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Re Morgan Inquest

Mr C Phillips & Dr R Adams

I have read June Raine's January 20th response to Mr Phillips Regulation 28 report.

If only as a gesture to offer solace to the Morgan family, submitting a Regulation 28 report and Dr Adams letter to NICE were likely well-intentioned. They haven't brought solace. MHRA's predictable response has made things worse. If you want to do more than gesture, you need to understand the key issues.

In Cardiff in the 1980s, there were many healthy volunteer studies involving SSRIs (mainly paroxetine) in which several volunteers, many of them in their 20s, became suicidal or hostile (a coding term for aggression and violence). One of them, a 23-year-old, committed suicide. In North Wales in 1999, we ran a blinded healthy volunteer trial of sertraline, in which two people, one of them a Family Doctor, became dangerously suicidal. The drug caused this. In Leeds in 1982, in a sertraline healthy volunteer trial, all subjects became agitated with one developing hostility and others suicidality. Pfizer concluded their drug had caused these reactions.

The weasel words both NICE and MHRA use leave it open to doctors like Dr Adams to figure a person's nervous state is the primary generator of any suicidality. In clinical trials of these drugs across a range of nervous conditions, those on SSRIs showed a doubling of suicidal events compared to placebo across all age groups. While a severe mood disorder can undoubtedly lead to suicidality, in the primary care cases for which these drugs are given it is more likely to be the drug that causes problems. The healthy volunteer studies confirm this.

Sam Morgan was pretty close to a healthy volunteer. It beggars belief it was anything other than his drug that caused his death. I invite you to consider the state of mind Dr Adams' prescription induced in him.

Unless MHRA and NICE state baldly that these drugs can cause suicidality and suicide, even in healthy volunteers, no amount of black boxing or other word tweaking will make much difference.

The words MHRA and NICE use make it more likely that a doctor, faced with Sam after a week on treatment, will increase his dose rather than stop the medication.

Regulators in contrast have found it possible to have something closer to the right kind of warnings about suicide for drugs like Siliq for skin conditions. So, this could be done for antidepressants – why isn't it. Well partly it's because MHRA don't want to admit to a mistake. But their justification for not taking action is what you need to understand.

In the case of antidepressants, their argument has been a risk-benefit one – we don't want to deter people who might be helped, indeed saved, by making warnings too obvious. And MHRA can point to notional support in the RCT data sent to them that shows more people with a rating scale benefit than people attempting suicide.

Quite aside from the fact many trials aren't sent to MHRA, and MHRA don't look closely at the data in those that are sent, the problem with this position is that it hinges on a primary endpoint. Primary endpoints hypnotize researchers, so they miss obvious things happening on treatment. Close to 100% of people taking an SSRI show genital numbing or irritability within an hour of taking their first pill but the trials MHRA have seen miss this entirely and there is no mention of it in the label.

Primary endpoints hypnotize regulators also. The primary endpoint of a trial is not the commonest thing a drug does – it's the thing a company wants to make money from. Strictly speaking far more people are harmed by an SSRI than not. This is not an argument for not having them – its an argument for full transparency about what we know.

Even sticking with just the data MHRA have seen and with rating scale scores as a primary endpoint, and disregarding things like genital numbing which are linked to some people being sexually dysfunctional for the rest of their lives, we now know that when these trials are amalgamated a greater proportion of people die on active treatment and there are a greater number of suicidal events on active treatment than on placebo.

MHRA's defense is that it is not their brief to consider this. They just look at the data from individual trials which do not show a statistically significant increase in suicidal events. (Some trials do, particularly in young people do, but this is ignored).

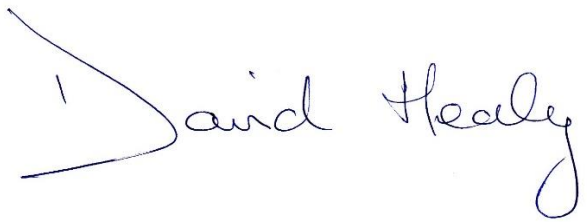
NICE essentially don't consider adverse events at all, so writing to them was a waste of time. They regard a ghostwritten literature as the highest form of evidence there is – better than the views of a clinician like Dr Adams.

Where does this leave us?

I have told MHRA and NICE their positions are inadequate and copied them in here. I have been doing this for over 20 years. Below is a Daily Telegraph piece from 1999 covering another inquest, I was involved in. I've invited MHRA and NICE to tell me where I am wrong because clearly to take these positions in public if I am mistaken would be wrong. They never have.

Ask yourself if any of the public reading this letter are likely to think you could do more. In the clip below, you will note the pharmaceutical company's response is that the care of patients is a doctor's responsibility. MHRA and NICE take the same position but are less likely to voice it.

