

Why we need to open up health research by sharing our raw data

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I shall start by giving answers to the questions posed by the organisers of this meeting. Is it ethical and efficient for the EU to allow essential medical research data to be shrouded in secrecy? The answer is clearly no. Can the health of EU citizens be effectively protected with very little or insufficient access to clinical trial data concerning the safety and secondary effects of a drug? The answer is clearly no.

Next, I shall explain why the answers are no. And why limited access to trial data leads to:

- unnecessary deaths of thousands of patients every year,
- unnecessary misery in millions of other patients
- unnecessary waste in terms of redundant research, and
- unnecessary waste of taxpayers' money.

Unnecessary deaths of thousands of patients

In the early 80s, researchers in the UK carried out a study of the drug lorainide, which was thought to be a good drug, as it could normalise dangerous heart arrhythmias after a heart attack. However, 9 people taking the drug died, compared to only 1 taking placebo (1). For commercial reasons, drug development was stopped and the results of the trial were never published or communicated to the society in other ways. Similar drugs made it onto the market and were widely used. Later, a large trial showed that such drugs kill people. At the peak of their use, these drugs are estimated to have caused between 20,000 and 70,000 deaths every year in the United States alone (2). Many of these deaths could have been avoided if the results of the lorainide trial had been known.

As another example, the drug maker Merck concealed for many years that its drug against pain, rofecoxib, better known as Vioxx, causes heart attacks. The use of Vioxx has probably caused about 100,000 unnecessary heart attacks in the United States alone (3), which correspond to about 10,000 deaths.

Anti-arrhythmic drugs and Vioxx also killed tens of thousands European citizens. And many of those who died on Vioxx were in perfect health, apart from a minor pain problem, for example after having played too much golf or tennis. At the same time, we wasted hundreds of millions of Euros, as Vioxx is no better than older, far cheaper drugs.

Unnecessary misery in millions of patients

Many trials are never published, and those that are published often present a highly selective and misleading version of the true results. These manipulations make doctors believe that drugs are far more effective than they really are, and also far more safe. Doctors in the EU therefore treat millions of patients every year who had been better served by not receiving any treatment at all. As all drugs have side effects, this leads to a lot of misery we could have avoided if we had had access to all the data.

As an example, the sales of the newer antidepressant drugs, the selective serotonin reuptake inhibitors (SSRIs), are now so high in Denmark that 7% of the whole population could be in treatment with such a drug every day for their entire life, from cradle to grave (4). Obviously, such massive use of drugs that affect the brain is not healthy, but yet again, the clinical trial data had been manipulated. One of the most widely cited trials was GlaxoSmithKline's 329 trial of paroxetine (Paxil), conducted in children and adolescents. In 2004, the Attorney General of New York State sued GlaxoSmithKline for repeated and persistent consumer fraud, which opened the company's archives. GlaxoSmithKline had told its sales force that the trial showed

"REMARKABLE Efficacy and Safety" (5), none of which was true. In internal documents, the company admitted that the study didn't show Paxil was effective, but after extensive torture of the data until they confessed, the published article reported positive effects. It was even worse for the harms. What is most important when treating depression is to decrease the suicide risk, but Paxil did the opposite. Eight children became suicidal on the drug versus only one on placebo. The publication, however, listed only one headache as being related to the drug. The suicidal thoughts and behaviour were called emotional lability or hospitalisation.

Unnecessary waste in terms of redundant research

An incomplete knowledge base leads to redundant research, which by its very nature is unethical, and informed consent is an illusion when patients and their doctors can only get access to biased information. It will also cause some patients to suffer and die unnecessarily. Researchers may, for example, include patients in trials of similar compounds as one that has been shown to be deadly because they are unaware of this.

Further, since the chance of publication depends on the magnitude and direction of the results, patients are being exploited for commercial or career gains, which is also unethical.

New research should not be done unless, at the time it is initiated, the questions it proposes to address cannot be answered satisfactorily with existing evidence, e.g. in Cochrane reviews. This requires access to all data from all previous similar trials, including access to raw data, as we generally cannot rely on processed data, which drug companies and researchers have shown to us in summary form.

