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Open letter to Karla Soares-Weiser
Editor-in-Chief, the Cochrane Collaboration

Complaint about Cochrane editors committing editorial misconduct

Dear Karla,

I hereby complain to you about what I consider editorial misconduct in the Cochrane Common Mental Disorders group. Briefly, while this group imposed ever increasing demands to our protocol about safe withdrawal of depression drugs in patients who wished to come off them, the group at the same time negotiated with another author group on the same issue secretly. The group rejected our protocol two years and four months after we first submitted it while it accepted the other authors' protocol. They subsequently published a Cochrane review, which is very embarrassing for Cochrane as it is full of marketing messages that are irrelevant for the review and of many misleading statements, as I shall explain.

The formal background for my complaint

Among Cochrane's ten principles are:

3 **Avoiding duplication of effort** by good management, co-ordination and effective internal communications to maximize economy of effort.

1 **Collaboration** by fostering global co-operation, teamwork, and open and transparent communication and decision-making.

Cochrane has always sought to avoid that two reviews cover more or less the same ground, which is what avoiding duplication of effort is about. Obviously, open and transparent communication and decision-making is also essential, as outlined in the first principle.

These two principles were violated to a substantial extent in relation to my review on withdrawal of depression drugs.

An account of the issues that led to rejection of our protocol

In June 2016, at a meeting in Oxford, I contacted psychiatrist Rachel Churchill, the coordinating editor of the Cochrane Common Mental Disorders group, who showed great interest in my proposal to do a review on withdrawal of depression drugs.

I employed a PhD student, Anders Sørensen, to help me with the work, and on 11 July 2017, we submitted a protocol for the review to the group. It became a highly protracted process. It took nine months before we got any feedback. We promptly responded to five pages of comments and submitted a revised protocol. Seven weeks later, we were told that further improvement was needed. We submitted a third version and were informed that we would hear from the group "shortly." However, three months later, when we had still not heard from the group, we asked for an update. We were told we would hear from the group "by the end of the week," which became another month.

On 11 February 2019, 19 months after we submitted our protocol, the managing editor wrote: "I am very sorry for the delays. I have prioritised your project and done everything in my power to speed up the process." This message made us suspect that her superiors in the Cochrane group had deliberately obstructed the process to wear us out so that we would withdraw the review ourselves while the group would not be seen as being uncooperative.

On 18 April 2019, Churchill responded that they had had received extensive peer reviewer feedback except one, due to be submitted when the reviewer was back from leave. The peer reviewers had "highlighted the lack of detail provided around scope and methods" and Churchill attached a 30-page document with no less than 86 points.

Four editors and three peer reviewers had provided individual comments, and the document took up 12,044 words including our replies to earlier comments. This was seven times more words than our original protocol. Sørensen wrote to me that our review was quite simple and that we just wanted to help people who wished to come off their drugs but weren't allowed to do so and he asked: "What kind of world is this?"

On 22 May 2019, Churchill sent the 8th peer review to us with this message: "I'm sorry that we cannot proceed with this protocol. I hope that all the peer review feedback we have sent will be helpful to you should you wish to submit elsewhere."

The final peer review provided an excuse for Churchill to reject our protocol. It was one of the worst I have ever seen and I have seen a lot. During my 40-year research career, I have published 97 papers in the "big five" (*BMJ*, *Lancet*, *JAMA*, *Annals of Internal Medicine* and *New England Journal of Medicine*), several scientific books, and 19 Cochrane reviews, so I think I know how to do good research.

The 8th peer review was as long as a research article, 1830 words, and, in contrast to the other seven reviews, it was anonymous. We asked for the identity of the reviewer, but this was not granted. We appealed Churchill´s rejection, responded to the comments from all eight reviewers and submitted a fourth version of our protocol.

Very few changes to the protocol were needed but that didn't matter. It was very clear to us that the final reviewer's mission was to protect psychiatry's guild interests. This was done by denying a long array of scientific facts and by using strawman arguments accusing us of things we had never claimed. I shall describe the main issues here (I have published a more detailed account).

