**Sex and Post SSRI EBM Dysfunction**

**Slide 1**: There is some great art work in this talk – done by Bill James who is listening in – and can answer all the important questions at the end. My part of the talk is about two things. One is a sexual dysfunction syndrome that may be new to you. The other is about a fault-line in Evidence Based Medicine (EBM) that this Post SSRI sexual syndrome reveals.

**Slide 2**: This view of Menai Bridge is one of the most iconic scenes in Wales. It’s a few hundred yards from where I used to live. Two thousand years ago, the Romans and Celts faced off against each other on either side of the Straits below. On the left is Ynys Mon, an island. On the right is the UK mainland. Ynys Mon is at the dead centre of the Western European Archipelago. If you draw a line from the Westernmost point of Ireland to the Easternmost point of England and the Northernmost point of Scotland to the Southernmost point of England, they intersect here.

The Romans never made it to Ynys Mon. The waters look calm in the picture, but even on a calm day the tide races. The Straits have an astonishing tidal fall. Both the Romans and the Celts set up nets to catch eels racing by in the rapids.

What’s this got to do with sex and EBM? Well, 2000 years later we still don’t know how eels reproduce – how they go about having sex.

The Bridge – built 202 years ago was the first of its kind in the world.

**Slide 3**: Engineers traditionally build safety into their systems. Although built a century before cars were dreamt of, Menai Bridge can take a string of juggernauts and coachloads of people – no problem.

We tend to figure, thanks to EBM, this is the way health is going. We used to have rickety old bridges incapable of holding much but now we have engineered health to be more like Menai Bridge.

**Slide 4**: It’s just the opposite. Health can never be engineered the way Menai Bridge was. It is always going to be more of a Rope Bridge. The problem is because of EBM the gaps between the slats on the bridge are getting wider and the slats are rotting. You are liable to fall through if you put your weight on them. More of us now die or are injured in our health systems and treatments compared with just a few years ago.

**Slide 5**: Here is another way to put it – getting us closer to sex. Most of us are more comfortable with the image of the Shower on the Left than the Bidet on the Right. We prefer a Top-Down to Bottom-Up approach as do our political and economic systems. Through to 1991, healthcare was about Bidets now its Showers. You could reframe the original EBM proposal of marrying evidence to clinical experience and patients values in terms of a marriage of Bidet and Shower – but in fact EBM got rid of Bidets.

**Slide 6**: Bidets went out of fashion on September 20th 1991. The year before an old-style Medical Bidet article described 6 cases of people becoming suicidal on Prozac. You took the drug away and the problem cleared up. You reintroduced it and the problem came back – by all standards of medical causality Prozac and other SSRIs caused suicide. There are maybe 300 drugs companies have quietly internally decided cause suicide.

Publicly it’s different. Defending Prozac, Eli Lilly faced an FDA Hearing at which they pitched their Shower – RCTs of Prozac - against the Bidet of clinical judgment calls and asked which are you going to believe the anecdotes or the science? This was a defence first adopted by the Pedophile Liberation Front 20 years earlier – the plural of anecdotes is not data. The original phrase is the plural of anecdotes is data - otherwise Google wouldn’t work.

Lilly recruited the most anti-Pharma journal, the BMJ, who published an article, the Beasley article, which supposedly showed no evidence in Lilly RCTs – or rather no statistically significant evidence - that Prozac caused suicidal events. In fact, the footnotes show there is a statistically significant increase in suicidal events on Prozac. Companies often put the truth out there in broad daylight – able to depend on the naivety of doctors and journals who think of themselves as the good guys to miss what is staring them in the face.

Lilly’s apparent success – the FDA didn’t agree the drug didn’t cause suicide - they agreed not to warn. But this meant the end of Bidets and the triumph of Showers – journals would no longer accept Case reports. Journals got a fortune from RCTs and meta-analyses of RCTs but nothing but trouble from Bidets. Drugs Bulletins vanished. We got Free Showers, Guidelines, instead which only mention benefits.