Unnecessary waste of taxpayers' money

The European governments have wasted billions of Euros on the purchase of oseltamivir (Tamiflu) in relation to the mild 2009 influenza epidemic (6). The drug maker Roche had omitted publishing most of their clinical trial data on Tamiflu and refused to share them with independent Cochrane researchers. Roche fooled the European Medicines Agency (EMA) into stating that Tamiflu reduces influenza complications, whereas the FDA stated that Tamiflu has not been shown to prevent complications (7). There is no convincing evidence either that Tamiflu reduces admissions to hospital or the spread of influenza to other people (6).

Tamiflu reduces the duration of influenza by 21 hours, which can probably also be obtained with far cheaper drugs such as aspirin and paracetamol. And, not to forget: Tamiflu has important harms, apart from the economic ones, but they were concealed to such an extent that the Cochrane researchers could not report on them.

Where should we go from here?

I have given some examples of bad behavior in drug companies. When confronted with this, drug companies usually talk about a few bad apples, but it is pretty much all the apples in the basket that are rotten. I know of similar examples of misconduct from all the major drug companies, and the reason is simple: The difference between an honest data analysis and a less honest one can be worth billions of Euros on the world market.

By sharing all our research data, including the raw data, we could save billions of Euros every year, and at the same time improve the health and longevity of the European citizens and reduce the amount of harm they are exposed to. A lot of research could be done at almost no cost on existing data, and the incentive for bias and fraud would be much reduced when other researchers can check the data.

International calls, including those from the European Commission, for sharing the results have mostly been restricted to publicly-funded research, but the distinction between publicly-funded and industry-funded research is an artificial and irrelevant one (7). As noted by The British House of Commons Health Committee, society's obligations towards the patients who participate in trials, and all other patients, must take precedence over commercial interests. Furthermore, the public is always a partner, contributing not only trial participants, but also the infrastructure needed for the research. And taxpayers contribute substantially,

both to research and by reimbursing drugs once they are on the market. There is no such thing as a free market for drug research and development.

Helped by the European ombudsman, my centre got access to unpublished clinical study reports and corresponding trial protocols at the EMA in 2010, after 3 years of struggle (7). This created an important precedent. We not only got access to the results but also to the raw anonymised patient data. This allows us to analyse the harms of the drugs, just as the patients reported them, before they were interpreted by a drug company.

I gave a lecture in April 2012 at a meeting where the EMA and 28 of the 30 European national drug agencies were represented. The atmosphere was very positive and there was a keen interest in providing easy access for the public to clinical trial data without restrictions, in line with the recommendation from The European Commission that data sharing (from publicly funded research) should mean that the data can be used for whatever purpose other researchers might find relevant, without needing to obtain permission from those who assembled the data (7,8).

We agreed that we needed legislation in the EU that could overrule national laws, which often impede access to all the data. Denmark and The Netherlands, for example, redact all narrative descriptions of adverse effects.

The regulators also noted that having "a third eye" on drugs has the potential of improving regulatory decision making, but said that, in the EU, the data protection officer goes against the attitude of the European ombudsman. The ombudsman has declared that the documents we requested do not identify patients by name but by their identification and test centre numbers, and he concluded that the only personal data that should be redacted are those identifying the study authors and principal investigators. Sadly, the Council of Europe's public consultation document related to revision of Convention 108 about the protection of individuals with regard to automatic processing of personal data from 27 April 2012 is all about protecting the citizens by requiring their consent for every use of the data (9). There is nothing in this document about anonymised data, which makes such protection, which would be detrimental for medical research, superfluous.

Convention 108 must be changed radically. If we ask the citizens whether they think an extremely small risk of identifying a particular patient while doing research on raw anonymised patient data is more important than the risk all patients currently run because the drug companies conceal serious harms of their drugs, I think I know the answer. Furthermore, EU drug regulators actually say in their guideline that the current European legislation requires patient information to be included in non-identifiable form in the marketing authorisation application submitted to competent authorities (10).

A drug regulator raised the concern that, by getting access to the data, aggressive anti-vaccine groups could publish misleading analyses, thereby harming the population. I argued that they already did this without having access to all the data and that - in an open society - we are used to filter information. For example, some newspapers are more reliable than others.

And please consider the alternative to open access to all data. Societies that have only one official version of the truth are not societies we would like to live in. Equally important, it is difficult to imagine a worse situation than the status quo, where people with vested interests so often distort the evidence for commercial or career gains, with no possibility for others to check what they have done.

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