We were accused of "painting a picture" about avoiding using antidepressants, which did not represent the scientific consensus. However, our review would not be a consensus report and it would not address the benefits of antidepressants. This was irrelevant, as our review was about helping people come off the drugs safely when they wanted to stop taking them.

We had written that, "Some patients refer to the discredited hypothesis about a chemical imbalance in their brain being the cause of their disorder and therefore also the reason for not daring to stop." The reviewer opined that we dismissed many decades of evidence relating to neurochemical changes observed in depression and wanted us to document that neurochemical theories of depression were incorrect. We responded that our review was not the place for such discussions and that the hypothesis of a lack of serotonin being the cause of depression had been discredited by many convincing studies.

In relation to this, the reviewer accused us of having suggested with no evidence that prescribers perpetuate untruths to justify drug prescription. There is plenty of evidence for this, and in some countries, over 80% of the patients ascribe their depression to a chemical imbalance. They did not invent this myth; the psychiatrists did. My deputy director and I showed in 2020 that 29 of 39 popular websites in 10 countries (74%) attributed depression to a "chemical imbalance" or claimed the drugs could fix an imbalance.

The reviewer wanted us to "Start with a statement as to why antidepressants are considered by the scientific community to be beneficial … in treating a broad range of highly disabling and debilitating mental health problems." We responded that our review was not an advertisement for the drugs and that it was not relevant to discuss their effect in a review about stopping using them.

We were asked to explain the concept of ongoing prophylactic antidepressant treatment, "a well-accepted clinical strategy," but this was outside the scope of our review. Furthermore, the randomised trials comparing maintenance therapy with withdrawal are seriously flawed because harms are introduced by withdrawal symptoms in the latter group, some of which mimic depression.

The reviewer wrote that we conflated disease reappearance with withdrawal symptoms. This was erroneous. We clearly did not, but many psychiatrists do, which is a major reason why many patients are treated for decades or for life.

The reviewer argued that it is not an acceptable definition of dependence when a drug that has been effective stops being effective when stopped. This is a strawman. We would never postulate anything so foolish.

The reviewer argued that most people who had taken antidepressants for extended periods could stop safely without either rebound of the disease or withdrawal symptoms. This is totally false, which we had documented and referenced in our protocol. The reviewer ignored recent research results, including that the Royal College of Psychiatrists in the UK reported in 2012 that of 817 people who had stopped taking depression pills, 63% experienced withdrawal symptoms.

As the reviewer seemed to believe in the chemical imbalance nonsense and mentioned thyroid diseases and insulin, we explained that antidepressants cannot be compared with drugs used to treat such diseases. People with myxoedema and diabetes lack thyroid hormones and insulin, respectively, whereas people with depression do not lack serotonin.

The reviewer accused us of having implicated very clearly – even though not having expressly stated it – that antidepressants are "bad medications" to be avoided, "especially as there is no mention whatsoever of the beneficial effects … I find this argument to be unscientific, and unacceptable in the context of the current evidence base." Another strawman argument. See also below about the Cipriani et al. network meta-analysis. These drugs do not have clinically relevant effects on depression.

The reviewer wanted us to remove this sentence: "the patients' condition is best described as drug dependence" arguing, with reference to the DSM-IV drug dependence criteria, that it is an unreasonable misappropriation of a term. We responded: "The official definitions of dependence are ridiculous and self-serving, in addition to serving the drug companies that have benefitted hugely from the false perception that only benzodiazepines cause dependence, not the SSRIs. Craving larger and larger doses as a criterion for dependence is absurd, as it means that no one who smokes 20 cigarettes every day is dependent on smoking cigarettes!"

Our three appeals

Churchill ignored us. After two and a half months of waiting for her reply, we complained to you (Cochrane's Editor-in-Chief, Karla Soares-Weiser, who is a psychiatrist), about the inappropriate, definitive rejection of our protocol. We flagged that our review was very important; that we had done huge work with it and could finalise it in a matter of days; that we had the expertise and were members of networks of people interested in this issue (I co-founded two such organisations, and was on the board in both); and that it was a very hot topic right now, in the UK in particular.

