

THE CARDINALS OF PSYCHIATRY

Professor David Healy MD FRCPsych – September 24th 2011.

Slightly over 10 years ago the previous Pope convened a meeting of US cardinals when it became clear that the Catholic Church faced a major child abuse problem (slide 1). We face a comparable crisis in psychiatry – and medicine. There is no medical pope but there are lots of Cardinals and it is not clear that our Cardinals are getting to grips with the crisis any better than the US Cardinals or Irish Cardinals have done.

There is a widespread recognition that there is a problem. In terms of pinpointing what is wrong, the answer most often heard today is that medical academics are paid by the pharmaceutical industry to give talks and to run clinical trials (slide 2). That they have conflicts of interest. Supposedly because they are paid, they offer views that suit the industry. This is not where the problem lies.

The Original Sin as it were lies in a drug crisis surrounding Thalidomide and a set of safeguards we put in place in 1962 to prevent a repeat.

Factor 1: Product Patents – The one True Faith

One part of the problem lies in a system that makes drugs available under product patents. Product patents were the system under which drugs were made available in the United States before 1962. Of 77 countries surveyed at the time by US officials investigating patenting systems, 28 allowed product patents and in these countries the prices of drugs ranged from 18 to 255 times higher than in the non-product patent countries.

The main European countries at the time offered process patents - if a company could find another process to synthesize a drug it too could bring the product to market. This system made it less likely that a company could make a fortune from one drug and encouraged them to hold a portfolio of compounds.

But after 1962 and the thalidomide crisis there was a switch to product rather than process patents and this is now the worldwide system. This lays the conditions for pharmaceutical companies to make blockbuster products out of their drugs. Blockbuster drugs are drugs that earn a billion dollars per year or more for a pharmaceutical company.

The first blockbuster drug was Zantac, a treatment for ulcers, in 1985. This was followed by antidepressants like Prozac. Some drugs like the statin, Lipitor, have pulled in revenues of \$13 billion per year for the company that markets them. I say market because companies are increasingly unable to make drugs. Pfizer did not discover Lipitor; they licensed it in (slide 3).

If we consider the mark-up for which these drugs sell, over the cost of the raw ingredients, a mark-up that in some cases rises to several thousand percent, these drugs are literally worth more than their weight in gold to pharmaceutical companies. As a result, the fortunes of many companies have come to depend critically on one or two key drugs. This means they have to hype the benefits of drugs and they have to hide the problems, as is brought out by a quotation from Leigh Thompson of Eli Lilly in connection with Prozac.

“I am concerned about reports I get re UK attitude toward Prozac safety. Leber (FDA) suggested a few minutes ago we use CSM database to compare Prozac aggression and suicidal ideation with other antidepressants in UK. Although he is a fan of Prozac and believes a lot of this is garbage, he is clearly a political creature and will have to respond to pressures. I hope Patrick realizes that Lilly can go down the tubes if we lose Prozac and just one event in the UK can cost us that.” (slide 4)

As regards conflicts of interest, a little noted conflict is that this system has been lucrative for the major shareholders of pharmaceutical companies. In the case of Lilly, the makers of Prozac and Zyprexa, company employees received over \$3 Billion worth of share options from the time Prozac came to market.

In terms of saving lives-souls, Product Patents are the equivalent of the Catholic Church insisting there is only one true way to salvation – that the alternate Christian or other routes just don't do it.

Factor 2: Prescription-only Status: Stockholm Syndrome

A second factor is the fact that all modern drugs are made available on prescription only. This was a system that was introduced in 1914 to control drug addicts. You could always get drugs on prescription from your doctor but we didn't have a system which meant that these drugs could be available on prescription only. In 1951 the system was extended to cover all new drugs. There was considerable opposition to extending a system designed for addicts to cover the entire population. But in 1962 because of the thalidomide crisis this arrangement was copper fastened in place (slide 5).

There are a number of aspects to this problem that were not considered at the time. In terms of conflict of interest this systems delivers most doctors several hundred thousand dollars per year – vastly more than academics make from giving lectures or doing other things for pharmaceutical companies.