This is not just the case for antidepressants, it holds for all on-patent drugs**. The greatest concentration of Fake News on earth centres on the drugs our doctors give us**. The ghosts hype the benefits to the point where negative trials are published as positive – and hide the harms.

**If you don’t make the first Bidet call and you rely on Showers to keep you in good clinical odour, you’re going to end up with a problem.** If you can’t recognise the harms your treatment causes, you can no longer see your patient. S/he becomes invisible.

If patients become invisible, then doctors do too. If drugs can only do good and cannot harm, then doctors are expensive prescribers and managers will figure on getting nursing staff, PAs and pharmacists, who are all cheaper, to do the prescribing.

**Slide 7:** There is a great thriller ***Malcharist*** about akathisia leading to suicide and the role of ghostwriting and data sequestration.

Let’s say I give Tom Perry an SSRI and he becomes suicidal and comes in and tells me he thinks the drug is causing it - the task of a scientist is to establish what is happening this person right in front of me who has taken a drug. If after listening, I agree with Tom the drug is more likely to have caused the problem than his condition, this is where solid knowledge, objectivity, comes from made even more solid if some other doctors and patients report the same thing.

If this view is at odds with the apparent evidence, a second scientific task is to explain the mismatch between the scientific literature and what Tom and I now think.

In the case of the SSRIs and suicide, the mismatch stems from the fact that close to 100% of the literature on these drugs was ghostwritten and in 100% of cases there is no access to the data from the clinical trials of these drugs. Regulators don’t see it, NICE don’t see it, the authors of papers don’t see it.

When you get to see the data, it becomes clear in the case of suicide and antidepressants that the evidence matches what Tom and I now think.

The wars about whether antidepressants cause suicide were pretty brutal. Fifteen years later, most prescribers in N America figure antidepressants don’t cause a problem and FDA only bowed to some pressure group like the Church of Scientology when they put warnings on the drugs.

How else to explain the data on antidepressants which show them to be the second most commonly taken drugs by teenage girls despite 30 out of 30 trials done being negative – the greatest concentration of negative trials for any indication ever in human history. Even the Prozac trials that led to its approval for children are negative. The published literature of course isn’t negative.

**Slide 8**: Compared with suicide, sex will be easy-peasy. Everyone wants to hear about sex. The media will lap it up.

The sex and antidepressants story starts with Frank Ayd in 1961. Ayd has just discovered the antidepressant effects of amitriptyline – one of the first tricyclic antidepressants. The best selling one.

The tricyclics were a treatment for melancholia for which SSRIs are totally ineffective. Melancholia causes suicide. The only treatment for it prior to 1960 was ECT – which Ayd had given his father on their kitchen table. Melancholia also causes loss of libido. Despite it being his drug, and being so personally aware of its benefits, and the difficulty in distinguishing between the effects of the illness and of the treatment, within a year of its launch Ayd reported that amitriptyline could cause sexual dysfunction.

**Slide 9**: I don’t want to show you a series of pictures of middle-aged white men, so here is something prettier. In 2001, Sandra Leiblum put Persistent Genital Arousal Disorder (PGAD) on the map. This is an horrific condition where women’s genitals go berserk. It can be trigged by the vibration of a car. It is so unpleasant they take gabapentin, 100 Botox shots to the vulval area – almost anything they think might help. Clitoridectomy pudendal nerve ablation – you name it, they’ve tried it.

There is a background story. Around 1970, George Beaumont joined Ciba-Geigy and was given the job of marketing clomipramine, which we now regard as the most potent antidepressant we have and is the drug the SSRIs come from. George had two ideas – one to market it for OCD.

His other idea led to a placement of stories in Britain’s popular press about a well-known starlet who was thrilled with clomipramine. The usual antidepressant dose is 150 mg. But taking 10 mg 30 minutes before sex cured her boyfriend’s premature ejaculation problem – and she was thrilled.

Clomipramine made major inroads into the OCD market. This brought Beaumont up against Isaac Marks, the leading behaviour therapist. OCD was the jewel in his behaviour therapy crown. Marks was a tough take-no-hostages hombre. He was quick to point out the hazards of clomipramine – one of his patients, a lady, a nun, was tortured by repeated orgasms on stopping clomipramine. This is probably a first report of PGAD – in the mid-1980s.