We emphasized that the Cochrane Collaboration should not mount ever increasing obstacles along the way for those who volunteer to do the work to help suffering patients but should be forthcoming and helpful.

You replied that we should use the official process and appeal to Chris Eccleston, Senior Editor for the Mental Health and Neuroscience Network and a professor of medical psychology. Before we did this, we appealed again to Churchill and noted that, although, according to Cochrane rules, we should have heard from the group within three days of an appeal, we had received no reply.

Two weeks later, Churchill wrote that our protocol was finally rejected already in April 2019 and that she only forwarded the final peer review in May to be helpful in case we would publish elsewhere. *This was not true*. She invited us in April to revise our protocol: "I'm sorry to have to inform you that we are unable to accept this protocol for publication as it stands. I'm aware this will be unwelcome news, but I'm wondering whether you and the rest of the author team would wish, once again, to try and address the feedback. Any new submission would clearly need to attend to the comments and feedback attached, but I hope these will be helpful to you."

We were convinced that Cochrane wasn't interested in helping patients come off their psychiatric drugs. Earlier, we had written to the editors that they "are making something, which is very simple, highly complicated. Our review has a very simple aim: to help patients come off drugs they want to come off." When asked if reducing withdrawal symptoms or coming off the drugs was most important, we replied that, "the most important outcome for patients wanting to come off drugs is whether they succeeded coming off the drugs. Reducing withdrawal symptoms is a means to achieve this."

Even though we had already stated in our protocol that, "Studies of interest are those aimed at helping patients, through various interventions, come off any antidepressant drug completely," three editors and one reviewer wanted us to specify whether reducing the dose was also an objective. We explained that "it is very easy to reduce the dose, as virtually all patients are overdosed, so this is not of any interest to us." An editor wrote that our primary outcome of "complete cessation of antidepressant drug use" should be more clearly defined, as it might not be cessation for life. We responded that we could not define a yes/no outcome more clearly: "It is not a matter of complete cessation for life, as a patient might fall ill again." Apart from this, no studies follow all patients till they are all dead.

Our appeal to Churchill was not assessed by her but by a co-ordinating editor from another Cochrane group, Rebecca Fortescue from the Airways group, who upheld the rejection decision.

Three days later, we appealed to Eccleston. We wrote that the demands on the protocol had increased steadily over two years and that we had tried our best to comply with them. We also noted that, even though Fortescue had provided a list of 11 documents she received from the review group in her 2.5-page assessment, it was not possible to see what all of them were about. However, it was clear that she

had not received our reply to the final peer reviewer or our revised protocol, as we had already complied with many of the issues she raised in the version we submitted to Churchill on 13 June 2019.

Fortescue mentioned a few new issues we could easily address. For example, we had written that, "Cutting the dosage in half as the first step is often possible because most patients are overdosed." Halving the dose each time was the official recommendation in the UK and other countries as well, but the hyperbolic receptor binding curves show that most patients are overdosed and that rapid dose reductions by 50% every time are dangerous.

According to Fortescue, "a reader can be left in little doubt about the review authors' stance on the relative harms and benefits of psychiatric drugs, which does not fully reflect the current international consensus and could cause alarm among review users who rely on Cochrane's impartiality." We noted in our appeal that, "We are a bit surprised about this comment." Cochrane is not about consensus but about getting the science right. And assessing the harms and benefits of psychiatric drugs was outside the scope of our review. So, we did not write about this issue in our protocol or offered any "stance."

Fortescue repeated criticism she had seen we had already responded to, and some of her criticism was plain wrong, e.g. "Lack of clear structure in the background, which fails to make proper use of the preferred sub-headings." We had used all the Cochrane preferred sub-headings and our background section was very clear.

Even though we had pointed this out repeatedly, Fortescue, the editors and the peer reviewers did not seem to understand that "Types of participants" were people taking pills who wanted to come off them. As the withdrawal symptoms are similar for any type of patient, disease or drug, this suggested a broad approach. However, Fortescue wanted to have a clearer description of the population, intervention and comparators, e.g. if we would include trials in migraine prophylaxis, chronic pain or urinary incontinence, and an editor asked for details about which ages, sexes, settings, diagnoses of depression, and types of antidepressants we would include, as if we were planning to do a randomised trial. The answer was: everything! The editors requirements made absolutely no sense.