Second it means that that when pharmaceutical companies market drugs they don't have to focus on the entire population. They only have to focus on a very small number of people who prescribe drugs – a very naive group of consumers - and they understand them better than these people understand themselves.

Third in August 1973, a bank robbery at the Kreditbanken in Stockholm triggered a 5-day siege with bank employees held hostage. After the siege ended, to the surprise of everyone many of the hostages, as if hypnotized, spoke well of their captors. "Stockholm syndrome" was born. Now recognized as common, the conditions that trigger this change in behavior are isolation, a fear that your life is at risk and kindness on the part of the hostage takers (slide 6/7).

Disease isolates us as profoundly as incarceration or anything else might. Our lives are at risk, and our doctors who control the exit to freedom are almost certain to be kind. But not a single doctor is trained to manage Stockholm syndrome, to suspect that our apparent insouciance or congenial conversation might conceal deep unhappiness with a proposed course of treatment or worse again alarm at new problems that have emerged on treatment.

Since 1973, doctors are increasingly likely to suffer their own variant of Stockholm syndrome. If something goes wrong with a treatment a doctor gives, even though the label may concede that the drug can cause the problem, the makers of the drug and the doctor's colleagues will deny that it is likely to have done so in any particular case. Speaking up about a problem, once the material of medical advance, is now a recipe for professional suicide. A doctor attempting to rescue a patient is likely to be accused of being a persecutor who victimizes the patient by withholding effective treatment.

Offers to describe problems at professional meetings are turned down. Journals are ever less likely to accept publications outlining a new problem. Invitations to apply for better jobs, to attend conferences, or simply to go with colleagues to local eateries funded by drug

companies are ever less likely to happen for doctors linked to adverse events. Those holding doctors hostage have been very kind indeed – there are ever fewer medical departments or medical conferences not awash with company support, when it comes to paying for meals with colleagues most doctors have forgotten what a credit card looks like, and of course in supplying drugs they supply the objects that make doctors desirable.

As a result bit-by-bit over the last 40 years any of us having a problem on treatment have been disappearing in front of the eyes of our doctors who in turn are increasingly inaudible and invisible to companies, academics and regulators. A key component of the fog that envelopes both us and our doctors lies in the published trials that have hypnotized everyone. Individual observations, the logic goes, are unreliable, while trials supposedly offer reliable estimates about the consequences of treatment. When a doctor does report an adverse event to regulators, the report is invariably parked as uncertain and unreliable information.

Finally to come back to the Catholic Church, of course children in particular are in a classic Stockholm syndrome position vis-a-vis priests and this has done much to generate the problems facing the Irish Church among others.

Factor 3 Controlled Trials: The Eye of the Needle

Following the thalidomide crisis in 1962, it was thought that in order to make a drug safer one of the protections might be to keep ineffective drugs off the market. Controlled trials were the way to do this. Accordingly after 1962, these were set up as the eye of the needle through which the pharmaceutical industry camel would have to get if it was going to get into Heaven (slide 8).

This was not a good system to achieve what was wanted – and indeed the belief that it is a good system makes it even more dangerous. There is no better symbol of the inadequacies of the system than the fact that the only drug that had been through a placebo controlled trial of this sort before coming to market as of 1962 was thalidomide which had been shown in a controlled trial to be an effective sleeping pill and to be absolutely safe.

The irony is compounded by the fact that the person who undertook this trial – Louis Lasagna – was the person who wrote the requirement for controlled trials into the 1962 legislation.

Factor 4: The Sacred Literature: Ghost Writing

When faced with claims of abuse, the Church has asked people to lift their eyes up from individual cases and to trust in a series of Ghost-written documents.

When faced with evidence of harm on drugs, our medical Cardinals do the same thing. They ask us to turn from individual cases of abuse (denigrated as anecdotes) to the evidence written up in controlled trials - by ghost writers. Close to 100% of the studies undertaken on pharmaceuticals that are on patent are likely to be ghost-written or managed by companies and the apparent authors are invariably Cardinals (slide 9).

What does ghost-writing buy? Well if you look at the suicidal acts that happened in the clinical trials that brought Fluoxetine, Sertraline and Paroxetine to the market, you find there is an entirely different distribution of acts in the published literature to what can be found when you get to see the raw data behind the trials (slide 10).

