To: Professor Danuta Wasserman, Head and Founder of the Swedish National Centre for Suicide Research and Prevention of Mental Ill-Health (NASP); Director for WHO Collaborating Centre for Research, Methods Development and Training in Suicide Prevention

Concluding Remarks

Regarding statements in Swedish radio about the Cochrane study *"Suicidality and aggression during antidepressant treatment: systematic review and meta-analyses based on clinical study reports"*

12 March 2016

Thank you for your mail dated 7 March. I realize at this point that I can't get any straightforward answers to my questions. It is however my hope that you in future talks and writings about antidepressants, children and suicide give a more balanced presentation about what we now actually know. Please consider these concluding remarks.

In your mail from 7 March you give the following comments to my earlier questions below (my translation of your mail):

> "The conclusion in the study "Suicidality and aggression during antidepressant treatment: systematic review and meta-analyses based on clinical study reports", published in British Medical Journal 2016, is much longer than the one you quoted in your message below.
>
> As for point 2 I want to refer to the National Board of Forensic Medicine and the Medical Products Agency who maybe can verify the data you refer to. Analysis of the effects of medicines is not part of the task of NASP (Swedish National Centre for Suicide Research and Prevention of Mental Ill-Health) Unfortunately NASP cannot assist you more, but I will thank you for your interest in these important questions.
> Kind Regards
> Danuta Wasserman"

Yes it is very true that there are more conclusions to be found in the BMJ study (the Cochrane review). [1] But my whole point here is that you don't seem to be in agreement with the research findings that *the risk of suicidality and aggression is doubled for children and adolescents when treated with antidepressants* and that *their effect seems to be below what is clinically relevant.* How can we otherwise explain your statement in Swedish radio: *"My conclusion is not to be more careful but my conclusion is to make it [the prescription of antidepressants] faster ..."* combined with other initiatives and better follow-up. In other words you recommend that antidepressants should be given *even earlier* and *not less* than now to children, adolescents and young adults.

I have in this mail conversation tried to get an answer if you really meant what you said with this remarkable statement, but I have not been able to get any clarification. So I suppose that you actually meant what you said, which is contrary to the conclusion in the BMJ article ("*we suggest minimal use of antidepressants in children, adolescents, and young adults, as the serious harms seem to be greater, and as their effect seems to be below what is clinically relevant")* and contrary to the text in the approved SPCs for all antidepressants.

As for point 2 – the research data about antidepressants, young women and suicide in Sweden: *I* don't need any form of help with this. I don't need to get the data confirmed by the the National Board of Forensic Medicine, the National Board of Health and Welfare, and the Medical Products Agency – *of the simple reason that the data are directly produced by these agencies.* My point here is that you – thanks to my efforts – are in possession of these very important data about young women, antidepressants and suicide. Neither you nor NASP did have these data before I sent them to you – 6 February 2015.

One important reason to update you about the current scene in Sweden was this: I have never seen any reanalysis from you of the data presented by you and Göran Isacsson in BMJ 20 years ago, where you wrote: *"A consistent finding in surveys of suicide is that about half of the patients who commit suicide are depressed."* And: *"Our most substantial finding, however, consistent with those of others is that few people are taking antidepressants at the time of suicide, although half of the people who commit suicide are depressed."* [3]

Well the current data – which you have in your hand since one year ago – show: *51% of young women (2006-2013) were prescribed antidepressants within a 12-month period before the suicide,* and that it is definitely not the case among young women that *"…few people are taking antidepressants at the time of suicide",* as toxicological analyses *found antidepressants in 41% of all young women who committed suicide (2013)?*

I think it would be honest to present what you know about the current scene as regards prescription of antidepressants and suicide rate among young women in Sweden.

In your comments you let me know: *"Analysis of the effects of medicines is not part of the task of NASP."* I don't know in which capacity (Head of NASP or Director for WHO Collaborating Centre for Research, Methods Development and Training in Suicide Prevention) you commented the findings of the Cochrane review, but I would say your statements in Swedish radio are *very much* an "analysis of the effects of medicines" [antidepressants]: *"Antidepressants save lives", "antidepressants are very good", "Antidepressants can cause adverse effects even in adults, but they are not life-threatening".*

I should also add the following:

You have probably seen the new scientific article about the increased prescription of antidepressants to children [4], creating headlines in the countries investigated. [5, 6] In the article (about Germany, the Netherlands, USA, UK and Denmark) we find that the prescription of antidepressants (0-19) in UK increased 54% in 7 years (2005-2012); in Denmark 60% (the highest increase in these five countries).