Although we explained to Eccleston that there was very little that separated us and the Cochrane Common Mental Disorders group after our latest revision, which Fortescue had not seen, he summarily rejected our appeal without a single comment. Apart from formalities, he offered only 56 words:

"I am very sorry that this title did not succeed because I agree with the importance of the question. I sincerely hope that you will both take what is done and complete it in another outlet. We need to stimulate a discussion on this important topic and it has become more important over time not less."

We appealed to you, Cochrane's Editor-in-Chief, on 2 October. On 5 November 2019, you upheld the rejection and explained why in just 72 words:

"I have had a chance to look carefully at the protocol, the editorial and the peer-review comments, together with your replies and the email exchanges between your team and the Review Group editors. The comments obtained from the open peer review process consistently indicated a lack of clarity regarding the review methods proposed and, despite more than one opportunity to address this, the protocol did not show sufficient evidence that this progressed."

You admitted that the review group had not treated us well: "I recognise that delays in the editorial process made for uncomfortable exchanges between the editorial office and you as authors, and I have

communicated this to the Review Group. However, having considered all the information, my final decision is to uphold the rejection of the protocol."

We wondered how you can call it an "open peer review process" when the final reviewer was anonymous, and we were ignored when we asked for his/her identity? We could not even check if the hangman had unacceptable conflicts of interest.

It took the review group two years and four months to reject our protocol for a very simple project and for no good reason.

Avoiding duplication of effort

Our protocol was finally rejected in November 2019 but already in February 2020, a similar protocol about withdrawing depression drugs was published in the Cochrane Library:

Van Leeuwen E, van Driel ML, De Sutter AIM, Anderson K, Robertson L, Christiaens T. Discontinuation of long-term antidepressant use for depressive and anxiety disorders in adults. Cochrane Database of Systematic Reviews 2020, Issue 2. Art. No.: CD013495.

It takes a very long time to get a Cochrane protocol approved and published, which means that this project must have been underway for many months, at the same time that the review group increased their demands to our protocol, pretty obviously in an effort of tiring us out, as already noted.

This double-dealing is totally unacceptable, particularly in a charity whose first principle is:

1 **Collaboration** by fostering global co-operation, teamwork, and open and transparent communication and decision-making.

And whose next principle is:

2 Building on the enthusiasm of individuals by involving, supporting and training people of different skills and backgrounds.

When volunteers who contribute to Cochrane's income for free by providing unpaid labour discover that they have been fooled by a review group, which is supposed to help them, it should not surprise anyone if Cochrane loses volunteers.

An analysis of the Cochrane review's Background section

Scientifically, I find that the outcome of kicking us out and letting other researchers do the Cochrane review is a bad one. Moreover, the review is far from being user friendly. The Cochrane review takes up 209 pages, or 110,770 words, the length of a full book, which is 23 times as long as our review of withdrawal from depression drugs of 9 pages.

I decided to study the huge Background section, which, with its 4239 words, is longer than most scientific papers. It is full of marketing messages that are irrelevant for the review and there are many misleading statements.

It is stated that "Maintenance treatment is provided to prevent recurrence of a new depressive episode after remission (Frank 1991)." There is no mention that every single maintenance trial ever carried out

is deeply flawed because many of the patients randomised to placebo experience withdrawal symptoms, which are erroneously interpreted as a relapse of the depression.

"Antidepressants have been shown to be efficacious in adults, compared to placebo, for acute treatment of major depressive disorder in the short term, although the effect is small (Cipriani 2018). In a previous Cochrane Review (Arroll 2009), authors found that for depression in primary care, between seven and eight people needed to be treated with an SSRI, and between seven and 16 people with a TCA, for one person to experience improvement in depression due to antidepressant use (i.e. number needed to treat for an additional beneficial outcome (NNTB))."