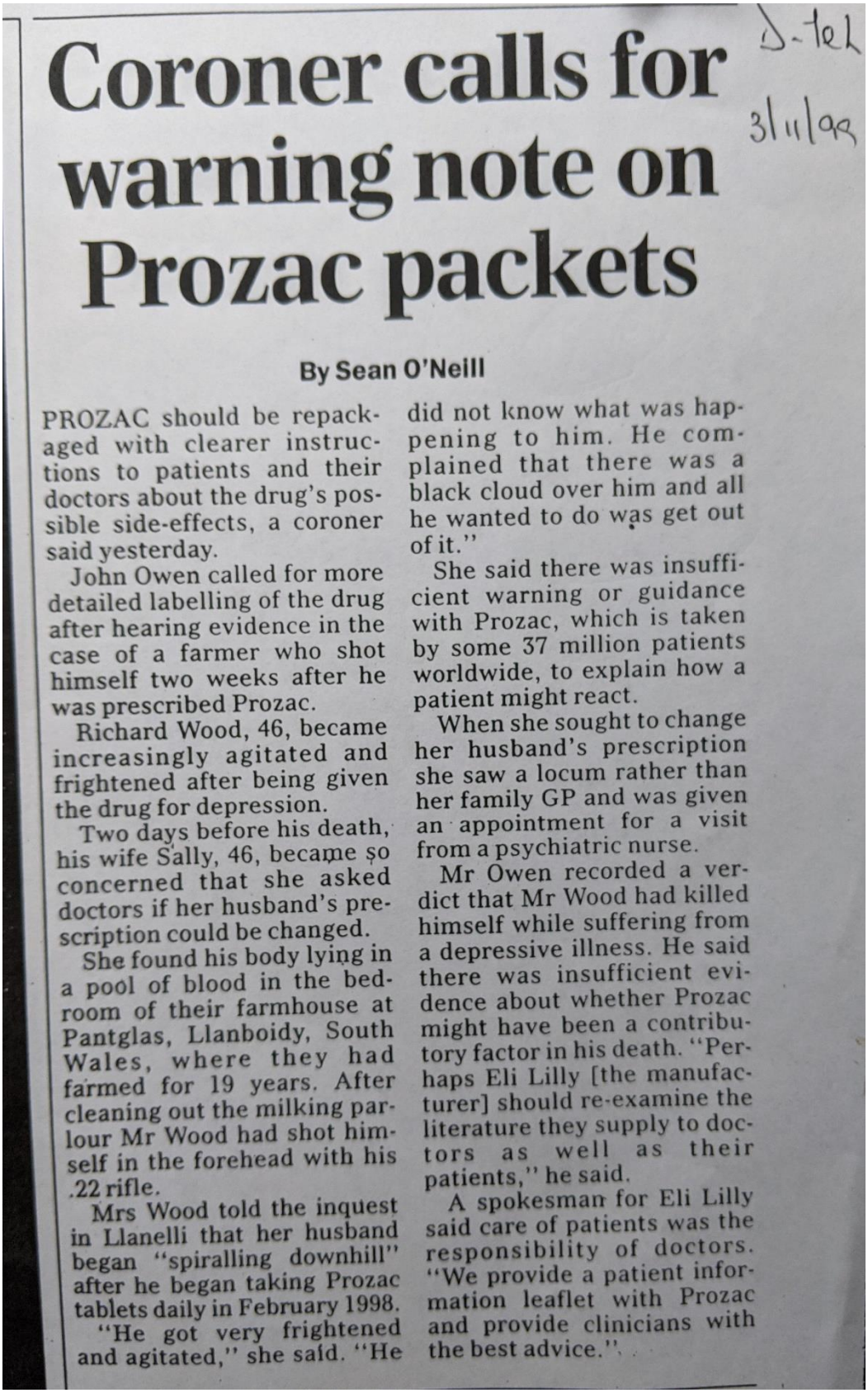
Yours sincerely



David Healy MD FRCPsych

cc J Raine, G Leng, S Nebhrajani

Daily Telegraph November 3rd 1999.



D-Tel
3/11/99

Coroner calls for warning note on Prozac packets

By Sean O'Neill

PROZAC should be repackaged with clearer instructions to patients and their doctors about the drug's possible side-effects, a coroner said yesterday.

John Owen called for more detailed labelling of the drug after hearing evidence in the case of a farmer who shot himself two weeks after he was prescribed Prozac.

Richard Wood, 46, became increasingly agitated and frightened after being given the drug for depression.

Two days before his death, his wife Sally, 46, became so concerned that she asked doctors if her husband's prescription could be changed.

She found his body lying in a pool of blood in the bedroom of their farmhouse at Pantglas, Llanboidy, South Wales, where they had farmed for 19 years. After cleaning out the milking parlour Mr Wood had shot himself in the forehead with his .22 rifle.

Mrs Wood told the inquest in Llanelli that her husband began "spiralling downhill" after he began taking Prozac tablets daily in February 1998.

"He got very frightened and agitated," she said. "He did not know what was happening to him. He complained that there was a black cloud over him and all he wanted to do was get out of it."

She said there was insufficient warning or guidance with Prozac, which is taken by some 37 million patients worldwide, to explain how a patient might react.

When she sought to change her husband's prescription she saw a locum rather than her family GP and was given an appointment for a visit from a psychiatric nurse.

Mr Owen recorded a verdict that Mr Wood had killed himself while suffering from a depressive illness. He said there was insufficient evidence about whether Prozac might have been a contributory factor in his death. "Perhaps Eli Lilly [the manufacturer] should re-examine the literature they supply to doctors as well as their patients," he said.

A spokesman for Eli Lilly said care of patients was the responsibility of doctors. "We provide a patient information leaflet with Prozac and provide clinicians with the best advice."