In breach of FDA and other regulations, companies have moved suicidal acts that happened in the washout-phase of trials or after the trial was over into the placebo arm making it seem like there was less risk from the active drug than there in fact is (slide 11). The control that ghost-writing gives has allowed many companies to effect similar or other manoeuvres for a range of side effects from heart attacks on Avandia to problems on Vioxx and other drugs.

How in these circumstances is your doctor going to know that there is this risk to these drugs? Well, she isn't. But both the regulators and our Cardinals know about it and although the dimensions of what happened have been known about for a decade no-one has been held to account.

Factor 5: Common Law & Canon Law?

But there is a further problem with trials. Fifty years ago before all these drugs were introduced doctors and patients were much more confident in the observations they made about whether treatments were working or not. Controlled trials have usefully brought to light the biases both doctors and patients may bring to such observations but the pendulum seems to have swung too far so that few doctors or patients find they are able to believe the evidence of their own eyes today. When patients get huge on the antipsychotic group of drugs if the controlled trial hasn't shown that actually happens, then it isn't happening.

Here's how it's done. The reliability of clinical observation is denigrated as poor and this problem can supposedly only be overcome by having 100s of patients exposed to a treatment. If there isn't any change on a pill then most of the observations should lie here right over the figure 1.0 (slide 12). If both doctor and patient come to the conclusion that good things are happening the curve will move over to the left. If they come to the conclusion bad things are happening the curve will move over to the right.

Now look at slide 12 which shows a statistically significant doubling of the risk of death on Drug A which may otherwise be very helpful for some condition. Now take drug B which can help the same condition but in this case our best data suggest there is a 4 times greater risk of death than on drug A. The data on drug B however are not statistically significant – perhaps simply because the company has ensured not enough patients are recruited to the study for there to be a risk of the inconvenient observations becoming significant (slide 13).

Now anyone working in a drug company or a regulatory body asked to treat her own child or parent or partner would use drug A rather than drug B because it is the safer drug to take. But when it comes to debate in the public domain these same people tell you drug A is the risky drug and there are no problems at all linked to drug B. No problems at all.

Here is the data on Prozac and suicide to bring home the point. When the first reports of people becoming suicidal on Prozac blew up, these were dismissed by the company, by the regulators and our Cardinals as anecdotes. The evidence we were told pointed the opposite way – that there was no risk. This is most clear in the case of an article in the BMJ in 1991 which purported to show all the trials done by the company and the data from those trials.

The distribution of the suicidal acts in this BMJ article shows an almost doubling of the risk of problems on Prozac compared to placebo. We can agree with the company that the increased risk is not statistically significant but it would be obvious even to a 12 year old schoolboy or girl that what the company then write which is that “data from these trials do not show that fluoxetine is associated with an increased risk of suicidal acts or emergence of substantial suicidal ideation among depressed patients” is just wrong (slide 14).

This is why I think a simple conflict of interest argument is wrong. 100,000 people read the BMJ. They are not all paid by the pharmaceutical industry to conclude there is no risk from

the drug. There are many people who read the BMJ that don't work in medicine. There are many that read the BMJ who work in the asthma field, the cardiovascular field. They don't have any vested interest to conclude that antidepressants aren't causing a problem. A 12 year old school child will see there is an increase in risk on this drug but all the professionals in the world it seems don't see it provided the data is not statistically significant.

Companies trade on this, as this quote from Paul Antony of Pharma shows (slide 15):

"FDA will send out this information, which they concede is just early signal information ... But I want you to think about it in terms of your reputation. It's really the reputation of a brand that's being signaled. **Imagine someone reporting that they had early information that you may be a child molester. I know that sounds extreme, but it's that type of thing.**

"It's just an allegation [However] that's what people will remember, and that's the reason there's a lot of concern about presenting early signal information when you don't really have any proof. It is very different than the kind of rigorous process we had in the past, where you had to do a trial, and it had to be statistically significant before you presented that".

What you see here is the most sophisticated version ever of the Doubt is our Product strategy pioneered by the tobacco companies in the 1960s (slide 16).