These marketing messages are invalid. Depression drugs are NOT efficacious in adults. The measured effects on the Hamilton scale, a difference of 2 over placebo, also in Cipriani 2018 (an effect size of 0.30 corresponds to a Hamilton difference of 2.3), is far below what is clinically relevant, as the least difference that can be detected is about 5-6 on this scale.

I have shown why the number needed to treat with a psychiatric drug to benefit one patient is largely an illusion. There are several reasons for this, but the most important one is that, for virtually all psychiatric drugs and clinical situations, more patients are harmed than those who benefit.

Harms and benefits are rarely measured on the same scale, but when patients in a placebo-controlled trial decide whether it is worthwhile to continue in the trial, they make a judgement about if the benefits they perceive exceed the harms. My research group did such an analysis based on clinical study reports we obtained from drug regulators. We found out that 12% more patients dropped out on a depression pill than on placebo ($P < 0.00001$). Thus, the patients consider placebo more useful than a depression drug.

This means that there cannot be an NNT for depression pills, only a number needed to harm (NNH). Our meta-analysis showed that this number is about 25.

Psychiatrists constantly tell the world how effective their drugs are by referring to NNTs. Technically, NNT is calculated as the inverse of the benefit difference. If, for example, 60% have improved on drug and 50% on placebo, NNT = 1/(0.6-0.5) = 10. But that is just the mathematics. The data such NNTs are derived from are highly flawed and here are the main problems:

1) NNT is virtually always derived from trials where the patients were already in treatment before they were randomised to drug or placebo. This means that many of those switched from a previous drug to placebo will experience withdrawal symptoms, which the psychiatrists interpret erroneously as disease symptoms. Therefore, the infallible recipe in the drug industry is that if you harm patients in the placebo group, you may conclude your drug works.

When the top among UK psychiatrists in 2014 tried to convince their readers that depression pills are highly effective, they claimed that they have an impressive effect on recurrence, with an NNT of around three to prevent one recurrence. But these trials did not assess recurrence but withdrawal symptoms in the placebo group. As only two patients are needed to get one with withdrawal symptoms when a drug is stopped, there cannot exist an NNT to prevent recurrence, only an NNH, which is two.

2) As psychiatric drugs have conspicuous adverse effects, the blinding in placebo-controlled trials is inadequate, which tends to exaggerate the measured benefit, as this judgment is highly subjective. If atropine is added to the placebo, the effect of tricyclics is only 1 on the Hamilton scale.

3) By far most trials are industry-sponsored, and fraud and other manipulations with the data are very common. We therefore cannot trust published trial reports. This became abundantly clear after one of my PhD students and I in 2010 opened up the archives at the European Drug Agency after we had complained to the European Ombudsman. Based on the regulators' clinical study reports, psychiatrist David Healy and I recently showed that fluoxetine in minors is unsafe and ineffective, in marked contrast to the claims in published trial reports.

4) The NNT only takes those patients into account that have improved by a certain amount. If a similar number of patients have deteriorated, there can be no NNT, as there is no benefit. Thus, a totally useless drug, which only makes the condition after treatment more variable, so that more patients improve and more patients deteriorate than in the placebo group, will seem effective based on NNT.

5) The NNT opens the door to additional bias. If the chosen cut-off for improvement does not yield the desired result, other cut-offs can be tried till the data confess under torture. Such manipulations with the data during the statistical analysis, where the prespecified outcomes and the statistical methods are changed after company employees have seen the data, are very common.

In psychiatry, NNT is so misleading that it should be abandoned altogether. We might instead use NNH. Since depression pills harm the sex life of about half the patients, the NNH is only two. Thus, by *not* using depression pills, we will preserve the normal sex life in one out of every two patients we do *not* treat. This leads to the conclusion that NNT in psychiatry - if used at all - should not mean number needed to treat but number *not* to treat in order to preserve the well-being of one patient. The reasoning I have outlined applies to all psychiatric drugs.

The Background section in the Cochrane review states that, "Evidence is insufficient to support or contest the efficacy of antidepressant medication for subthreshold and mild depressive disorder (Cameron 2014)."

