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To Norwegian National Research Council
(grants 133897/320 and 154642/320)

cc Ingrid Melle
Robert Whitaker

Re: the TIPS study, which was supported by Norwegian National Research Council

Dear Torbjørg Øyslebø,

thank you so much for your email from 20 February where you say that it is a very important issue that I address and that the Research Council is very concerned about this. You also wrote that you had talked to professor Ingrid Melle and that she had promised to reply to our questions.

I wish to draw the Council's attention to the fact that Dr Melle, in her reply to me in an email, copied to you, from 28 February did not address my questions about the causes of deaths appropriately. Melle explained, among other things:

"The Hegelstad et al 2012 paper is a personal follow-up of all patients included in the original TIPS study (1997-2000); ten years after start of first treatment. The paper does not indicate 49 deaths, as stated in your letter. After re-reading the letter and the paper several times, I think you have misread the papers Figure 1. This figure is a flow-chart of participants and attrition at the different follow-up points (one, two, five and ten years) . The figure gives at each step a cumulative account of the reasons for non-attendance. They are not supposed to be summarized further. The figures given for the last time period is the study total, 16 deaths in the intervention site and 12 deaths in the non-intervention site a total of 28. The same account is given in the text."

My comment to this is: Figure 1 in this paper is seriously misleading because flowcharts always show numbers of patients who were lost or died during the course of a study. This means that we did not misread the paper. The way we read the flowchart was correct, which is why we arrived at 28 + 21 deaths, or a total of 49 deaths. The authors made a serious mistake, also because they did not write anywhere in the text that they had used a flowchart in a highly unusual way (which we have never seen before) adding deaths from earlier time periods to those that occurred in later time periods. They only write: "Figure 1 provides an overview of the flow of participants through follow-ups at 1, 2, 5, and 10 years." See the flowchart on the next page.

More importantly, Melle did not respond fully to our concerns. In my paper from 21 Sept 2017, which I had enclosed (Psychiatry Ignores an Elephant in the Room. https://www.madinamerica.com/2017/09/psychiatry-ignores-elephant-room/), I explained that it is surprising that 8 young people died from physical illness and asked: What were these illnesses exactly and what were the cardiovascular illnesses? If some of these people suddenly dropped dead, it could be because antipsychotics can cause QT prolongation.

Melle did not detail at all the causes of these deaths in her email to me but merely repeated them in a table (see below).

FIGURE 1. Overview of Patient Participation in a Long-Term Follow-Up Study of Early Detection in Psychosis

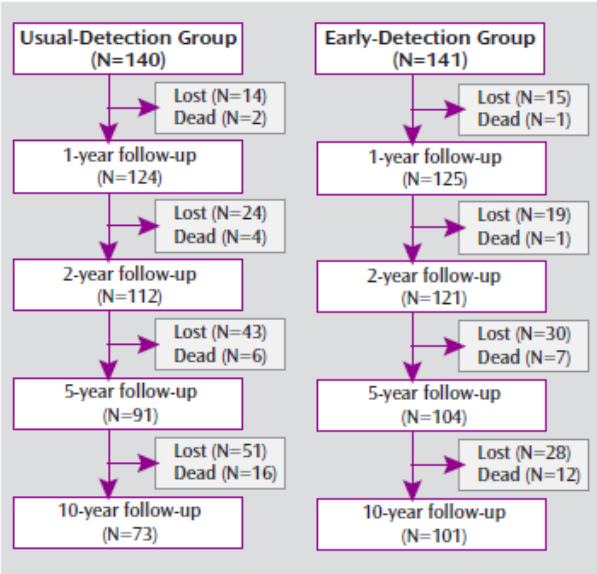

Table 1. Causes of death during the first ten years after start of treatment.

	N	%
Alive	**250**	**89.0**
Suicide	**16**	**6**
Confirmed suicide; violent means	*4*	1.4
Confirmed suicide; other highly lethal means	*5*	1.8
Confirmed suicide; drug overdose or other intoxications	*2*	0.7
Confirmed suicide, other means	*2*	0.7
Probably suicide; drug overdose or other intoxications	*3*	1.1
Other causes of death	**15**	**5**
Accidental drug overdose	*5*	*1.8*
Accidents	*2*	*0.7*
Natural death, cardiovascular illness	*3*	*1.1*
Natural death, other illnesses	*2*	*0.7*
Natural death of unknown causes	*3*	*1.1*

31 deaths in 281 patients who were only 29 years on average when they were included in the study, and who were followed up for 10 years, is a very high death rate (11%).

Melle's study might give us a unique insight into why so many patients with schizophrenia spectrum disorders die so young. Such knowledge could be used to treat the patients better in future thereby avoiding some of these deaths.

Melle wrote to me that the data on causes of death were attained through blind linkage on person-numbers by Statistics Norway and Statistics Denmark, and contained the full information available to the doctors writing out the death certificates.

Since detailed information exists about the causes of death, I request to see this information, which can be sent to me in an anonymised format so that I cannot identity the 10 patients who died due to accidents, cardiovascular illness, other illness or from unknown causes. Eight of these deaths are called "natural deaths", although it is not in any way "natural" to die so young of, for example, cardiovascular illness.

We need to know in detail why these 10 patients died. Antipsychotics were used liberally in the study and some or all of the deaths could have potentially been caused by the drugs the patients were on, which often involve polypharmacy. The only information I have been able to find on drug usage in the two papers is table 2 in Hegelstad's paper, which says that 121 patients out of 174 (70%) were still on antipsychotic medication after 10 years. This is an extremely high usage of antipsychotics. In contrast, in Lappland where the Open Dialogue model is practised, only 33% of 71 patients were ever treated with antipsychotics, and after 5 years, it was only 17% who were on them (Seikkula J et al. Psychotherapy Research, 2006;16:214-28).

It is curious, considering the high death rate, that the authors nowhere discuss whether the deaths could have been caused by the drugs and do not even tell their readers about the drugs the patients were on. I would of course be highly interested in seeing deails about drug usage after 10 years, if such data are available.

I reiterate what I noted in my first letter to you, that this is a vitally important issue. When young people who are receiving antipsychotics die, we need to know why they died in order to reduce the risk of death in future.

I also wrote, in the article I had attached:

"In contrast to the authors of the TIPS study, professor of psychiatry Merete Nordentoft, Copenhagen, was forthcoming when I asked her about the causes of death for 33 patients after 10 years of follow-up in the OPUS study, also of patients with a first-episode psychosis.[3] I specifically mentioned that suicides, accidents and sudden unexplained death could be drug related. I received a list of the deaths and Nordentoft explained that no one had a heart related cause of death registered but that this was probably because they were so young. In the certificates she had seen some patients had simply dropped dead, one of them while sitting in a chair. This is how it should be. Openness is the way forward if we wish to reduce the many deaths that occur in young mental health patients."

Finally, Melle asks me: "Since you are writing with a Nordic Cochrane Centre letter-head, Im curious if Cochrane has any plans for doing anything in this area?"

I am not sure I understand the possible relevance of this question. Why would I *not* use the letterhead for the Centre I established in 1993? Cochrane is an international organisation with tens of thousands of members and there are many Cochrane reviews on antipsychotics, which Melle undoubtedly is aware of. She likely also knows that we are very active at the Nordic Cochrane Centre in this area. We do research on psychiatric drugs and have recently published several important papers in the BMJ and other prestigious journals.

Yours sincerely,

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