We now know stopping SSRIs is the most common trigger to PGAD. Clomipramine is the drug from which the SSRIs come. Serotonin reuptake inhibitors includes many antihistamines, some tetracycline anbiotics, and pain killers like tramadol

**Slide 10:** PSSD – Post SSRI Sexual Dysfunction – is pretty well the opposite of PGAD. You have numb genitals and no orgasm. My first brush with PSSD came in 2000, when a woman in her 30s told me she had sexual dysfunction from her SSRI – citalopram. Could it be the bromide element to citalopram HBr she asked – not a bad guess.

I reassured her the problem would clear when she stopped the drug. She replied she’d been off treatment for 3 months and she could take a hard-bristled brush and rub it up and down her genitals and feel nothing. We tried a lot of obvious things like Viagra but nothing helped.

Here you see Stormy Daniels. All erotic points are covered so you are safe to use the image on Facebook. Donald Trump is also here. His head is on the brush - although he looks a little floppy rather than hard bristled.

The first journal reports appeared in 2006. It is now clear that by that stage many people had the condition for well over a decade without relief. The first report of PSSD to the British regulator was in 1991, since when the regulator has had over a thousand reports and done nothing about them.

**Slide 11:** A similar condition, Post Finasteride Syndrome (PFS) was reported in 2011, and drug taken by young men in their teens and early twenties to try and combat hair loss. Again, it is clear people had been enduringly affected for a decade or more before the first published reports.

In 2014, a post retinoid Sexual Dysfunction (PRSD) was reported following a use of isotretinoin for acne. People again had been affected for decades before from this drug that was on the market since 1984. PRSD appears to have led to a homicide in Chicago in 2006 when a man killed the doctor who gave him Accutane and PRSD.

**Slide 12**: The core features of these conditions are a genital numbing, a muting of orgasms or inability to orgasm, with a subsequent loss of function and libido.

A lot of those affected report an emotional disconnection or blunting or general anhedonia that may be as bad as the sexual problems. They also report other sensory disturbances.

On RxISK.org we have had over a thousand reports of PSSD and related conditions from over 30 different countries. These conditions can happen to all ages, both sexes, all ethnic groups. PSSD can start after 2 – 3 tablets. Or like Tardive Dyskinesia, it may only become apparent there is something badly wrong when treatment is stopped. Some recover after months or years, some remain affected for life.

We don’t know where the problem lies. Most people with PSSD think their brain must be affected but I think it lies in skin and is a peripheral sensory problem. Our brain is not the boundary between us and others – our skin is and we know little more about it than we do about the sex lives of eels. It is a mysterious domain – which is so strange.

**Slide 13:** The distress of these conditions is intense. Many have killed themselves. Others seek medical assistance in dying (MAID) – and it will be interesting to see what the new Canadian provisions for MAID might make of this. The distress is made worse for people by getting ridiculed by doctors and other healthcare staff – drug has left your body months ago and you still think it is causing the problem. Access google and you will be ill for life – you need an antidepressant dude or maybe trauma therapy.

We have a fund of $125,000 on RxISK for anyone who comes up with an answer.

I am sure there is a Nobel Prize waiting for the person who finds the answer – it would change our ideas about receptor theory entirely. Imagine if we could give a few doses of a drug and produce an enduring good effect?

Here is where Sex begins to crash into EBM.

The SSRIs derive from clomipramine which we knew from two decades previously caused genital numbing. The 2-week healthy volunteer trials of these drugs in the 1980s showed severe sexual dysfunction in over 50% of volunteers – in some cases dysfunction that lasted after treatment stopped.

Despite this the clinical trials of these drugs portrayed them as being linked to sexual dysfunction in no more than 5% of cases. The story for doctors like me was - it clears when treatment stops.

How does more than 50% become less than 5%? Easy. You don’t need ghostwriters and don’t need to hide the data (except the healthy volunteer data). You just run an RCT. Dangle a primary endpoint in front of investigators and the problem vanishes – especially anything that could be a manifestation of an illness.