This is terribly misleading. The evidence is absolutely clear that these drugs are ineffective for *all* degrees of depression, even for very severe depression. The reported effects in flawed trials that favour active drug over placebo are very small for all depression severities, e.g. 2.7 for patients with a baseline Hamilton score above 23 which is considered very severe depression, and 1.3 for milder degrees. Moreover, it is likely just a mathematical artefact that the effect seems to be slightly larger in severe depression. Since the baseline scores for severe depression are larger than for mild depression, any bias will influence the measured result more in patients with severe depression than in those with mild depression. If we assume that the bias due to insufficient blinding is 10% when estimating the effect in the drug group and, for the simplicity of the example, that there is no bias in the placebo group and no improvement between baseline and the final visit, then a Hamilton baseline score of 25 would still be 25 after treatment. But because of the bias, there would be a 2.5-point difference between drug and placebo. If the baseline is 15, that difference would only be 1.5.

"Evidence suggests that continuation of antidepressant treatment is effective, as it reduces risk of relapse and recurrence by 50% to 70% (Geddes 2003; Glue 2010; Kaymaz 2008), although none of the trials on which this conclusion was based measured withdrawal effects (Cohen 2019; Hengartner 2020; Recalt 2019)." These trials are so flawed that it is misleading to write that antidepressant treatment has a huge effect, 50-70%, on recurrence. The authors should have stated that there is no reliable evidence that the drugs reduce recurrence.

Similarly, it is misleading to write that "Antidepressant treatment duration of up to one year results in lower relapse rates among responders compared with treatment discontinuation in anxiety disorders." The expression "results in" means that the authors take it as a fact that the drugs reduce the risk of relapse, and their only reservation is that "withdrawal confounding bias may lead to overestimation of the effects of antidepressants (as many symptoms of withdrawal overlap with domains on an anxiety score)." They should have said that there is no reliable evidence that the drugs reduce recurrence.

"The effect of most antidepressants fully develops after some weeks, indicating that neurophysiological changes in brain tissue (e.g. changes in sensitivity and frequency of receptors) occurring in the presence of a constant level of active ingredients are necessary for improvement in depressive symptoms (Machmutow 2019)." This is highly misleading. One cannot say that the effect fully develops after some weeks when the effect even after seven weeks is so small that it is not clinically relevant and when there is a very gradual and slow separation of the Hamilton scores on drug and on placebo:

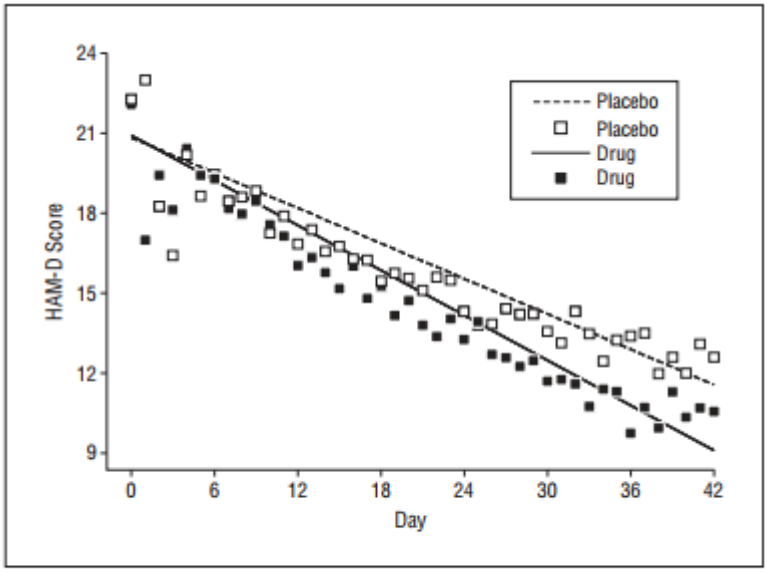

Figure. Observed vs estimated depression severity time trends for drug vs placebo in 37 adult and geriatric studies. HAM-D indicates Hamilton Depression Scale.

"However, suggesting that a single biochemical deficiency is the cause of depression and that antidepressants work by correcting chemical deficiency is not correct." Cochrane does not treat author groups equally. We were heavily criticised by the 8th reviewer for having written that the hypothesis about a chemical imbalance in the brain being the cause of depression had been discredited.