The real Burn in Hell moment comes in this quote from Ian Hudson, then head of Global Safety in GSK, asked if paroxetine – Seroxat/Paxil can make people suicidal says (slide 17):

A: It is impossible, on an individual case basis, from individual reports, to assign causality ... That's why, when we have issues, we review all the available data and make a determination .. whether there is an issue or not.

Q: Okay. Do you believe that it is possible that Paxil has caused any person worldwide to commit an act of homicide or suicide?

A: I have seen no evidence to suggest that at all.

This is Burn in Hell because GSK and other companies on issues such as suicide, birth defects or other problems – regularly on the basis of individual cases make judgements that it is almost certain that their drug has caused a problem.

While Hudson was saying this GSK and other companies and regulators had compelling trial data on file showing the increased risk on Seroxat.

The crisis only came to a head some years later when an article appeared in the BMJ showing that when the accumulated scientific literature was assembled that the increase in risk had become statistically significant. What slide 18 shows is that from 1988 – two years before the first reports appeared that people became suicidal on Prozac – the clinical trial data showed a 3-fold increase in risk. Despite this regulators and Cardinals and company personnel said the evidence from abused people was at odds with the "science" – and who are you the public going to believe?

It was only 15 years later that the regulators were prepared to say there was an increase in risk. Even though there is no increase in risk from the clinical trial data – all that had happened was that an accumulation of data had made the risk significant.

What you need to know is that we are now systematically training doctors these days to make exactly that kind of mistake the whole time. They are being trained to say that if the results are not statistically significant you don't pay any heed to them. Our problems are going to get worse – not better.

While articles like the BMJ article remain unpublished and while companies fail to undertake the studies to properly explore the issue, companies, regulators and our Cardinals take thousands of convincing treatment induced injury cases and consign patients and their families to Limbo, and continue to claim in public there is no issue.

This is true for Vioxx, where in the controlled trials of 4,300 patients taking it there were 17 heart attacks. In the 4,300 patients taking placebo in just the same trials there were 4 heart attacks. But the data were not statistically significant so the company could publish an article in a journal read by 100,000 people from all over medicine and from all parts of the world and depend on people to say there is no increase in heart attacks on Vioxx. The Avandia story is exactly the same story.

Factor 6 The Inquisition

When I was growing up most Irish authors were banned in Ireland. The Church could impose its will on what we were allowed read or not. I suspect we pride ourselves now on having overthrown this layer of control that in some circles might even be called tyranny (slide 19).

More recently, John Cornwell as you see here wrote two books – one on Prozac, suicide and homicide and one on Pius XII. Those of you schooled on Dan Brown's Da Vinci code will no doubt think that JC will have had far more difficulties with the Vatican since than he had with Lilly. Quite the contrary. Lilly threatened to sue him in many different countries and have made his life far more difficult than the Vatican have (slide 20).

This is not surprising. When Joseph Glenmullen's Prozac Backlash came out, the *Boston Globe*, *Newsday* in New York, and other media outlets received a number of unsolicited critiques of the book. These included a commentary from John Greist of the University of Wisconsin, a witness for Lilly in the Wesbecker case. Another was by Graham Emslie, a leading advocate of SSRIs in children. A third came from David Dunner, a clinical trialist for Lilly and member of the 1991 FDA panel on Prozac. A fourth came from Harvey Ruben of Yale. All followed a standard line about the devastating disease that was depression, the weight of research behind Prozac, and the patients who would commit suicide because they had been scared off treatment (slide 21-26).

In one commentary Tony Rothschild claimed to be "disheartened that Dr. Glenmullen bolsters many of his arguments and proves his hypotheses by borrowing liberally from others' work including my own....at no point did Dr. Glenmullen consult me directly to question my studies, two of which he conveniently uses to prove his argument".

I had tried unsuccessfully to contact Rothschild to talk about just this. It was well known that Carol Locke, the senior author on the Rothschild and Locke publication, stood by her view that the study pointed toward a causal relationship between Prozac and suicidality. Jerrold Rosenbaum from Massachusetts General, who apparently owned up to not having read the entire book, was also quoted in the material sent to the *Globe*. When approached by the *Globe* and asked about his consultancy with Lilly, he claimed that pretty well every senior figure in psychopharmacology had consultancies with a range of different companies—that in fact it was impossible to function in this world without these links.

