah, yeah, we need to do both.

[21.08 PH] Now, we need to talk about the FITNET Trial, which is a trial you're recruiting for at the moment, after we've heard a bit from Steely Dan ...

[21.15 music ...]

[24.13 PH] Esther, tell us a little about the new research trial you're doing, the FITNET Trial, because rather perversely for Radio Bristol, that doesn't apply to young people in Bristol, does it? Tell us about why you're doing this research, and what you hope to achieve.

[24.25 EC] Yes well we've talked about how common this illness is, 1% of kids missing a day a week of school; we know the evidence shows that if they access a specialist treatment they're much more likely to get better than without. The problem for me, or the problem for these children more importantly, is that in the UK very few of them have access to treatment, and it really bothers me that we have an important illness, a treatment that can work, and that most children can't get it. And so this trial is designed to try and see if we can get specialist treatment to children at home, and children will have either FITNET or activity management.

[24.59 PH] So, explain what FITNET is, we haven't done that.

[25.00 EC] FITNET is internet delivered CBT. So the children will get a lot of information, will be doing all the stuff they're doing when they come see us in clinic – but they'll be doing it at home. They'll have a therapist who they'll have contact with and sessions with, once a week to begin with, then every two weeks, at home, online.

[25.16 PH] Who will actually make the diagnosis, will that be done online as well?

[25.20 EC] So the local GP and paediatrician would be needed to make a diagnosis, and then we do a whole load of screening and we essentially check the diagnosis very carefully before they come into the trial.

[25.32 EC] So I think it's a really interesting study; it was shown to be effective in the Netherlands where 63% of children seemed to make a full recovery at 6 months.

[25.43 PH] One of our listeners has texted in and said he read that actually, that recovery wasn't sustained over time, that six months later there was no difference – is that correct?

[25.54 EC] Oh, people have really made a mistake on this. So, in the FITNET Trial, they were offered FITNET or usual care for six months, and then if they didn't make a recovery in the usual care, they were offered FITNET again, and they were then followed up at 2 to 3 years, so of course what happened is that a lot of the children who were in the original control arm, then got FITNET as well, so it's not surprising that at 2 or 3 years, the results were similar. However, their recovery was still very high, it was still in the same region of about two-thirds.

[26.28 EC] And I think it's really important to say, that in the FITNET trial, children who got FITNET at the start, were better very quickly, compared to those at three years. And if you were a parent of a child, you know, you'd want your child to get better as soon as possible, and these are CHILDREN, teenagers, you can't leave them three years to make a recovery, they need to get treatment too.

[26.54 PH] But staring at a screen can be a high energy activity for young people, and a lot of them do enough screen-staring already; isn't it something slightly counter-intuitive to deliver their therapy online? I understand that making them travel to a clinic miles away is completely exhausting, but is staring at a screen a good thing to do for chronic fatigue syndrome?

[27.09 EC] Well, I am more interested in getting them therapy at home, than worrying too much about them staring at the screen. And for me, it's completely intuitive that children should have treatment delivered in a medium that they're very comfortable and familiar with. So we talk a lot

with teenagers, we have tested the FITNET internet platform to destruction with teenagers, and teenagers tell us they want stuff online, they want stuff at home, they don't want to travel, they like the media that they're very familiar with.

[27.40 PH] With Skype, what I'm worried about is that if this is very successful, I'm going to be out of a job; I like to think I'm kind and compassionate, I have a 90 minute consultation when I first see patients and try and make the diagnosis, I do lots of empathy and compassion and understanding, and reinforce that it's a real illness. If it's shown that actually doing online CBT is as or more effective than me, then we're out of a job, aren't we ?

[28.00 EC] You know what I think [...] there are lots of different forms of this illness, and there are also different children who want different things. I think that children have the right to choose how they get seen, and what treatment they have to offer. So if we show that this treatment is effective, as far as I'm concerned children should still have choice; if they want to do Graded Exercise Therapy, which a lot of children do, they should have it. If they want FITNET, which a lot of children seem to want, they should have it. And if they want to see you, Phil, they should have that as well.

[28.30 PH] So like every illness, there are different therapies because there are different types of illness and different people that work for different. So, tell us the response you've had so far since FITNET was announced.

[28.39 EC] I have been overwhelmed with children, teenagers and parents from all over the UK, asking to be able to come into this trial. It's something – I also want to say – there are people who are trying to stop our research, but they are only a tiny minority, compared to the overwhelming number of teenagers and parents who are absolutely desperate to take part in research, and desperate for treatment and help.