Even though one of the main drivers establishing the Cochrane Collaboration in 1993 was to assist patients in their decision making, the whole Background section is about what doctors think, e.g. "Reviews suggest that 30% to 50% of long-term antidepressant prescriptions had no evidence-based indication supporting their use." There is no mention that many patients would like to come off the drugs, which should have been the key motivation for the authors to do their review. The tone in the review is highly paternalistic rather than being cooperative in relation to patients.

There is nothing in the Background section about that the tapering should be hyperbolic not linear, which is essential if one wishes to minimise withdrawal symptoms. The authors quote a NICE

guideline from 2009 but do not criticise it for recommending linear tapering. This is one of the many sad developments in Cochrane. Those of us who started Cochrane in 1993 were willing to criticise the authorities. The current leadership wants to please the authorities, and in many cases also the drug industry, which this Cochrane review abundantly demonstrates.

The abstract of the Cochrane review

The abstract of the Cochrane review is 915 words, four times as long as the 236 words in the abstract of our withdrawal review, and its results section is 5 times as long as ours (531 vs 106 words).

The Cochrane abstract states as a fact that discontinuation "may increase" the risk of relapse (10 studies for abrupt discontinuation and 13 studies for tapered discontinuation) whereas, in both cases, there was only one study that described the risk of withdrawal symptoms. This is highly misleading because these studies did not distinguish relapse from withdrawal symptoms, which the authors themselves acknowledge elsewhere.

The Cochrane authors included 33 studies involving 4995 participants and concluded that "Future studies should report key outcomes such as *successful discontinuation rate."*

Our little abstract is far more meaningful and informative than the Cochrane abstract. The entire Results and Conclusions sections are these:

"RESULTS: We included 13 studies (2085 participants). Three compared two withdrawal interventions and ten compared drug discontinuation vs. continuation. The success rates varied hugely between the trials (9% to 80%), with a weighted mean of 47% (95% confidence interval 38% to 57%) and a median of 50% (interquartile range 29% to 65%). A meta-regression showed that the length of taper was highly predictive for the risk of relapse (P = 0.00001). All the studies we reviewed confounded withdrawal symptoms with relapse; did not use hyperbolic tapering; withdrew the depression drug too fast in a linear fashion; and stopped it entirely when receptor occupancy was still high.
CONCLUSIONS: The true proportion of patients on depression drugs who can stop safely without relapse is likely considerably higher than the 50% we found."

The lengthy Cochrane abstract does not mention the most essential issues:

1) The length of taper is highly predictive for what the trial authors called relapse.

2) All the studies we reviewed
- confounded withdrawal symptoms with relapse
- did not use hyperbolic tapering
- withdrew the depression drug too fast in a linear fashion; and
- stopped it entirely when receptor occupancy was still high.

3) The true proportion of patients on depression drugs who can stop safely without relapse is likely considerably higher than the 50% we found.

Final considerations

As already noted, Cochrane is keen not to disturb guild interests and the financial interests of the drug industry. The Cochrane review gives precise but entirely misleading estimates of the benefit in the

form of number needed to treat to benefit one person, but it does not offer estimates for the most serious harms.

I looked briefly at the main text and also searched on "suicid" in the text. Even though the Cochrane review is very detailed and mentions suicidality and suicide in many places, it does not say that depression drugs double the suicide risk, both in children and adults. It does say in the Background section that there is a "higher risk of agitation and suicide at the beginning of treatment, or when dosage is increased." But this is inadequate for two reasons. First, there is also a higher risk of suicide when the dose is lowered. This only gets mentioned indirectly later: "Typical antidepressant withdrawal symptoms or discontinuation symptoms, such as flu-like symptoms, insomnia, nausea, imbalance or vertigo, sensory disturbances, hyperarousal (anxiety and agitation), and suicidality (Valuck 2009), can occur when doses of any antidepressant are stopped, missed, or reduced." The review does not mention with one word the most dangerous withdrawal symptom, akathisia, which increases the risk of suicide, violence and homicide.

