Research fraud, prisoners and ADHD drugs in Sweden

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The study was hailed in media and used for new prescription guidelines. But the actual disastrous results were concealed. No one – except the researchers involved – knew that 26% of the subjects receiving the "ADHD drug" Concerta in high dose relapsed into addiction *the first week* when released from prison, or that 41% had relapsed the first two weeks.

This is a short story about research fraud and how one can turn a disastrous result into a success. How one can recommend "the new treatment" as an important step to help prisoners – even fooling the government to issue guidelines saying that the treatment seems to make prisoners drug free.

We are talking about a Swedish study, published in the scientific Journal Addiction, and lead by Professor Johan Franck at Karolinska Institutet and Clinical Director of the Stockholm Centre for Dependency Disorders, assisted mainly by psychologist Maija Konstenius.

In the study, financed by the tax payers with 4.5 million SEK (605,000 US dollars), 54 prisoners, "with ADHD" and a background as amphetamine addicts, got methylphenidate (Concerta) in a high dose (N=27), or placebo (N=27). The "treatment" was started some weeks before the release date. The released prisoners were to visit the clinic twice a week to get the drug (classed as a drug with high abuse potential in the same class, Schedule II, as cocaine) *in a very high dose* – most of them 180 mg – or to get sugar pills. When visiting the clinic they should also provide a supervised urine specimen.

The study was officially presented as a "double-blind, placebo-controlled randomized study" – meaning that neither the study subjects nor the researchers should know who got what (active drug or placebo). But it doesn't take much to figure out that this was utterly false: Of course the experienced drug addicts immediately knew if they got the narcotic drug in a high dose or if they got sugar pills. And why bother to come to the clinic to get a sugar pill?

In actual fact this was the whole idea with the study: The study subjects receiving sugar pills *should* drop out fast, and then be counted as "relapsed to addiction". As Professor Johan Franck wrote in his application papers for the study: "It can be expected that those who get randomized to placebo will cut the contact with the clinic." And so they did!

Actually 7 of the 27 persons (26%) who got sugar pills didn't provide any urine specimen at all – they fell off the first week (!); they never even came to the clinic, or didn't leave any urine specimen *if* they arrived. *And were immediately counted as a "positive for illegal drugs" – to a value of 90% of actual positive urines.* And were so counted (twice a week) for the remaining 22 weeks. *After two weeks* in freedom 21 of the 27 persons (78%) receiving sugar pills had dropped out from the study – meaning there were only 6 persons left in the group!

Of course their drop-out created a *tremendous* amount of "positive urines" (even if dropping out was counted with a value of "only" 90%). And that's how the "result" of the study was created. The main result being the *difference* in positive urines between the group receiving the narcotic drug Concerta and the group receiving placebo.

But *what was the actual result for the group receiving Concerta*? No one knew as this was not at all told in the published article about the study: "Methylphenidate for attention deficit hyperactivity disorder and drug relapse in criminal offenders with substance dependence: a 24-week randomized placebo-controlled trial" (Addiction. 2014; 109(3):440-9), by Franck, Konstenius and colleagues (available here http://onlinelibrary.wiley.com/doi/10.1111/add.12369/pdf).

And here we really get into scientific misconduct. Part of the definition of research fraud is "misrepresentation of the research process … for example through incorrect use of methodology, dishonest inclusion or exclusion of data, deceptive analysis of data that intentionally misrepresents their interpretation …" (http://www.codex.uu.se/en/etik6.shtml)

And in this study, which first of all was misrepresented as a "double-blind study", data about what happened with the persons receiving Concerta were *deliberately* excluded to such an extent that it was impossible to understand even for the most careful reader.

Let's look at some of the results for the Concerta group – which emerged when the underlying documents for the study finally were released, after vivid requests using the Swedish Freedom of Information Act. We could then see that:

- **7 of the 27 subjects in the Concerta group (26%) relapsed into addiction – had actual positive urines – *the first week* of release from prison; the same week when most of them reached the maximum dose of 180 mg of the legally prescribed stimulant drug (Concerta).**
- **11 persons (41%) relapsed in the first *two* weeks after release.**
- **20 persons (74%) relapsed during the study – did leave *actual* positive urines (5 dropped out without leaving positive tests, 2 completed with no relapses).**
- **7 of the 9 persons who *completed* the study, who were present at week 22 in freedom, had relapsed into addiction. The 7 subjects had 2, 3, 9, 9, 10, 12, 23 relapses – in average 10.**
- **18 persons (67%) dropped out of the study before it was over.**

But this was not known to the enthusiastic, uncritical media representatives reporting that prisoners now – finally – should get the help they really needed. Media couldn't understand that the real results were "drowned" in a sea of unimportant comparisons with the dropped out placebo group. The results in the study became "positive" as the persons in the placebo group reacted as was expected – they left the study *fast*! And this of course affected all areas of the study: positive tests, time to first positive test, assessment of "ADHD symptoms", and of course, retention in the study. Neither did media know that the study was disapproved from the beginning with scathing words in the internal document from the assessor at the Swedish Medical Agency (MPA), the well-known Professor emeritus in psychiatry Lars Gunne. The later approval of the study was more to be seen as a political decision.

The press release from the researchers at Karolinska Institutet (14 October 2013) did distort the actual results even more, presenting the study with the headline "ADHD medication effective for persons with addiction"; saying that the higher dose ("double compared to what has been used in earlier studies") gave the effect that the subjects got "less relapses in drug abuse, got decreased ADHD symptoms and stayed longer in treatment".

