

An Analysis of Use of Prozac, Paxil and Zoloft in USA 1988--2002

The IMR Patient Flow Model has been used to analyse the usage of the SSRIs Paxil, Prozac and Zoloft in the US since each drug was introduced. The results for Paxil were given in an open letter to Congressmen Barton and Greenwood (Ref.1). The letter also introduced the IMR Model and summarised its development and capabilities. This report will answer three questions with results produced by IMR.

- 1) How many US patients have consumed these drugs since date of introduction ?
- 2) How many US patients have continued to use these drugs for many years ?
- 3) How many US patients may have been killed by drug induced suicide in the first weeks of use ?

Numbers of Patients.

The IMR model starts in the year of introduction and uses specific Inman usage profiles for each drug (Ref. 2) The known quantity of medication has been consumed by approximately 67.5M patients. Although it is possible that some patients may have switched between drugs and this would reduce the number of unique patients. Nevertheless a probable 8M new SSRI patients in 2002 indicates the magnitude of the potential harm, particularly as these drugs have little or no proven efficacy above placebo for the majority of conditions for which they are now prescribed.

Table 1: New Patients on Prozac, Paxil and Zoloft.

Year	New patients Starting on Drug in current year			
	Prozac	Paxil	Zoloft	Total
1988	899,856			899,856
1989	1,547,442			1,547,442
1990	1,947,338			1,947,338
1991	426,619			426,619
1992	1,787,521		213,790	2,001,310
1993	1,020,216	850,205	2,373,784	4,244,205
1994	2,863,022	1,467,859	1,677,421	6,008,302
1995	2,280,438	1,289,065	2,171,122	5,740,625
1996	2,328,614	1,653,982	1,940,201	5,922,796
1997	2,622,047	2,106,261	1,675,933	6,404,241
1998	2,663,209	2,037,645	2,106,666	6,807,520
1999	1,855,358	1,861,142	2,068,905	5,785,404
2000	1,380,479	2,330,549	2,292,718	6,003,747
2001	1,610,645	1,887,306	2,463,645	5,961,595
2002	1,805,015	3,046,058	3,041,536	7,892,609
Totals	27,037,820	18,530,071	22,025,721	67,593,612

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Long Term Use

Although the majority of patients are forced to drop out during the first year of use, many patients remain on SSRIs for many years, some out of choice, but some become dependant and cannot withdraw. GSK have now been forced to admit that 25% (not 2% as they previously claimed) of patients will have “difficulty” in withdrawing (June 2003).

Other long term patients confuse their drug induced withdrawal symptoms and believe that these are their own original condition and that therefore the drugs must be making them well. The lack of thoroughness of coroner investigations and the inadequacy of post-mortem analyses means that there is no data to indicate how many suicides may be triggered by attempted SSRI withdrawal. Table 2 presents the probable size of the long term patient cohorts on each drug and their duration of dependence as at the end of 2002.

Table 2: Numbers of US patients in Long Term Use.

Duration of use by US Long Term Patients as at end 2002				
Time on Drug	Number of Patients			
	Prozac	Paxil	Zoloft	Total
1 year or more	2,831,468	2,565,975	2,894,978	8,292,421
3 Years or more	2,167,664	1,601,950	1,823,505	5,593,119
5 Years or more	1,669,161	945,426	1,142,992	3,757,579
7 Years or more	1,032,343	446,904	684,143	2,163,390
10 Years or more	382,243	57,483	173,215	612,941
12 Years or more	206,911	-	-	206,911

None of these drugs have ever been scientifically validated for such long term use either in terms of efficacy or permanent central nervous system damage. The cost implications are phenomenal. For example, the cost of keeping 2.163 million patients on these drugs for 7 years is over 20 billion dollars, (much of which are tax dollars). This money could have funded alternative more effective and far less dangerous therapies. Table 2 is a snapshot at the end of 2002, the whole picture is dynamic, the duration and cost of long term use will continue to grow as time passes, Paxil and Zoloft are relatively young so their long term populations and costs will increase.

This table illustrates the scope of IMR to analyse long term patient cohorts in detail for any SSRI. New patients, drug induced harm and costs can all be derived from one coherent base, founded on the published work.

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Drug Induced Suicides.

The IMR model uses some internal sequences to calculate the growing population of patients from the amount of medication that was consumed. But in order to calculate the probable number of drug induced suicides it is necessary to have a suicide rate per given number of patients at risk. This suicide rate must be provided externally and must relate to actual trials and studies, it cannot be generated by IMR. In view of the serious implications of the tables 3 and 4 that follow, it is most important to briefly review the sources to give provenance to the chosen rates.

All new patients or volunteers on SSRIs regardless of their mental condition, child or adult, face a finite risk of drug induced suicide in excess of any risk of suicide that they had before medication. GSK presented randomised clinical trial (RCT) results to the MCA for Seroxat in 1990 in their UK licence application. This showed that Seroxat was 8 times more likely to cause suicide or suicide attempts than placebo giving a rate of 236 suicides per 100K patients, zero for placebo. After some debate the application was withdrawn.

GSK then manipulated the results of the same trial, shifting suicides from Seroxat onto placebo, and re-applied in 1991. The adjusted figures showed that placebo was now twice as dangerous as Seroxat, giving a rate for Seroxat of 168 suicides/100K patients and an incredible 361/100K for placebo. This affront to medical ethics, logic and common sense did not dismay the MCA and on the basis of this data the MCA granted the lifetime UK licence for Seroxat, which was never to be scientifically and critically reviewed subsequently. This dangerous, inexplicable and incompetent approval in the UK undoubtedly influenced the FDA to follow suit 2 years later when the Paxil licence was granted.

