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Medicine's secret archives: How patients are harmed by the concealment of knowledge

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No one knows how many mothers' and babies' lives have been saved by the obstetrical forceps. This device has been part of the standard equipment of every maternity room for about 250 years. However, a shadow lies over the success story: after the Chamberlen brothers developed the device at the beginning of the 17th century, the brothers and their descendants used it for 3 generations, but kept it a secret from other obstetricians. While thanks to the forceps the Chamberlen family became rich and famous, at the same time women and babies were still dying elsewhere because the device was not available.

The story of the obstetrical forceps is one of the oldest documented examples showing what consequences secrecy in medicine can have. In an article published in the journal *Trials*, researchers at the German Institute for Quality and Efficiency in Health Care (IQWiG) compiled over 60 examples illustrating how the dissemination of medical knowledge has been impeded. For this purpose, they assessed hundreds of articles from journals and other sources, which covered areas including treatment for psychiatric disorders, pain, heart and circulatory disease, skin disease, cancer, and infectious diseases. A wide range of interventions was affected: from drugs and vaccines to medical devices such as ultrasound or devices for wound care. The collection reads like the script for a crime series.

Concealment is common

In science the phenomenon is called "publication bias", i.e. bias through selective publication. This occurs on two levels: On the first level complete studies remain unpublished. For example, an analysis of 90 drugs that had been newly approved in the US showed that they had been tested in a total of 900 trials. However, even 5 years after approval, 60% of these studies were unpublished. On the second level only selected outcomes from studies are published. Nowadays researchers have to specify in a study protocol which outcomes they want to measure and how they are going to analyse them. Comparisons of protocols and journal articles of studies showed that in 40% to 60% of studies, results had either been completely omitted or analyses changed. "In this way study results are often presented in a more positive way than is actually the case," says Beate Wieseler, Deputy Head of IQWiG's Drug Assessment Department.

This does not only affect studies sponsored by the pharmaceutical industry. In their paper, the IQWiG authors also cite an analysis in which 2000 studies on cancer topics were analysed according to sponsorship. The proportion of published studies was extremely low: of the industry-sponsored studies, 94% were unpublished; however, even 86% of university-sponsored studies were also unpublished. "Due to legal regulations, regulatory authorities are also sometimes obliged to withhold data," says Thomas Kaiser, Head of the Drug Assessment Department.

Patients are harmed

The concealment of knowledge often has consequences for patients. On the one hand, it can result in delays to the implementation and dissemination of beneficial interventions (as was the case with the obstetrical forceps). However, it is more common that bad news and reports of failure remain unpublished. "As a result, physicians and patients use treatments that are actually futile or even harmful," says Beate Wieseler. For example, researchers estimate that drugs prescribed

in the 1980s to prevent irregular heart beat cost tens of thousands of lives, because early signs of dangerous adverse effects were not published.

Appeals are insufficient

IQWiG's search for documented examples of publication bias was triggered by the Institute's own experience in its daily work, as was recently the case, for example, in the assessment of reboxetine, a drug used to treat depression: the pharmaceutical company Pfizer only provided previously concealed studies to IQWiG after subjection to public pressure. In the previously unpublished studies, the results for reboxetine were considerably worse than appeared to be the case in published studies. "For many years, not only patients but also physicians have been deceived," says Beate Wieseler.

The collection of examples published in *Trials* shows that the tendency to conceal unfavourable results or results that do not fulfil one's own expectations is so widespread that appeals and proposals for voluntary solutions will not be able to solve the problem effectively. "The increasing registration of studies in public registries is an important first step," says Thomas Kaiser. "However, in order to protect patients, we need legal regulations, so that results of all clinical trials are published swiftly and completely."

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