We assume RCTs focus on the commonest effect of a drug and tell us all we need to know about a drug. Some rare effects might be or effects that happen after the trial period ends.

But genital numbing happens in close to 100% of cases within half an hour of the first dose of treatment – this is vastly more common that any antidepressant effect. Dangle a primary endpoint in front of investigators and you can make anything vanish.

**Slide 14:** Here is the second point about EBM.

Clinical practice and all science is a judicial exercise not an algorithmic one. To make judgment calls you must be able to cross-examine the witness or the data.

Walter Raleigh brings this point home. He was executed in 1618 for supposedly getting on too well with the Europeans. The people making these claims about him never came to Court to be cross-examined. After his execution, British and other legal systems introduced a Hearsay Rule. Unless we can cross-examine people in court the things they say will not be heeded.

In the case of adverse event reports, regulators don’t take patient details and don’t follow patients up. So if Tom Perry goes on an SSRI and gets PSSD and wants to take David Healy to Court, saying regulators have thousands of cases of this and have had them for ages, will lead Healy’s lawyers to say Hearsay your Honor. Perry’s point will be thrown out.

In contrast, the RCT data will remain in. RCTs were given an exemption from the Hearsay Rule in the 1970s. It was possible at that point though to bring authors of papers into Court who knew the patients in the trial and what happened to them – just as it was possible to bring the authors of Case Reports into Court – as happened to me.

Since the early 1990s many of the trials that brought these drugs on the market had non-existent patients. The non-existent patient problem has gotten much worse in recent years.

No author on an RCT now will have met any of the existing or non-existing patients in the trial.

**People are the trial data – the figures put into statistical sausage machines are not the data nor are the statistical outputs.**

For instance in a 15-year-old boy in Study 329 went on Paxil in Dallas and dropped out with intercurrent illness. This code means the company don’t have to submit any adverse event data or narratives on him. The 80,000 pages on this trial tell you nothing about him.

An internal company email says he was picked up by the police because he was outside waving a gun around and threatening to kill people. Holy Shit he’s on our drug. You’d like to ask the kid what happened. If he and his mother say nothing like that ever happened before he entered the trial you have a very different story to company efforts to pass him off as bipolar – without using the word. This happens a lot in drug and vaccine trials. He is the data.

**Slide 15**: We decided to test the system. We sent a petition to FDA, and EMA asking them to ask companies to mention enduring sexual dysfunction in the labels of their drugs.

I wrote mentioning we could provide named reports of people with PSSD with contact details and doctors’ letters specifying the person had been on an SSRI and there was no other way to explain their problem. We made it clear the point was to offer EMA/FDA an opportunity to cross-examine people. EMA said yes – FDA didn’t respond.

People with PSSD are unwilling to have their name in the public domain but we got over 80 people to send named reports at short notice and over 30 doctors to confirm.

When the material arrived at EMA, per procedure the regulator immediately removed all names and never followed anyone up.

If you report to companies, they are legally obliged to follow you up. They check your medical records to find out if you had an ingrown toenail at the age of 2 they can blame your PSSD on.

But these follow-ups end up with them including all sorts of things like violence, suicide and other serious problems in the drug label under the heading Other Reports when there is no way to explain what happened other than as an effect of their drug. They know that doctors and the public will dismiss these as reports by Scientologists and Flat Earthers and see the company as wonderfully transparent for including them. These are the most solid cause and effect material on the label.

Companies now ask people to report to regulators – not to them. Sounds like they are being responsible. Conflict of interest people will cheer – yes progress. This is a case of the good guys being outwitted yet again. Think about it.

EMA say they license drugs on the basis of a Risk-Benefit analysis. Ask them how they do that and they say they depend on RCTs. The assumption is the primary endpoint of an RCT is the most common effect. But in the case of SSRIs the harms are far more common and when it comes to dead bodies there are more in the treatment arm of trials than the placebo arm. This It blows a hole in the whole notion of Risk-Benefit analyses – regulators don’t know what they are doing.

