

Publication of entire Cochrane review obstructed for 5 years

AS ALREADY NOTED, OLE OLSEN AND I WERE NOT ALLOWED TO publish the major harms of screening in our 2001 Cochrane review¹ and therefore we published them in the *Lancet* instead.^{2,3} It would take another 5 years before the harms came out also in *The Cochrane Library*, and we didn't get there easily. In fact, the series of events I shall describe here are highly unusual for an academic journal and not something I would wish others to go through.

Our disputes with the Cochrane Breast Cancer Group were discussed in correspondence in the *Lancet* in early 2002,⁴ but the editor-in-chief, Richard Horton, alerted readers that much bigger issues were at stake:⁴

Some senior scientists have said to me that this debate should not be taking place in public. Screening mammography is, they argue, too important for women's health to have its image damaged by questioning the technique's efficacy and safety. Such paternalism assumes that women cannot decide for themselves whether the available evidence supports or refutes the case for mammography. Discouraging a discussion with women about the evidence for and against mammography is more harmful for women's health, not less, if doctors truly believe that patients should be active partners in making decisions about their care.

Horton also noted:

When Cochrane reviewers [us] produce a review at odds with the opinions

of Cochrane editors, the normal process of peer review and negotiation will resolve many of the differences. But if a difference remains, let the scientists doing the review publish what they wish to say – it is, after all, their work. The editors can present their own view as a supplementary discussion or comment. That way, the debate proceeds properly, each side is given its voice, accusations of censorship are avoided, and the public sees science as a truly collaborative process, in which differences of opinion are not only respected, but also welcomed.

In his letter in the *Lancet*, the chair of The Cochrane Collaboration Steering Group, Peter Langhorne, alluded to the uniqueness of the Cochrane process when he remarked:

First, Cochrane editorial groups are committed to try to publish reviews – rejection is very much a last resort. Second, because limited resources must be used responsibly there should only be one Cochrane review addressing a particular question. It therefore needs to be comprehensive and balanced.

I addressed the limitation of this arrangement:

Should a Cochrane researcher become dissatisfied with the Cochrane editorial group he cannot choose another Cochrane journal for publication to obtain the Cochrane stamp of approval – a quality stamp that, in the case of mammography screening, seems to have been important given that the Cochrane review was eagerly awaited by many policy-makers.

The monopoly situation creates a potential for editorial abuse, and we felt the editors had clearly overstepped their limits. We were willing to negotiate how the harms should be presented and discussed but not to have them deleted.

Langhorne arranged a telephone conference to resolve our dispute with the Breast Cancer Group. He was keen to avoid further damage to the collaboration and therefore asked me to disclose our reply to a letter the Cochrane editors had submitted to the *Lancet* about the dispute. I replied that suppression of academic freedom could be far more damaging to the collaboration and noted that I had already received the Cochrane editors' letter from the *Lancet* and had responded to it. Furthermore, I felt it would be inappropriate for me to circulate my reply to the conference attendees, as Langhorne requested.

When Langhorne insisted, I noted that Horton had made it very clear that in his view, the collaboration 'should not, repeat not' ask me to disclose the contents

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of my letter. With Horton's permission, I also forwarded his comments to me about this:

It smacks of censorship and I know of no example where one protagonist has had the right to review the comments of another protagonist pre-publication. That is my public view and I would be happy for you to restate it in full – ie, with the reason behind it rather than just the advice to keep your letter confidential. The way forward, and again I have said this to all parties, is to convene a discussion between you and John Simes. That way, any factual misunderstandings can be ironed out. It is then up to John to revise his letter, and only then for you to amend yours in the light of his changes.

John Simes accepted this.

At my request, Drummond Rennie participated at the meeting in his capacity as an editor of a major medical journal, *JAMA*. Rennie pointed out that majority voting in an editorial group, such as that which had occurred with our review, was not a good way to solve disputes between authors and editors, or between the editors themselves. He agreed with Horton about giving freedom to authors when disputes cannot be resolved, and to let the dissenters have their saying in an accompanying editorial.

Cochrane editors stonewall our Cochrane review

Although the teleconference went well, the process of updating our review was subsequently obstructed by the Australian-based Cochrane Breast Cancer Group. I continued my enquiries about when I would get the Cochrane editors' comments, but to no avail. I gave up after 11 months and contacted Langhorne, who asked the group for a response. Still no reply, even though it was The Collaboration's chair who had asked.

