

A GIJN GUIDE

Investigating Health & Medicine



By Catherine Riva and Serena Tinari / Re-Check.ch



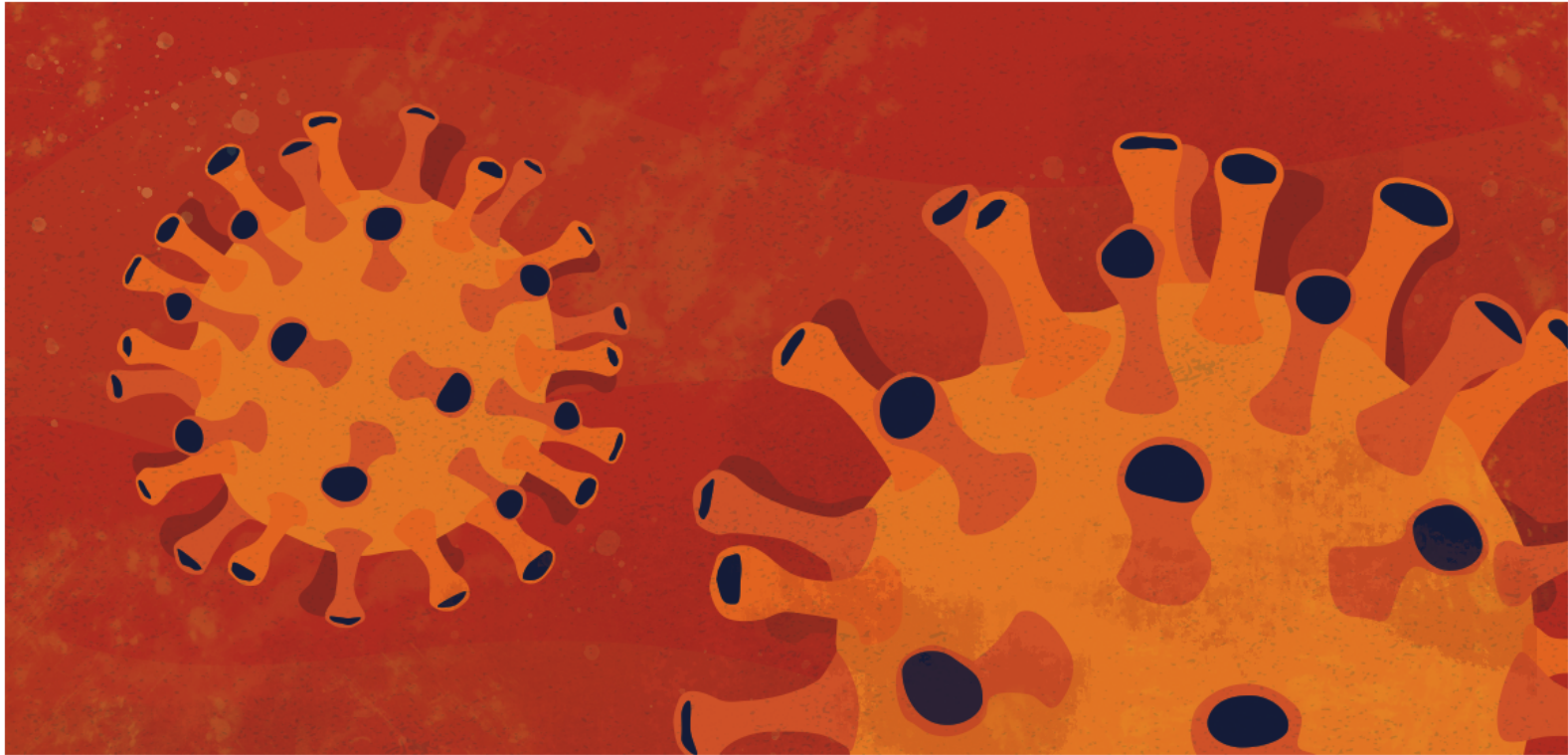
Global Investigative Journalism Network

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PREFACE

COVID-19



Investigating health care is complex and challenging. Reporting in this field means reading lengthy documents and getting well-acquainted with medical jargon. Numbers and statistics are also part of the game. Although the learning curve can be steep, in this specialized area of investigative journalism you'll never run out of stories. Truly global, it's compelling and engaging. Still, suddenly becoming a medical investigative reporter, as many have had to do during the COVID-19 crisis, can be frustrating and full of pitfalls. This guide will provide reporters with the basic knowledge they need to dig deeper into many aspects of COVID-19, a complex area of reporting, as well as other public health issues which can be equally challenging. We start with a few brief tips and tools for better reporting on COVID-19.

COVID-19 STATISTICS

First of all, keep in mind that COVID-19 is the name of the disease caused by the Coronavirus SARS-CoV-2. In this guide, for the sake of keeping it simple, we are referring to the [pandemic as COVID-19](#). Remember that any number makes sense only if put in context. For example, before suggesting that a COVID-19 metric or statistic is unusual or extraordinary, make sure to find out what a normal metric would be in the context of a viral infection, or its potential consequences for a patient's health, or the way a symptom is normally addressed in any given hospital setting. Providing context is the only way to assess whether a phenomenon has really never been seen before, or is common in the world of health care.

This global crisis is producing a huge volume of research, published at breakneck speed. Most of these studies are not going through the usual process of review.