The commentaries sent to *Newsday* in New York included a delicious covering letter from Robert Schwadron of Chamberlain Communications Group: "The book preys on the fear of people with clinical depression, and may prompt some people to abandon their medication

and seek medically unproven alternatives for a debilitating disease with potentially life-threatening consequences.. If we can offer you any information, or some balance to a story you may be planning, we would be more than happy to oblige. We can arrange for interviews with spokespeople from Eli Lilly and Company, as well as with independent researchers from the medical community (slide 27).

Chamberlain Communications Group were Lilly's PR agency in New York. The *Globe* materials came from Rasky Baerlein, another PR group working for Lilly (slide 28).

This is not all I have many articles that have been through the peer review process and been accepted in the best journals, only to be held up by the legal department of journals too scared to publish for fear of the pharmaceutical industry. The ultimate symbol of this is when Index on Censorship self-censored the publication of materials that were all entirely in the public domain (slide 29).

But in addition as the following freedom of information documents show there is probably someone here in the audience today whose brief it is to see if I can be sued (slide 30):

103 Healy long term strategy.

Thank you for the message outlining your strategy to counteract Dr David Healy's claims re: Prozac and violence. Send a letter to Healy designed to get him to stop discussing a study that he has never done. Have a third party expert in the audience at BAP to ask Healy questions when he presents.

Just last Thursday Healy was quoted in a Cincinnati paper saying Prozac causes violence and suicide...X has asked that we go back to legal and determine if we can sue Healy under UK law.

104 Huge turn out... Good talk. Lesson no sponsor if Healy present in future.

When inside pharmaceutical companies I find evidence that colleagues, Cardinals of Psychiatry, have been consulted to get information on Healy that might be potentially damaging (slide 31).

And in talks such as this one recently by David Nutt at the Royal College of Psychiatrists meeting in the UK, I am labelled as a scaremongerer (slide 32).

This slide is interesting in that it makes clear that Dr Nutt feels he cannot brand me as a treatment denier or illness denier - the libel is Scaremongerer.

There may be many here today who deny mental or other illnesses exist or deny that medical or psychiatric treatments do any good – I would say to you the industry will not be very interested in you because neither the public at large nor doctors in general will go along with this – despite all the evidence of abuse you see here today.

Being a Scaremongerer however involves mastering the science – you cannot make claims about the hazards of a treatment without being sued unless you have the science right.

One suggestion I have is that the highest aspiration anyone should have is to be a Scaremongerer. We should turn this word around – make it a badge of honour, like Gay Pride or Mad Pride. It is precisely for this reason that drugs were made available on prescription only so that doctors might ferret out their hazards and in the belief that doctors would have what it takes to stand up to pharmaceutical companies. The average person facing Pharma was like a child in the hands of a priest who could threaten eternal damnation but doctors would be neither children nor accomplices in the face of abuse.

Final Acts of the Tragedy

We are facing a true tragedy – a system put in place with the best of intentions to prevent injuries from drugs in general but symbolized in particular by injuries to babies in utero is now leading to just the outcomes it sought to avoid.

In the case of the SSRIs as the evidence mounts that these drugs cause birth defects, doubling the rate of major malformations, doubling the rate of miscarriage, increasing rates of voluntary terminations and more than likely leading to learning disabilities/autism in a significant number of children born to mothers on these treatments, we have nevertheless a mounting use of these drugs. Where antidepressants were once used rarely in pregnancy they are now among the most commonly used drugs – up to 15% of pregnant women.

This use is actively promoted by our Cardinals, who collectively make it almost impossible for articles to get published drawing attention to the issues. It is a world where articles can only get published in Vogue or other such outlets – outlining the case of Gina Fromm who for instance when she became pregnant in 2004, did a range of things that few women would have done in 1962 – she took cold rather than hot showers in case she might harm her baby, stopped eating yoghurts and incinerated any chicken because of the risk of bacteria from listeria to salmonella. She balked at taking prenatal vitamins, though she had been taking Paxil following a fleeting episode of anxiety. She continued to take it through her pregnancy; she had found stopping difficult and her doctor reassured her it posed no risk to her baby. On February 2nd 2005 her son Mark was born with congenital heart defects (slide 33).