In March 2003, 1½ years after the publication of our curtailed Cochrane review, we had still not heard anything from the Cochrane editors. Therefore, we submitted a revision of our review, which was now out of date, as additional, important data had been published in the Swedish 2002 meta-analysis (see Chapter 10). We had reinserted the data on treatments, had expanded our explanations why these data were reliable and had made some compromises in an attempt to accommodate the editors.

The silence continued. In June, I informed the Cochrane editors that it had written about itself that, 'Reviews will not be published in parts (eg reporting on

some outcomes in one issue, and other outcomes in the next).’ I reminded the editors that it was now almost 2 years since we published our curtailed review. Again I asked when I could expect a response. And asked once more. Dead silence.

In September 2003, I told Langhorne that there were now epidemiological data from the United States and the United Kingdom that clearly confirmed the results the Breast Cancer Group had not allowed us to publish in 2001 – namely, that screening causes about 30% overdiagnosis and overtreatment. I added that the pro-screening lobby had consistently tried to suppress and even ridicule this important information. I also warned that the longer it took, the more the suspicion of censorship would grow, as we had received reports of such worries from many people already in 2001, both in and outside the collaboration.

It was like ringing a bell. I received an email from two of the group’s editors, Simes and Wilcken, the next day. But their reply didn’t follow standard editorial practice. It mentioned two peer reviews, but they were not enclosed, only a summary of them. Therefore, we couldn’t reply to them, and we couldn’t tell if they were written recently or some time ago.

We were now convinced that the group was doing what it could to get rid of us. We were told that the two anonymous peer reviewers both strongly recommended against publication and furthermore that our review was not acceptable for publication and that further revision of the review was unlikely to resolve the issues. That was a smart move, leading to a catch-22 situation. By denying us the possibility of updating the review, the group could withdraw our published review at a later stage with the argument that it was outdated. That would be easy to do, as *The Cochrane Library* is an electronic publication that gets regularly updated.

Complete denial of the most important harm of screening continued. The editors talked about ‘unsubstantiated claims of harm’ and remarked that in the longer run the number of surgical procedures would tend to become the same in the control groups as in the screened groups, which was not only wishful thinking, but plainly wrong.

I informed Langhorne about the permanent roadblock the same day, and he offered to contact the collaboration’s newly appointed publication arbiter, David Henderson-Smart, who had a specific remit to address disagreements between authors and editors.

I also asked Drummond Rennie for advice. He replied that the Breast Cancer Group had taken an unbelievable time over all this and furthermore noted that The Cochrane Collaboration is committed to having only one version of a review, which is tantamount to saying that in an area of debatable science there is only one correct answer and one correct version, which is completely anti-science. He suggested that, in exceptional circumstances, there could be two versions of a

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Cochrane review, e.g. that of the authors and that of the editors, with an accompanying explanation that it was not possible to agree on the final version. That would be in the fine tradition of science, which acknowledges that information is often hard to interpret, and ‘unless Cochrane makes it as a scientific enterprise, it cannot and should not survive’.

Langhorne and I agreed with Rennie. Langhorne added that, in his capacity as editor of the Cochrane Stroke Group, he increasingly found himself disagreeing with the way some reviews had been analysed, but as no one could say which was the more correct approach, the solution was to publish both sets of analyses.

My co-author, Ole Olsen, and I had undertaken a huge piece of work together and had had our happy moments when we found the proof of a suspicion we had shared for a long time. Systematic reviewing has similarities to detective work and faces similar difficulties. It is difficult to detect what is *not* there, when it has been carefully removed from the scene of the crime. This requires experience, and one of the peer reviewers on our Cochrane review actually remarked that, with all its details, it looked like a court case.

But what we had gone through was also very stressful, and Olsen had left our centre, informing the Breast Cancer Group that he didn’t want to contribute to the review any longer. The group asked me to find another co-author, as it was its policy to have at least two authors on reviews, which is reasonable, as two detectives see more than one. I promised to do so and asked the group to send their comments on treatments in the meantime but was told I wouldn’t get them before I had found an additional author. I informed the group that Donald Berry was the new co-author. However, he pulled out when he realised that the amount of work involved was too much for his busy schedule. The Breast Cancer Group raised concerns about Berry’s withdrawal as co-author, and Rennie felt this was a particularly specious reason to turn our review down. I published the updated Cochrane review in 2006 with Margrethe Nielsen from the Danish Consumer Council, who later became a PhD student with me on a different subject, psychotropic drugs.