We find that the response to this from the WHO director of mental health Dr Shekhar Saxena is to raise serious questions [5], and from the Minister of Health in Denmark to say that it is disappointing to see doctors not abiding by the guidelines and demanding an investigation into the matter. [6] We can easily compare this with the situation in Sweden, where the annual prevalence of antidepressant use (0-19) in 7 years (data available only from 2006) up to 2013 increased 59% (the same increase as in Denmark). However the prescriptions in Denmark to 0-19 have decreased slightly from 2010 up to 2014 – but in Sweden we see an increased prescription level year by year. Updated figures for Sweden

show an increase both up to 2014 and 2015. *From 2006 to 2015 the prescription of antidepressants in Sweden (0-19) in*creased 85%! [7] *For adolescents 15-19 we see an increase with 105% (!) in the years 2006-2015.* ***One in twenty teenage girls (15-19) in Sweden got antidepressants 2015!***

I would like to see your concerns about that disastrous situation in media.

I copy the data in this mail also to the Ministry of Health and Social Affairs. It must be interesting for the Minister for Health Care to get updated information about the prescription of antidepressants to children and adolescents in Sweden and the relation to the increase in suicides.

The Ministry must also ask the question: Will the programs from NASP about suicide prevention lead to an even higher prescription level of antidepressants (earlier and faster)?

Kind Regards,

Janne Larsson
Reporter
janne.olov.larsson@telia.com

[1] Tarang, Sharma et al, Suicidality and aggression during antidepressant treatment: systematic review and meta-analyses based on clinical study reports. BMJ 27 Jan 2016,doi: 10.1136/bmj.i65) http://www.bmj.com/content/352/bmj.i65
[2] Sveriges Radio, Antidepressiva en risk för unga (Antidepressants a risk for young people), 29 January 2016, http://sverigesradio.se/sida/avsnitt/668111?programid=412 Antidepressiva kan öka självmordstankar hos unga (Antidepressants can increase thoughts about suicide in young people), http://sverigesradio.se/sida/artikel.aspx?programid=406&artikel=6355574
[3] Isacsson G, Holmgren P, Wasserman D, Bergman U. Use of antidepressants among people committing suicide in Sweden. *BMJ.* 1994 Feb 19; 308(6927):506–509. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2542784/
[4] Bachman et al, Trends and patterns of antidepressant use in children and adolescents from five western countries, 2005–2012. European Neuropsychopharmacology 2016, http://dx.doi.org/10.1016/j.euroneuro.2016.02.001
[5] BBC, Anti-depressants: WHO concern over use by children, 8 March 2016, http://www.bbc.com/news/health-35756602
[6] Politiken, Minister kritiserer læger: I må ikke udskrive depressionsmedicin til børn (Minister [for Health] criticizes doctors: You must not prescribe antidepressants to children], 9 March 2016, http://politiken.dk/forbrugogliv/sundhedogmotion/ECE3107128/minister-kritiserer-laeger-i-maa-ikke-udskrive-depressionsmedicin-til-boern/
[7] The National Board of Health and Welfare, The Register on Prescribed pharmaceuticals in Sweden, http://www.socialstyrelsen.se/statistik/statistikdatabas/lakemedel

From: Anna Johansson
Sent: Monday, March 7, 2016 4:37 PM
To: Jan Larsson
Cc: Danuta Wasserman
Subject: SV: (Answer needed) Regarding statements in Swedish radio about the Cochrane study "Suicidality and aggression during antidepressant treatment: systematic review and meta-analyses based on clinical study reports"

Bäste Janne Larsson,
Slutsatsen i studien "Suicidality and aggression during antidepressant treatment: systematic review and meta-analyses based on clinical study reports", publicerad i British Medical Journal 2016, är mycket längre än det du citerade i ditt meddelande nedan.