Nevertheless, EMA asked companies to mention PSSD in drug labels. Why? Possibly because companies want to start replacing SSRIs with newer more expensive drugs. The only people able to get a drug’s harm recognised are pharmaceutical companies.

**Slide 16:** At almost the exact same time as EMA said they would ask for a warning, BMJ featured sex on its front cover. See the media love sex. Apparently, the Brits are having less sex than they did 10 years ago. Similar evidence has emerged from the US and its probably true of the whole Western world.

The article blamed depression. The implication is antidepressants will solve it. But its only melancholia, a very rare condition that causes a loss of libido. The conditions that SSRIs are given for are like the nerves for which benzodiazepines were given in the 1980s – conditions that if anything might lead us to have more sex if we were still on benzos. Not however while we are taking SSRIs.

15% of the populations of Western countries are now on these drugs – primarily because they can’t get off them. This means 20% of us or more are not making love the way we would wish to. In some deprived parts of the country the figures may hit 50%.

If you’re a Trump supporter, you may be concerned at the fact that its mainly Caucasians who are affected – the Great Replacement is for real. If you aren’t Caucasian, it might be worth thinking twice before joining the chorus that we have to combat the stigma of detecting and treating mental illness in our communities.

The 15% of people stuck on treatment for the most part figure their sexual function will return if they could just get off the drugs. For some this might happen. For many, things may be worse rather than better. We just don’t know.

Stuck on these drugs? Yeah, that was something we saw in healthy volunteer studies of SSRIs in the 1980s also. Up to 80% of people had problems getting off after exposures of only 2 weeks. Yet we could bring these drugs on the market as non-dependence producing antidepressants to replace the horrific dependence from benzos. There were more reports of dependence on one SSRI alone, paroxetine, within 3 years of its launch in the UK than from 20 years of reports all benzodiazepines combined. But this made no difference.

How did we manage this? Not by ghostwriting or data sequestration. It’s the primary endpoint trick again. RCTs are the gold-standard way to hide adverse events.

**Slide 17:** This question about Sex and what we are doing to ourselves is one instance of the problems dealt with on a broader front in Shipwreck of the Singular just published.

First: The publisher – Samizdat Health - is a Writer’s Co-operative for books.

We live in a world poised between Biden and Trump. Trump and QAnon turn to conspiracy theories. While you can see the point about a conspiracy, if you claim one with no evidence it’s pretty primitive – childish.

Biden is childish too. He has a delegated narcissism issue. Delegated narcissism is where a child is watching a spectacular sunset with a father from a hilltop and after its over ask – Daddy can you do it again? Biden saying we follow the science is the same thing.

Maturity means you weigh an issue up on its merits and almost certainly in collaboration with others – not by following them. It means Bidets not Showers. If you have anything you figure the world needs to hear about and publishers don’t seem interested, think about us.

Second: This Sex and Drugs story gives you an example from the wider Shipwreck argument which is that Life Expectancy in the West has been falling for the last 5 years. The commonest explanation is inequality and a lack of access to health services. Poverty contributes to disparities in health, but an increasing amount of health service input itself is now a cause of morbidity and mortality, as symbolized best by the data on polypharmacy and evidence for better outcomes after deprescribing.

We are wandering into a danger zone by relying on the algorithm approach to medicine that is now called EBM – the Shower approach.

Medical Care and science is a judicial not an algorithmic process. A Bidet approach. When reporting on adverse events, we need an agency to report to who will keep the professional and the patients name on the report so that when Tom Perry tries to get justice for what has happened him he can call on people and their doctors to whom this has happened who are willing to come into Court to testify. We don’t have an agency like this. The closest things we have is RxISK.org.

If someone else like Alan Cassels came to testify and be cross-examined about his PSSD, perhaps with his doctor, Courts could not throw this evidence out. The legal system would seize up.

But leaving names on reports and being willing to testify requires Courage. Care of this kind is an act of Courage.

**Slide 18:** The last slide is tricky because I can’t sing. But this needs singing to the tune of Life is a Cabaret as sung by Lisa Minelli:

*Life is a Bidet, my chum. Come to the Bidet*.