The letter of rejection from the Breast Cancer Group from September 2003 noted that international working parties had reassessed the evidence and had concluded that screening was of value. I remarked that this was a judgemental and not a scientific statement, and that Cochrane reviews are about presenting the scientific evidence on benefits and harms and letting the readers make up their own minds. They are not policy documents. Therefore, I suggested – to ensure a fair process that distinguished appropriately between science and politics – that we should invite experienced editors from highly respected general medical journals to handle our review.

I met with Langhorne and Henderson-Smart a month later and we agreed that I should ignore the rejection from the editors and submit a revision, with a reply to the comments. We did this in November 2003, with the hope that it could be published in April 2004 (*The Cochrane Library* came out quarterly at that time). However, it took another 3 years.

In January 2004, we submitted yet another version, as advised by the publication arbiter who had also asked the group to find additional peer reviewers. Nothing happened. Four months later, I noted that I believed the group had a serious conflict of interest and that I couldn't understand it could be so difficult, as I could easily suggest dozens of skilled people, both pro- and con- screening, who would agree to peer-review our work within a couple of weeks.

I asked about the peer reviews several times and for a deadline, but after 10 months, no reviews and no deadline. The group's arrogance was unbelievable.

A second publication arbiter, Kay Dickersin, director of the US Cochrane Center, became involved. In December 2004, we discussed breaking the dead-lock by moving forwards without waiting for the missing peer reviews. Only a week later, a letter arrived from Wilcken that included three peer reviews. I wondered whether this was merely a coincidence but, again, they were undated, just as those we had received a year earlier. But there was a big difference. The new peer reviews were excellent and remarkably consistent, and it seemed to us that the reviewers' interest this time was to get as close to the truth as possible, rather than to protect screening.

That was certainly a new development. As we agreed with almost all the comments, it would be very easy for us to respond. *But we didn't get the opportunity!* Our update was flatly rejected: 'It is with regret that we inform you that on the basis of this feedback, the CBCG [Cochrane Breast Cancer Group] is unable to accept the review update.'

This appeared to be, in my view, an abuse of a monopoly situation. The rejection at this stage, with no possibility of appeal, was not only entirely inappropriate; it also went against Cochrane principles. What is more, one of the reviewers noted:

The novel contribution of this review is the information reported on the relative increase in mastectomies and radiation among screened women irrespective of the quality score for a trial. This is important information to be communicated to women who are considering undergoing screening mammography.

The second reviewer stated: 'Overall this is a carefully done review', and the third suggested various changes we could easily make. *Thus, there wasn't the slightest objective reason for rejection.*

I was reminded of Kafka again and I appealed to Dickersin. In my appeal, I mentioned another reply on a related issue we had received from the group just 2 days earlier. Karsten Juhl Jørgensen and I had submitted a protocol to the group for a systematic review on the harms of radiotherapy for breast cancer, as these were very poorly elucidated in randomised trials and were virtually absent in systematic reviews. Interestingly, our proposed review was rejected with the argument that it would not 'offer patients and practitioners an opportunity to balance evidence of harms and benefits within the same review'. What can one say? The same editors had made sure that our published Cochrane review on breast screening *did not allow such a balance*. It seems that the group's rules changed ad hoc, depending on the circumstances; therefore, we abandoned that review.

Stalemate, it seemed. But the publication arbiters now decided to discuss the issues not only with the chairman but also with the whole democratically elected Cochrane Collaboration Steering Group. Five months later, we were asked to reply to the comments and to submit a new version. Most important, the steering group had decided that all benefits and harms should be examined in the review and also that the Breast Cancer Group needed to provide us with an itemised list of what needed to be addressed for the review to be publishable, incorporating the points raised by the peer reviewers and the editorial team.

It was the first time in 3½ years that we received specific suggestions for escaping from the Kafkaesque process. Kay Dickersin offered her assistance with the language, which was very helpful. She had extensive experience with breast cancer and with consumer issues through her active involvement with the US National Breast Cancer Coalition. This evidence-based group consists primarily of women who have been treated for breast cancer, and it has been described as being perhaps the world's most influential medical consumer lobby group.⁵

Three days before we submitted the revised review on 27 November 2005, the Cochrane Breast Cancer Group informed me that our review would be peer-reviewed again. I wrote back that I had understood that it was now up to the editors to look at the paper. Wilcken replied that he would send our paper on 'to reviewers', not to *the* reviewers. That was not a clear reply, and I remained nervous. I enquired again and was then told that it would be sent to the previous reviewers, not new ones (which would have been the fifth time our Cochrane review was getting peer-reviewed).