Beträffande punkt 2 vill jag hänvisa till rättsmedicinalverket och läkemedelsverket som kanske kan verifiera de uppgifter du hänvisar till. Analyser av läkemedelseffekter ingår inte i NASP:s uppdrag.
Tyvärr kan inte NASP bistå dig mer, jag vill dock tacka dig för ditt intresse för dessa viktiga frågor.

Med vänlig hälsning,
Danuta Wasserman
genom

Anna Johansson | Administration
Nationellt centrum för suicidforskning och prevention av psykisk ohälsa (NASP)
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Från: Jan Larsson [jan.olov.larsson@telia.com]
Skickat: den 27 februari 2016 21:47
Till: Anna Johansson
Kopia: Danuta Wasserman
Ämne: (Answer needed) Regarding statements in Swedish radio about the Cochrane study "Suicidality and aggression during antidepressant treatment: systematic review and meta-analyses based on clinical study reports"

To: Professor Danuta Wasserman, Head and Founder of the Swedish National Centre for Suicide Research and Prevention of Mental Ill-Health (NASP); Director for WHO Collaborating Centre for Research, Methods Development and Training in Suicide Prevention

Regarding statements in Swedish radio about the Cochrane study *"Suicidality and aggression during antidepressant treatment: systematic review and meta-analyses based on clinical study reports"*

27 February 2016

Thank you for your mail dated 23 February. To my surprise you didn't answer *any* of my questions. With this letter I will try to rephrase the questions to make it easier to answer.

You answered in Swedish (below), but as I think this communication is interesting for an international audience, considering your prominent position, I have translated your mail like this:

> "Regarding your questions I first refer to the Cochrane study: *"Suicidality and aggression during antidepressant treatment: systematic review and meta-analyses based on clinical study reports"* published author: T Sharma Nordic Cochrane Centre, Rigshospitalet, Blegdamsvej 9, Department 7811, 2100 Ø Copenhagen, Denmark and to my interview in Vetandets värld. The interview was given in Swedish and can in full be picked up here: http://sverigesradio.se/sida/avsnitt/668111?programid=412
>
> I further refer to the National Board of Health and Welfare, with the task of giving knowledge and support to the area of health care, to IVO [the Health and Social Care Inspectorate] with the task to follow up and evaluate how the health care area functions, and to the Medical Products Agency."

My original letter (below) shows that I am well acquainted with the Cochrane study—after all my questions about your statements were based on the content of this study. I have also listened to the whole interview, my quotes in the original letter are from that same interview. Probably my text also indicates knowledge about the work and function of the Swedish Government Agencies you mention.

I refer to what I wrote before and would be happy to get a clear answer to these questions:

1. Are you in agreement with the conclusion in the Cochrane study, *"Therefore we suggest minimal use of antidepressants in children, adolescents, and young adults, as the serious harms seem to be greater, and as their effect seems to be below what is clinically relevant"*?

2. Can you confirm that you have got the research material for Sweden (sent 6 February 2015) showing that *51% of young women (2006-2013) were prescribed antidepressants within a 12-month period before the suicide,* and that it is definitely not the case among young women that *"…few people are taking antidepressants at the time of suicide",* as toxicological analyses *found antidepressants in 41% of all young women who committed suicide (2013)?*

Kind Regards,

Janne Larsson
Reporter
janne.olov.larsson@telia.com

From: Anna Johansson
Sent: Tuesday, February 23, 2016 9:21 AM
To: Jan Larsson
Cc: Danuta Wasserman
Subject: SV: (Answer needed) Regarding statements in Swedish radio about the Cochrane study "Suicidality and aggression during antidepressant treatment: systematic review and meta-analyses based on clinical study reports"

Bäste Janne Larsson,

Beträffande dina förfrågningar hänvisar jag till dels Cochrane studien *”Suicidality and aggression during antidepressant treatment: systematic review and meta-analyses based on clinical study reports”* published author: T Sharma Nordic Cochrane Centre, Rigshospitalet, Blegdamsvej 9, Department 7811, 2100 Ø Copenhagen, Denmark och till min intervju i Vetandets värld. Intervjun gavs på svenska och kan i sin helhet hämtas på: http://sverigesradio.se/sida/avsnitt/668111?programid=412

Vidare hänvisar jag till Socialstyrelsen som har i uppdrag att ge kunskap och stöd till vården och omsorgen, till IVO som har i uppdrag att följa upp och utvärdera hur vård och omsorg fungerar, och till Läkemedelsverket.

