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The opposition to «bureaucratic obstacles to medical research» is part of the propaganda which has as its primary objective the promotion of the sale of pharmaceutical drugs.

What happened to Dan Markingson?

Early in the morning of 8 May 2004, Mary Weiss received the worst message a mother can hear: her son Dan Markingson had taken his own life. Weiss had long warned the doctors treating her son that this might be the outcome. Less than two weeks earlier she had in desperation left a message on the doctor's answering service (1): «Do we have to wait until he kills himself or someone else before somebody does something?»

In the autumn of 2003 Dan Markingson became seriously ill with paranoid and other delusions. When on 12 November he threatened to kill his mother if he was «asked» to do it, Mary Weiss became frightened and called the police. Dan was admitted to Fairview University Medical Center in Minnesota and put on risperidone by the doctor. Stephen C. Olson was of the opinion that Dan was psychotic and dangerous, and therefore two days later he sought to have him compulsorily detained in a psychiatric hospital because he «was in no state to make his own decisions». On 17 November a clinical psychologist also recommended compulsory detention. In Minnesota, patients who are compulsorily detained can avoid psychiatric hospital if they are willing to follow the treatment programme recommended by the psychiatrist, a «stay of commitment». Olson requested this for Dan on 20 November, permission was granted and he proposed that Dan should participate in a study funded by the pharmaceutical industry. On 21 November, with no next of kin present, Dan Markingson signed a form on which he consented to participate in the CAFE study (Comparison of Atypicals in First Episode) (1, 2). How was it possible that Dan, who a few days earlier was assessed as «in no state to make his own decisions», was suddenly competent to give his consent to participate in a clinical drug trial?

The study appeared credible (1, 2). The purpose was to compare the effect of three «atypical» antipsychotic drugs – quetiapine, olanzapine and risperidone – all approved by the Food and Drug Administration (FDA). The study was financed by Astra-Zeneca, the manufacturer of quetiapine (Seroquel). What was less clear was that this was a «non-inferiority study», i.e. a study the purpose of which was none other than to show that none of these drugs was inferior to the others. To determine a significant positive difference between various treatment alternatives is difficult. To set up a trial in such a way that nothing is significantly different from anything else is easy. If what is needed in order to obtain a statistically significant treatment effect is a certain number of patients and a defined difference between the groups that are to be compared, all that is required are sufficiently small groups in order for the difference between them *not* to be significantly different. «Non-inferiority» studies have only one purpose: to give the manufacturer of the drug in question an endorsement to market it as being equally good as the other drugs in that group. These clinical studies do not give participating or future patients any benefit in terms of treatment. Are those who participate given a clear message that they are involved in a marketing exercise, not research?

The CAFE study was not just devoid of clear benefits for Dan Markingson, it also entailed an exposure to risk for him. For example, there was no opportunity to take the patients off the drug they had been put on through the double-blind process, even if it was not effective, and there were restrictions on how many drugs they could take to alleviate side effects. The patients in the CAFE study thereby had fewer treatment alternatives than others (1).

When Mary Weiss discovered that her son had been recruited to be part of a clinical study, she repeatedly attempted to protest – without being heard. She telephoned and wrote to Stephen C. Olson, who headed the study, and to Charles Schulz, who was in charge of the psychiatric unit at the hospital, and told of her concern about the change in her son – not least what she perceived as his «inner rage». Schulz replied that «it is not obvious to me how you think those treating him should be able to deal with this». It was after this that Mary Weiss called in with her telephone message.

In the years that have passed since Dan Markingson's tragic death, numerous individuals, groups of researchers and organisations have attempted to initiate an independent enquiry on the CAFE study, especially since several of the researchers were financed by the pharmaceutical companies. All requests have been rejected. In October 2013 a group of more than 170 researchers in health law, health ethics and research, among them former and current editors of medical journals, sent a letter to the University of Minnesota. In it they urgently requested an open investigation of the study (3). This exhortation was also refused.

The Declaration of Helsinki regulates medical research. The latest version (4) reminds us that «while the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects» and that «medical research involving human subjects may only be conducted if the importance of the objective outweighs the risks and burdens to the research subjects». If this had been followed, Dan Markingson would not have been enrolled into the CAFE study. How many others have been exploited?

We often hear that there are many «bureaucratic» obstacles in the way of medical research; that declarations of consent, conflict of interest forms, research protocols and applications to ethics committees delay medical progress. At the close of the year there is reason to stop and ponder whether this is true – or whether it is part of the propaganda which has as its primary objective the promotion of the sale of pharmaceutical drugs.

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