And so national media reported the news: “ADHD medication instead of drugs”, “Less relapses with ADHD medication”, and “Researchers at Karolinska Institutet have seen that methylphenidate, a stimulant medication, effectively lowered ADHD symptoms and drug dependence if given in an individually higher dose compared to what was done before. This is an epoch-making work …”

An “epoch-making work” where 41% (!) of the persons who got the drug relapsed within two weeks, where 67% dropped out from the study and where 7 of the 9 persons who completed the study had relapsed in addiction, in average 10 times?

This is how media can be fooled by a distorted, manipulated presentation of data.

But it gets worse.

Presenting treatment guidelines based on distorted research data

The manipulations of scientific studies (mainly by pharmaceutical companies) have led to numerous articles in medical journals in recent years; articles showing how the companies have control over the “scientific process” and that the end results are often determined already by the design of the studies. Honest academic researchers and patient representatives have demanded transparency, that the actual research results – not only the distorted published versions – become available for independent researchers and the general public.

This study by Franck and Konstenius is an excellent example of the need for transparency, for gaining access to the actual results, the underlying data.

It has taken several court decisions and three critical decisions from the Swedish Parliamentary Ombudsmen (JO) to get the researchers in this area to understand what the good Swedish Freedom of Information Act actually means, and that the real research results are not their own property.

And we come to the underlying documents, needed to understand *the real results* of this study – as given above.

These documents must of course be available for government agencies analysing the results of the study, especially when this analysis is forming the basis for national treatment recommendations. As in the on-going project with guidelines for treatment of drug abuse from the Swedish National Board of Health and Welfare.

Preliminary guidelines were issued in March 2014. In these the following conclusion could be found: “In amphetamine dependence and concurrent adhd *methylphenidate* can be used to treat the amphetamine dependence, as it seems to have an effect on *a drug-free condition*.” [Emphasis here.] (http://www.socialstyrelsen.se/Lists/Artikelkatalog/Attachments/19405/2014-3-24.pdf Swedish)

The project leader (Branting) at the National Board of Health and Welfare explained in a mail that this conclusion was reached from the study by Franck and Konstenius [and from a smaller, actually even more failed study, by the same researchers].

The next logical question, was of course about the research data available for the National Board of Health and Welfare in its analysis. It gave this incredible answer:

“Our expert had no other data to work with than the two published articles …”

Meaning that the National Board of Health and Welfare, in its important work with scientific guidelines, didn’t care more than the media to analyse the objective, underlying data for this study. The Board just used the distorted published data, and suddenly “treatment” with a high dose of methylphenidate had found its way into the preliminary guidelines for treatment of drug addiction.

We can assume that the uncritical expert (at the University of Lund) would be red in his face if he found out what his words about methylphenidate bringing about a “drug-free” condition corresponded to in the real world: 41% of the research subjects reverting to illegal drugs within two weeks; 77% of the persons *completing* the study having in average 10 relapses in 22 weeks.

But it gets worse.

It turned out that the important objective research data I had gained access to via the Freedom of Information Act were not *available* at the National Board of Health and Welfare. So of course the Board and its project leader would welcome these important documents, so that they could make a real scientific analysis of the research project (at least that would be the assumption).

And so I sent the most important documents to the project leader. As this one **http://jannel.se/Underlag1.pdf** , in which one can see, week by week, which persons in the Concerta group and in the placebo group who provided actual positive urines (“1,00”), which persons in the groups who did not turn up/dropped out from the study (“0,90”) and which persons who provided negative (clean) urines (“0,00”). From this, one can work out the results presented above. Number two: “retention” in the study (to be read in relation to the first document) **http://jannel.se/Retention.Underlag.pdf** and the self-assessed ADHD symptoms, which really just shows that the placebo group didn’t have a chance to write anything at all, as most of them dropped out right away, **http://jannel.se/Haga.CAARS.SUBscales.pdf**

The Board acknowledged the receipt of the documents, but wrote: “…we need to get it [these underlying research documents] verified by the research group in order to include it in our position.”

This was of course a positive development: The Board now had the needed documents for an independent analysis of the study, and needed only to get the accuracy of the documents verified.

But one month later (29 October 2014) the Board writes this: “We have judged that the information we need to evaluate the study can be found in the published article. We have therefore not had any contact with the research group about these basic documents.” I asked the project leader how they could find the results I have described above in the published article by Franck and Konstenius, but got the answer: “This matter is now closed.”

Thus we have come to the bizarre situation that the Government Agency evaluating the scientific evidence for different treatments was *refusing* to accept the real objective results

in a project, and instead was relying on a distorted, manipulated presentation – actually *knowingly* forming its conclusions in the area on research fraud.

But in the end the National Board of Health and Welfare had to change its mind about the recommendation, *even if one used the easy way out.*

The preliminary guidelines were changed. The study was no longer said to give evidence about methylphenidate having an effect on a drug-free condition. Instead it was said that "the scientific evidence is insufficient and that research is expected". It was said that due to a high drop-out rate the risk for bias is high. And so, even if the linked documents had not been evaluated, the National Board of Health and Welfare concluded: "It is not possible from the study to assess effects of ADHD symptoms or substance abuse from treatment with methylphenidate of persons with ADHD and concurrent amphetamine dependence."

We have for some years now seen a small group of researchers from Sweden (Franck/Konstenius, Ginsberg, Lichtenstein, Tiihonen) publishing articles internationally about criminality as a genetic defect ("dysfunction"), claiming that 40% of all prisoners "have ADHD", and pushing "treatment" with narcotic stimulant drugs in a high dose as the "solution" to the biologically based criminality.

It's time to ask some critical questions and examine the real results of their research.

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