Med vänlig hälsning,

Danuta Wasserman

genom

Anna Johansson | Administration
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Please consider the environment before printing this e-mail.

From: Jan Larsson
Sent: Monday, February 8, 2016 7:39 PM
To: Danuta.Wasserman@ki.se
Cc: anna.johansson.4@ki.se
Subject: Regarding statements in Swedish radio about the Cochrane study “Suicidality and aggression during antidepressant treatment: systematic review and meta-analyses based on clinical study reports”

Dear Danuta Wasserman,

I would really appreciate to get an answer to the questions below.

Kind Regards,
Janne Larsson

From: Jan Larsson
Sent: Sunday, January 31, 2016 10:39 PM
To: Danuta.Wasserman@ki.se
Subject: Regarding statements in Swedish radio about the Cochrane study “Suicidality and aggression during antidepressant treatment: systematic review and meta-analyses based on clinical study reports”

To: Professor Danuta Wasserman, Head and Founder of the Swedish National Centre for Suicide Research and Prevention of Mental Ill-Health (NASP); Director for WHO Collaborating Centre for Research, Methods Development and Training in Suicide Prevention

The text below also in PDF **http://jannel.se/LetterDanutaWasserman.pdf**

Regarding statements in Swedish radio about the Cochrane study *"Suicidality and aggression during antidepressant treatment: systematic review and meta-analyses based on clinical study reports"*

The article *"Suicidality and aggression during antidepressant treatment: systematic review and meta-analyses based on clinical study reports" from the Nordic Cochrane Centre was published in BMJ 27 January 2016.* [1] *Two days later you made extensive comments about the* article *and the subject in national Swedish radio.* [2]

I would like to get some clarifications about the statements you made in the radio program. As you have a prominent position internationally I write this in English so that an international public has the chance to read and understand your answer.

First, I would like a clarification about your comments on the prescription of antidepressants to children and adolescents. The Cochrane review made it clear that despite the serious shortcomings identified in the studies about antidepressants, the research team had been able to confirm that *"the risk of suicidality and aggression doubled"* for children and adolescents. They concluded, also with reference to earlier results: *"Therefore we suggest minimal use of antidepressants in children, adolescents, and young adults, as the serious harms seem to be greater, and as their effect seems to be below what is clinically relevant."* [1] In the SPCs for *all* SSRI:s we can also read: *"Suicide-related behaviours (suicide attempt and suicidal thoughts), and hostility (predominantly aggression, oppositional behaviour and anger) were more frequently observed in clinical trials among children and adolescents treated with antidepressants compared to those treated with placebo."*

However when the reporter in the radio program asks, with reference to the Cochrane review, *"can't a conclusion also be that you have to be more careful not to prescribe antidepressants to children, adolescents and young adults"*, you say that *we are already careful* and then give the following remarkable statement: ***"My conclusion is not to be more careful but my conclusion is to make it [the prescription of antidepressants] faster ..."*** combined with other initiatives and better follow-up. In other words you recommend that antidepressants should be given *even earlier* and *not less* than now to children, adolescents and young adults. We should, when evaluating that statement, know that the prescription of SSRI antidepressants to young persons (10-19) in Sweden ***doubled*** 2006-2014, and that 6.2% (!) of young women (15-24) got a prescription for antidepressants 2013 (see below about suicides among young women in that age group). [3]

My question: Do you really mean, what you say, that the result in this Cochrane review should *not* make prescribers "more careful" (and this despite the doubling of the prescriptions in Sweden since 2006); that you instead recommend that antidepressants are given *faster* (earlier) to children and adolescents?