Two recent inquests in which I gave evidence bring out the deeper problems. One was Shane Clancy's inquest in April 2010 (slide 34). This young man put on citalopram had a classic adverse reaction to it, becoming suicidal early on. His doctor continued the treatment and a few weeks after starting treatment he killed himself and another young man in terrible circumstances. The deaths bore all the stigmata of SSRI induced problems. I gave testimony to this effect at his inquest and the jury agreed that it was not possible to return verdicts of suicide (and by extension homicide).

Some of the senior Irish Cardinals got involved in the case – engaging the media and others before, during and after the case, stating that antidepressants came with no problems and that the tragedy in this case would be if publicity led to a drop in the use of antidepressants. The Irish College were pressed into making a statement supporting the use of antidepressants.

The reaction from a retired senior academic was as follows: "I am afraid I agree with Healy - the College is plain wrong. There is no such thing as a college statement which is circulated to the membership simultaneous with its publication, without opportunity for comment or vote and "in unison" with a body 100% financed by drug companies, and with personal hostile references to expert testimony at an inquest with families still in grief. And this on the heels of a dreadful multiprofessional letter even before the inquest began. Extraordinary and outside my experience. If I were not retired I'd dissociate and publicly resign" (slide 35).

The second case involved Yvonne Woodley a woman in her early 40s also put on citalopram who had a classic case of treatment induced agitation that worsened as her dose was increased to the point where she hung herself in her house with her children downstairs (slide 36).

In this case as in the Clancy case, company spokespeople insisted that they did not believe citalopram had contributed to the problem and gave the impression that they did not believe it could contribute to the problem.

The coroner however asked the medical representative for the company – can your drug cause people to commit suicide? In response to this Dr Chris Muldoon had no option but to agree it could.

Companies **are legally obliged to agree that their drugs cause people to commit suicide**. Our Cardinals are not legally obliged. And here is where they offer one of the greatest services they can to companies – they can and regularly do offer Apologias for industry. They have become industry's way around the law and any moral code that may apply in this domain. They state in public that not only did the drugs not cause a problem in the Clancy or Woodley cases but that they cannot cause a problem. Done behind closed doors this behaviour is one thing; taking the issue to the media is quite another.

At the height of the controversy about antidepressants and suicide in children in 2004, when US regulators issued a black box warning on the drugs, the American Psychiatric Association issued a suicide note. They stated "The American Psychiatric Association believes that antidepressants save lives" (slide 37). If the drugs work well and are free of problems given how much psychiatrists cost to employ, it would be better for health systems to employ nurses or pharmacists who can prescribe. APA should have said "The American Psychiatric Association believes that Psychiatrists save lives" (slide 38).

The Irish College has made a comparable mistake. Doctors need to wake up to the politics of the situation.

Some of you here might like to see the demise of Irish psychiatry, maybe even Irish medicine. This talk is however delivered in the hope that psychiatrists and doctors can save themselves, in the belief that we are better off with good doctors than without.

There is a vision here about what good care involves - that needs doctors if it is to be realized. Just as Freud and Jung made us aware of the biases underpinning what patients say so that not all claims of abuse are based in reality, but we have since learnt to our cost that many are, so also controlled trials have made us aware of the biases doctors and patients bring to treatment but while aware of these biases both doctors and patients have somehow to regain the ability to believe the evidence of their own eyes.

This lecture, however, is also delivered in the belief that we are not witnessing a crisis about conflicting interests where this refers to relatively small amounts of money but we are witnessing a much more profound conflict.

"If clinical trials become a commercial venture in which self-interest overrules public interest and desire overrules science, then the social contract which allows research on human subjects in return for medical advances is broken" (slide 39).

"At a time when health has become a common credo for all social classes, ethnic groups, both sexes and all age groups, concealing or distorting "our" data, data that we literally risk our lives to generate, amounts to an abuse of a sacred trust. This is an abuse that cannot continue without the active participation of our Cardinals" (slides 40, 41).

Note:

The use of the term Cardinals in this context refers to some but not all Senior Academics in a medical discipline.