Again, the delay was grotesque, and repeated requests, both from me and from Dickersin, to get a reply from the group led nowhere. We were told that not all of the three peer reviewers had responded, and I requested a deadline for this but I didn't get one. It took another 7 months before we finally got the message that our updated review was accepted for publication. The updated review was

published in October 2006 and was very well received. This was 6 years after we first submitted it. That could be a record for editorial delay, as our revisions took up very little of these 6 years. It is also revealing to compare this with the process at the *Lancet*. We submitted our full review on 10 September 2001 and it was published 40 days later.

On 13 March 2009, we submitted the second update of the Cochrane review, which included a new trial, the UK Age trial in women about 40 years of age. This time, our contacts with the group were fine and uneventful, and the update was accepted without peer review and published in October 2009.⁶

Lessons for the future

At one time, when I was particularly frustrated, one of the two publication arbiters, Henderson-Smart, replied that it would be better to be a tortoise than a hare in this matter. He alluded to Aesop's fable again when he later wrote, 'Slow and steady – sticking to the course (scientific principles) – wins the race.' He was right. The Cochrane review is the most comprehensive scientific evidence there is about mammography screening in one place, and it has benefited from the fact that so many people became involved with it.

What I have described is the most high-profile conflict in The Cochrane Collaboration's history. It concerned one of the most controversial and hugely expensive interventions that have ever been introduced in healthcare. The NHS in the United Kingdom has never invested more in implementing a new type of clinical practice.⁷

The conflict can be analysed from different angles. The overriding perspective for us was ethics. Women should not be denied information about the most important harm of screening. This harm was a well-guarded secret before we stepped into the scene and published our findings in 2000 in the *Lancet*.⁸ The screening advocates kept quiet about overdiagnosis, as they were afraid it would deter women from attending screening. Such utilitarian ethics are a form of unsolicited paternalism, which is only acceptable if one deals with incompetent patients, e.g. unconscious patients or children. Women are not children, and the prevailing paternalistic attitude is therefore not acceptable.

The conflict is also interesting from a Cochrane perspective. The Cochrane Collaboration is a charity that aims to help people make evidence-based decisions about healthcare interventions. It builds on volunteerism, and the editorial teams for each of its 52 review groups have been recruited on a somewhat first-come, first-served basis. This means that many editors lack training in issues related to

editing, publication ethics and conflicts of interest. Another key value is collaboration, which is helpful, but difficulties are created when hard decisions need to be made that not everybody will agree with.

With a strong leadership, it would have been easy to demand of the Cochrane Breast Cancer Group that it publish the data on harms shortly after our *Lancet* paper with these data came out. On the other hand, it was a strength that the collaboration's steering group wouldn't tolerate that the huge work we had done on the review was thrown in the dustbin by the Breast Cancer Group.

An editor-in-chief was appointed in 2008, but before this happened, the freedom for Cochrane groups to set their own standards sometimes resulted in unusual demands that do not exist in other scientific journals. For example, when performing a review on soft laser therapy for unwanted hair growth with a dermatologist, the Cochrane Skin Group told me that they required a consumer as co-author. It is not clear to me why a woman with too much hair on her upper lip would become a good author of a scientific paper. We found one, but as she didn't contribute in any meaningful way, the group allowed us to publish without her name on the review.

The Cochrane Breast Cancer Group also told us that it was keen to have a consumer as co-author. We had concerns about this, e.g. a woman who had already made up her mind and entered a screening programme might not be a good choice. We replied that we would provide the consumer input ourselves, as Ole Olsen had been a consumer pregnancy and childbirth advocate for many years, and this was accepted.

The Cochrane Anaesthesia Group required that all author teams must have access to a BSc-, MSc-, or PhD-qualified statistician. I argued that I knew an excellent statistician who had never been formally educated in statistics but had worked his whole life as a statistician, and also that I had authored 12 Cochrane reviews without having needed support from statisticians. The group accepted my arguments and now explains that a statistician is someone who has the skills to perform a meta-analysis.