Second, I would like to get an answer about your comments on adults and antidepressants. The Cochrane review made it clear that the *true risk* for serious harm remains unknown for both children and adults. It is said that misclassification, misrepresentation and under-reporting of harmful events found in the studies may have led to *"serious under-estimation of the harms"*. Peter Götzsche, one of the researchers, said: *"What I get out of this colossal under-reporting of suicides is that SSRIs [antidepressants including Prozac] likely increase suicides in all ages."* [4] In an Editorial in BMJ it is said: *"With doubts about the efficacy and effectiveness of antidepressants and evidence that they can produce such serious adverse reactions as suicidal and aggressive tendencies, regulators and the public need access to more comprehensive and reliable data."* [5]

But what did *you* say about this in the radio program? The answer: You turned this into something else. Instead of taking up the dishonest design and reporting of the harms of antidepressants you made it into an issue of "the young brain" versus "the adult brain". You said about the findings in the review, for children and adolescents: *"… it depends on brain development. We don't know for sure, but the young brain reacts differently than the adult brain".* You even make these comments about the prescription of antidepressants to adults: *"Antidepressants save lives", "antidepressants are very good", "Antidepressants can cause adverse effects even in adults, but they are not life-threatening".* [2]

My question: Don't you think the radio audience should have been informed that your comments about the young and the adult brain had *nothing* to do with the findings in Cochrane review, and that the audience should have been informed about the misclassification, misrepresentation and under-reporting of harmful events found in the studies – leading to a "serious under-estimation of the harms" done by antidepressants?

Third, you are well informed about the current catastrophic situation with antidepressants and suicide among young women (15-24) in Sweden.

We should compare the current situation with what you and Göran Isacsson wrote 20 years ago – also in BMJ. You wrote: *"A consistent finding in surveys of suicide is that about half of the patients who commit suicide are depressed."* And: *"Our most substantial finding, however, consistent with those of others is that few people are taking antidepressants at the time of suicide, although half of the people who commit suicide are depressed."* [6]

The current situation in Sweden is that 6.2% (!) of young women (15-24) got a prescription for antidepressants in 2013. There is a covariance between the sharply increased prescription of antidepressants and the increase in the number of confirmed suicides among young women. We can now see that the young women who commit suicide to a large degree were treated with antidepressants, within 6 and 12 months before the suicide. On average, *51% of the women (2006-2013) were prescribed antidepressants within a 12-month period before the suicide and 41% within a 6-month period.* Please compare this with your estimate 20 years ago that *"half of the patients who commit suicide are depressed".* [7, 8]

And it is definitely not true for this group of young women what you wrote 20 years ago: *"…few people are taking antidepressants at the time of suicide".* Instead we *now* find that a *very high percentage* of young women have taken antidepressants immediately prior

to death. In 2013 toxicological analyses *found antidepressants in 41% of all young women who committed suicide.* [8]

My question: Don't you think the radio audience should have been informed about the current catastrophic situation as regards antidepressants and suicide among young women in Sweden?

Janne Larsson
Reporter
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Sweden

[1] Tarang, Sharma et al "Suicidality and aggression during antidepressant treatment: systematic review and meta-analyses based on clinical study reports. BMJ 27 Jan 2016,doi: 10.1136/bmj.i65) http://www.bmj.com/content/352/bmj.i65
[2] Sveriges Radio, "Antidepressiva en risk för unga" (Antidepressants a risk for young people), 29 January 2016, http://sverigesradio.se/sida/avsnitt/668111?programid=412 "Antidepressiva kan öka självmordstankar hos unga" (Antidepressants can increase thoughts about suicide in young people), http://sverigesradio.se/sida/artikel.aspx?programid=406&artikel=6355574
[3] The National Board of Health and Welfare, The Register on Prescribed pharmaceuticals in Sweden, http://www.socialstyrelsen.se/statistik/statistikdatabas/lakemedel
[4] The Week, Antidepressants can raise risk of suicide in under -18', 28 January 2016, http://www.theweek.co.uk/69030/antidepressants-can-raise-risk-of-suicide-in-under-18s
[5] Moncrief, "Misrepresenting harms in antidepressant trials", BMJ *28 Jan* 2016*;* 352 doi: 10.1136/bmj.i217, *http://www.bmj.com/content/352/bmj.i217*
[6] Isacsson G, Holmgren P, Wasserman D, Bergman U. Use of antidepressants among people committing suicide in Sweden. *BMJ.* 1994 Feb 19; 308(6927):506–509. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2542784/
[7] Data from the National Board of Health and Welfare, accessed via FOI requests and via The Register on Prescribed pharmaceuticals in Sweden.
[8] Unpublished data from the National Board of Forensic Medicine, accessed via an FOI request.