In 1993, epidemiological studies (Ref.3) carried out by the Drug Safety Research Unit on a cohort of 50 K patients who were using various SSRIs found gross rates of suicide as follows:- 269 deaths/100K for Seroxat, 244/100K for Prozac and 173/100K for Zoloft. The weighted average from the whole study is 219/100K. These gross figures must be reduced by an estimate of suicides that might have occurred in that population if they had never received medication. This additional data, provided by a study on 460K people over 5 years, suggests a cautious figure of 60/100K (Ref.4). The result is that the average SSRI may typically cause at least 160/100K suicides in excess of the suicides that may occur without medication.

Both clinical and epidemiological studies suggest that it would be quite justifiable to run IMR with an average SSRI induced suicide rate of about 160/100K. However, in the interests of careful science and caution, a range of excess rates between only 32 to 104 drug induced suicides per 100K patients has been chosen to predict the range of total drug induced deaths. To put it another way, the results have been calculated using rates of one fifth to three fifths of the excess induced suicide rates that have been measured in actual clinical trials and epidemiological studies on SSRIs.

Although all SSRI patients are at risk of induced suicide and other harm at every dose transition (starting, stopping and increasing dose) the drug induced withdrawal suicides and mid treatment dose change suicides are not included in this analysis.

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Table3 (Below): Drug Induced Suicides in the US (rate of 32/100K patients)

Year	Excess (Drug Induced) Suicides			
	32 deaths per 100K new patients			
	Prozac	Paxil	Zoloft	Total
1988	292			292
1989	501			501
1990	631			631
1991	138			138
1992	579		69	648
1993	331	275	769	1,375
1994	928	476	543	1,947
1995	739	418	703	1,860
1996	754	536	629	1,919
1997	850	682	543	2,075
1998	863	660	683	2,206
1999	601	603	670	1,874
2000	447	755	743	1,945
2001	522	611	798	1,932
2002	585	987	985	2,557
Totals	8,760	6,004	7,136	21,900

Table 4 (Below): Drug Induced Suicides at rate of 104/100K patients.

Year	Excess (Drug Induced) Suicides			
	104 deaths per 100K new patients			
	Prozac	Paxil	Zoloft	Total
1988	936			936
1989	1,609			1,609
1990	2,025			2,025
1991	444			444
1992	1,859		222	2,081
1993	1,061	884	2,469	4,414
1994	2,978	1,527	1,745	6,249
1995	2,372	1,341	2,258	5,970
1996	2,422	1,720	2,018	6,160
1997	2,727	2,191	1,743	6,660
1998	2,770	2,119	2,191	7,080
1999	1,930	1,936	2,152	6,017
2000	1,436	2,424	2,384	6,244
2001	1,675	1,963	2,562	6,200
2002	1,877	3,168	3,163	8,208
Totals	28,119	19,271	22,907	70,297

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Table1 shows that, in 2002, 7.8 million Americans became new users of either Paxil, Prozac or Zoloft and therefore they faced a net risk of induced suicide that is not likely to be lower than 32/100K and very probably is higher than 104/100K. Nevertheless, even using these cautionary rates, somewhere between 2500 and 8200 excess suicides may have occurred in 2002 alone due to these drugs.

Whatever the value of the suicide rate, it was not zero. At least two thousand Americans may have died in 2002 who were not warned of the possible lethal outcome of their SSRI medication. This is the consequence of a dysfunctional drug safety regulation system in which the drug manufacturers have not only failed to disclose evidence of great harm but also have infiltrated virtually every organisation that could criticise, study and report on their drugs with scientific objectivity. This is compounded by the doctors who continually fail in their duty to report possible adverse effects, (i.e. suicide within days of starting the drug), associated with the dangerous drugs that they prescribe so frequently and so readily for virtually all the problems of life, culture and society.

But the spotlight must now fall on the FDA (together with the other national regulators,) to explain why it has been so unreactive, unaware and in such positive denial of the possible harm and deaths caused to the American population by the drugs that it has approved since 1988.

The significance of this paper is that for the first time some credible numbers are available to assist the FDA who confidently assert, without any knowledge of the number of patients at risk and the extent of harm that the “benefits of the drug outweigh the harm “. Now with the IMR results “harm/ benefit ratios” can be discussed scientifically and three very serious questions can be asked.

- 1) What processes have the FDA used to measure the “benefit” for SSRI drug users?.
- 2) How many “units of benefit” equate to one drug induced suicide ?
- 3) How many drug induced suicides will the FDA tolerate before robust regulatory intervention is provoked ?

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6 June 2004

- Ref1: Open Letter to Congressmen Barton and Greenwood “Number of US Citizens at risk to SSRIs” : Graham Aldred : 27 April 2004.
- Ref2: PEM Report No .6: Paroxetine : William Inman et al : 1993: Pharmacoepidemiology & Drug Safety: Vol 2 393-422.
- Ref3: A Comparison of paroxetine etc by observational cohort studies. FJ MacKay et al: 1997: Pharmacoepidemiology & Drug Safety: Vol 6 : Supp 3: 5-11.
- Ref 4 Modelling Suicide Risk in Affective Disorders: A P Boardman & D Healy: 2001: Eur. Psychiatry vol 16: 400-5.