[29.02 PH] Do you accept that people are legitimately allowed to question stuff, to apply to look at data if they want to ? I mean, it's part of the therapeutic process is to have patients and carers asking awkward questions, and challenging us.

[29.12 EC] Yeah, and that's why we have lots of Frequently Asked Questions on our website, and as we get questions we post responses. And particularly for example the long term recovery rate, it's very important for us to go out and say, "actually if you go back and read that paper again, a lot of the people with children in the control arm, ended up with FITNET".

[29.28 PH] Finally, one of the big controversies about Chronic Fatigue Syndrome is Graded Exercise Therapy. We said that one of the diagnostic criteria for Chronic Fatigue Syndrome, is that even a small amount of exercise can absolutely wipe someone out for several days, particularly in the severe stages of the illness. A lot of people say they were given Graded Exercise Therapy and it made them even worse, that the activity absolutely floored them; and that whenever you offer it in a research trial or therapeutic approach, you should warn people of the potential harm. Are you doing that ?

[29.52 EC] So the evidence, the best evidence that you can ever get is what's called the Systematic Review, it's when you look at all of the papers, and all of the research that's ever been done, and you combine the data. And the largest systematic review, of over 1,500 people was absolutely clear, there was no evidence of harm.

[30.11 PH] So what do we mean by Graded Exercise Therapy ? It means you're doing it incrementally, little by little, rather than risking somebody crashing and burning – is that right ?

[30.18 EC] Well I think that's an important point. So if you just tell someone to just go and do exercise, I would expect that they would get their symptoms made worse. In fact, what we're doing in our trial, and what all the trials do, is to usually reduce exercise at the start. So in children with Chronic Fatigue Syndrome, quite a lot of them are still trying to do sport or ballet or stuff like that, and what we're trying to do is say, actually, don't go and do all of this exercise, do less ...

[30.43 PH] So you're actually restricting their exercise, instead of allowing them what they want to do ?

[30.45 EC] ... and I want to say something – which is that we interviewed all the children in our trial – they really like Graded Exercise Therapy – and the only complaint that we've had is that we're restricting their activity too much. So this isn't about making children go and do more exercise, that's probably why we don't see harm in our trials, compared to patient report of harms, which is probably more about someone saying 'go and do more exercise' or themselves doing more exercise.

[31.14 PH] Okay, so most people listening to this will be in the Bristol area, or the Bristol and Bath area – if that's the case, then the FITNET trial isn't applicable for them, it's for people who are outside the area.

[31.23 EC] [if] FITNET's not applicable, they can come and see you or they can come and see me, and they can get face to face contact. We believe that the only way to advance research in this area is that every child (rather like with cancer) every child should be offered a trial.

[31.39 PH] Okay, and if people want to find out more about it, and about FITNET, more about the research that's being done, more about your interpretation of the PACE Trial or whatever, is there one website you can direct them to, that has all this information up there ?

[31.46 EC] So if they want to find out about FITNET, they can go onto the FITNET.NHS website; if they want to find out about our research, all our papers, they are online and readily accessible.

[31.57 PH] And what about any sort of charities ? What I've found is really important with all illnesses, is that often the best support comes from other people going through the same stuff – to support you, and give you tips how to cope – are there any good charities and resources you would recommend ?

[32.06 EC] Well, we recommend the Association for Young People with ME [AYME], a great national charity and a load of great resources, that we work very closely with.

[32.15 PH] Thank you. And what do you see, how optimistic are you about the future – do you envisage one day, looking forward 5 or 10 years, we will actually have a drug therapy that we can use for Chronic Fatigue Syndrome ? I know I use occasionally amitriptyline and occasionally melatonin to help people to sleep. But do you think there will be either in a subset of patients or a lot of patients, a pharmacological therapy that will dramatically improve, if not cure, their symptoms ?

[32.33 EC] Dunno, I think it would be nice if there were a drug therapy for patients with chronic Fatigue Syndrome, but I'd also say to you that most of the parents and most of the children that come to my clinic, don't want medicine, they'd much rather do other stuff that gets them better, rather than take a tablet. I think in ten years' time we'll understand the different types of Chronic Fatigue Syndrome, and hopefully we'll have better treatment that works in a higher number of patients within each subtype.

[33.02] [thank you etc]