In dealing with a fourth group, the Cochrane Cystic Fibrosis and Genetic Disorders Group, we needed to involve both the publication arbiters and the editor-in-chief, David Tovey. The group refused to send our Cochrane review for peer review before we had found a third author who was a content area expert. We explained that we had plenty of access to such experts, but that they didn't necessarily have to be co-authors, and that it would be impossible to add an author when the work was already done, as such an author would become guest author, a practice uniformly condemned by journal editors. The group provided us with comments from such an expert, who had numerous conflicts of interest in

relation to the exceedingly expensive intervention we had studied, which may cost up to US\$150 000 annually for each patient in the United States. The group even wrote to us that this expert would be willing to become co-author. In my opinion, this is inappropriate editorial conduct. But as I couldn't persuade the group's editor, I described the case in an anonymised fashion on the email discussion list of the World Association of Medical Editors, of which I am a member. There was no sympathy with the group's attitude. Tovey proceeded cautiously and also involved a person outside The Cochrane Collaboration, Elizabeth Wager, chair of the independent organisation Committee on Publication Ethics, which is a forum for journal editors and publishers, with thousands of members, that handles difficult issues, thereby setting precedents. The deadlock ended when Tovey told the group to send our work out for peer review without demanding a third author. We didn't find convincing evidence that the drug we studied is effective.⁹

It is a big challenge for The Cochrane Collaboration that its editorial teams – in contrast to general medical journals like the *Lancet*, *BMJ* and *JAMA* – to a large extent are based on content area experts. Specialists often share the same opinions, prejudices and biases, and it can be very difficult to get a review accepted that provides evidence challenging their beliefs. Being a Cochrane director, I should perhaps not praise our own organisation, but I think the collaboration has performed exceptionally well for a grass-roots organisation. However, the time has come where impartiality and professionalism – with adoption of the best available standards for journal editing, as expressed in international guidelines and policies for editors – must be the norm for all Cochrane editors. It is the challenging task of the editor-in-chief to ensure that this comes true.

Welcome results in France

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In France, our results were much appreciated by the highly respected medical journal *La Revue Prescrire*. This journal aims at providing French doctors unbiased information about interventions, and it also has editions in English.¹⁰ *Prescrire* is a non-profit continuing-education organisation, committed to better patient care; it is wholly financed by its subscribers and accepts no advertising or other outside support. Its editors are healthcare professionals who are specially trained in *Prescrire*'s methods and who are free from conflicts of interest. Thus, it is exactly the type of journal we need to help us decide what is right and what is wrong about healthcare interventions, and I hope we may one day say also about Cochrane editors that none of them have conflicts of interest.

Prescrire published a series of very detailed articles on mammography screening

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in 2006 and 2007, with numerous references. The editors sent me their drafts to ensure they had not misunderstood anything. I was very impressed by their work; there was virtually nothing I could contribute. The way the editors at *Précrire* work with the scientific issues offers a startling contrast with how screening supporters and their like-minded editors work. It was such a nice break from the usual screening muddle and wishful thinking to assist the editors of this journal.

I shall mention only one thing from the series. The editors wrote that French women are not being informed in an honest and balanced way, which is in violation of the law; furthermore, they noted that information coming from the French Cancer Institute and other bodies is biased.¹¹ Déjà vu! Just like in other countries. Why haven't the women protested?

References

- 1 Olsen O, Gøtzsche PC. Screening for breast cancer with mammography. *Cochrane Database Syst Rev*. 2001; (4): CD001877.
- 2 Olsen O, Gøtzsche PC. Cochrane review on screening for breast cancer with mammography. *Lancet*. 2001; **358**(9290): 1340–2.
- 3 Olsen O, Gøtzsche PC. Systematic review of screening for breast cancer with mammography. *Lancet*. 2001 Oct 20. Available at: <http://image.thelancet.com/extras/fullreport.pdf> (accessed 5 May 2010).
- 4 Letters. Screening mammography: setting the record straight. *Lancet*. 2002; **359**(9304): 439–42.
- 5 How consumers can and should improve clinical trials. *Lancet*. 2001; **357**(9270): 1721.
- 6 Gøtzsche PC, Nielsen M. Screening for breast cancer with mammography. *Cochrane Database Syst Rev*. 2009; (4): CD001877.
- 7 Gray JA. Breast screening programme. *BMJ*. 1989; **298**(6665): 48.
- 8 Gøtzsche PC, Olsen O. Is screening for breast cancer with mammography justifiable? *Lancet*. 2000; **355**(9198): 129–34.
- 9 Gøtzsche PC, Johansen HK. Intravenous alpha-1 antitrypsin augmentation therapy for treating patients with alpha-1 antitrypsin deficiency and lung disease. *Cochrane Database Syst Rev*. 2010; (7): CD007851.
- 10 Prescrire in English. Available at: <http://english.prescrire.org/spip.php?article214> (accessed 3 November 2010).
- 11 [Mammography screening: honest and balanced information] [French]. *La Revue Précrire*. 2007; **27**(288): 762.