At the Cochrane Colloquium in Lyon in 2001, my research group gave a lecture called "Anatomy of the Cochrane review." We analysed all 1000 Cochrane reviews published in issue 1 of the Cochrane Library in 2001. One of our findings was that the median length of the text in a Cochrane review was 15 pages.

As illustrated by the Cochrane withdrawal review of 209 pages, Cochrane has developed into a highly ineffective organisation, which is why its main funder, the UK National Institute for Health and Care Research (NIHR), has cut all funding to the UK based Cochrane review groups from 31 March 2023.

On 23 April 2021, Professor Ken Stein, Director of the Evidence Synthesis Programme at the NIHR spoke at a webinar about the work in the UK Cochrane groups and their future funding (see details in my 2022 book, "The decline and fall of the Cochrane empire," which is freely available. He criticised Cochrane quite substantially for much the same reasons as I did when I was an elected member of the Cochrane Governing Board. He said the writing had been on the wall for eight years, which was exactly the period when Cochrane's CEO, journalist Mark Wilson, ruled the organisation and destroyed it. About the failing scientific integrity, Stein noted that, "This is a point raised by people in the Collaboration to ensure that garbage does not go into the reviews; otherwise, your reviews will be garbage."

In a review of my book, "Death of a whistleblower and Cochrane's moral collapse," UK child and adolescent psychiatrist Sami Timini writes: "… it was because Professor Gøtzsche was prepared to call out the lowering of scientific standards in Cochrane that the hierarchy felt compelled to plot his demise … one of the worst show trials ever … in a manner that mirrors how the drug industry operates … the death of Cochrane rather than the whistleblower …"

Leaked recordings from the secret board meeting that expelled me, which I have described in my two books about Cochrane's downfall, include the following:

Board member David Hammerstein, previous member of the European Parliament, said: "Every single conflict between the central executive board and Peter is about an issue where the central executive board takes the side of the pharmaceutical industry. And I can document this ... and we'll be able to open up ourselves to a unified brand and more funding." Hammerstein warned that Cochrane was setting a dangerous precedent whereby industry representatives only had to "write a complaint to Cochrane and then Cochrane caves in under the pressure."

BMJ's Editor-in-Chief agreed. A week after my expulsion, she wrote that Cochrane should be committed to holding industry and academia to account, and that my expulsion from Cochrane reflected "a deep seated difference of opinion about how close to industry is too close."

The size of Cochrane reviews has been constantly increasing since 2001 by a process that can best be described as the meat extender method, but where is the beef? I have calculated that the median size of a Cochrane review, all included, was 26 in 2001, 41 in 2012 and 79 in 2023.

I have the following questions:

1) When did the Cochrane Common Mental Disorder group approve the title for the Cochrane review about antidepressant drug withdrawal, published by Van Leeuwen et al.?

2) When was the first version of the protocol for this review submitted to the Cochrane Common Mental Disorders group?

3) Do you agree that it was inappropriate that the Cochrane Common Mental Disorders group was negotiating with another author group about a similar review as ours at the same time as it increased its demands to our review all the time and exposed us to huge delays before they responded to our submissions? If so, will you reprimand the group in case it still exists? I have been told that all the 24 UK based review groups will close due to lack of funding.

4) Will you take steps to ensure that the surviving Cochrane review groups adhere to the ten principles of the collaboration?

5) Will you take steps to ensure that the Cochrane drug withdrawal review becomes less misleading and with no marketing-like messages like those used by the drug industry (see my comments above)?

6) Will you take steps to ensure that Cochrane reviews in general, but particularly those in mental health, become less misleading? A case in point is that virtually every single placebo-controlled trial of depression drugs and neuroleptics include patients who were already in treatment with the same or a similar drug before they were randomised, which means that these trials do not compare a drug with placebo but with a drug withdrawal group. Therefore, Cochrane reviews of the placebo-controlled trials of psychiatric drugs are generally highly misleading because they do not take this huge bias into account when they report the results, let alone mention the existence of the bias.

7) Will you take steps to ensure that Cochrane reviews become much shorter and more user friendly in future?

Best wishes

Peter C Gøtzsche