GIJN has [compiled](#) official and unofficial sources of COVID-19 data. An additional and valuable source for COVID-19 data is [Our World in Data's COVID-19 statistics and research landing page](#). For Europe, [EuroMOMO](#) is an excellent source that offers insight and hints for many investigations even if you're not reporting on Europe. Remember that many factors play a role in determining how data is collected and filed, and there are many different approaches and confounding factors involved.

Stick to the Best Available Scientific Evidence

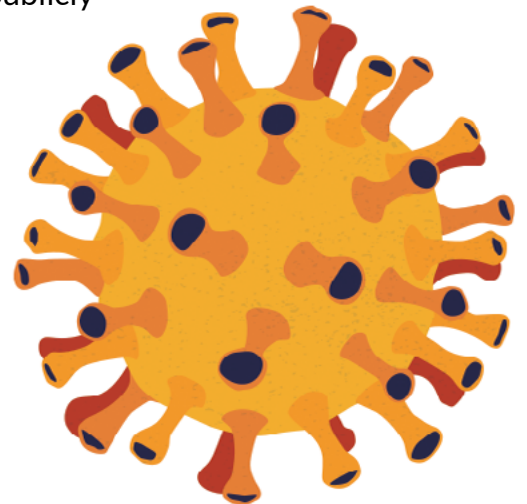
The World Health Organization (WHO) has a [website](#) listing published studies on COVID-19. As you'll discover from reading this guide, there are major differences among the studies in terms of design and significance. Also, this global crisis is producing a huge volume of research, published at breakneck speed. Most of these studies are not going through the usual process of

review and many are observational, which do not allow us to come to reliable conclusions. In a nutshell, there is a lot of noise at the moment in the world of medical research, and it can be difficult for a journalist who doesn't specialize in this field to make sense of it.

To make sense of what's going on, we recommend the Evidence-Based Medicine approach – a methodology that uses the best current research to evaluate patient care. The Oxford University Centre for Evidence-Based Medicine ([CEBM](#)) has a [COVID-19 Evidence Service](#) which publishes rapid reviews and analysis using some of the most solid methodologies available. On this website you will find accurate summaries, written in relatively plain language, on the best available evidence about many angles of COVID-19. Which are the reliable published studies on the benefits for the general population of wearing face masks? Where are we in terms of scientific proof for understanding the transmission mechanisms of the virus? What is the available knowledge about its mortality and the efficacy of this or that intervention? Evidence Service contributors are independent scholars who dig out, analyze, and summarize what we know, and don't know, about the science on COVID-19.

Who's the Expert?

Scientists from various fields of specialization speak publicly about COVID-19. But in medical science there are considerable differences among the many specialist areas of expertise. It's a good idea to discuss COVID-19 with infectious disease epidemiologists and vaccine safety epidemiologists, as they possess expertise specifically in the spread and management of epidemics and pandemics.



Models Should Come with a Warning

Models are mathematical simulations that project possible outcomes, such as how many people are likely to become infected from a particular virus over a given period of time. As scholars Carl Heneghan and Tom Jefferson put it in their piece [Modelling the Models](#): “All models, be they prospective or retrospective, if they are based on scientific principles have substantial uncertainty as to their starting point and are incompatible with oracle-like statements of certainty.” Their level of reliability depends on many factors, especially by the data that informs them. Early COVID-19 models were developed at a time when little data was available. Moreover, epidemics are

Models should come with a warning, and if you're using them for your journalism, carefully consider all the potential confounding factors and methodological weaknesses.

non-linear and rather chaotic, making it even more difficult for any model to be predictive of what is

going to happen. All these limitations mean that all models should come with a warning, and if you're using them for your journalism, you should carefully consider all the potential confounding factors and methodological weaknesses.

Beware of Media Reporting about Health Claims

Reports in the media may be flawed, are often not evidence-based, and much of the time rely on government and industry press releases. This guide deals extensively with how to independently assess research claims and frequently cites the work of [HealthNewsReview.org](#), which has experience in appraising health and medical claims as they are published by the media. HealthNewsReview.org is doing outstanding work related to COVID-19. It often focuses on the media landscape in the United States, but its key findings apply to all countries, and it can be a great inspiration for your journalism.

Beware of Oversimplification

Nothing is straightforward or simple in the current global situation. Be especially skeptical about information influenced by industry or relayed by governments. Take the time to independently assess the evidence, cross-checking the information, and bearing in mind that conflicts of interest and complex agendas are ubiquitous in the field of health care. Comparing countries can be a difficult exercise and one prone to pitfalls, as differences and confounding factors might play a relevant role. If you need to compare, make sure to adjust the comparison for multiple factors, such as average lifespan, which often differs from one country to another – an issue that is especially important with COVID-19 as most recorded death cases have been of the elderly. Also, consider that countries use different definitions for COVID-19 cases and deaths.

Don't Forget Health Issues Besides COVID-19

All public health interventions, medical or non-medical (such as physical distancing and wearing face masks), come with consequences. Make sure to examine the evidence on both the benefit and the harm of any intervention your government may introduce in the framework of COVID-19. Are there adverse effects to be expected, and are they transparently communicated to the public? Also, remember that in public health, long-term and all-cause or overall mortality are more important than short-term data which will be revised frequently as issues are clarified.

In addition, it may seem that COVID-19 is the only health issue at the moment.

GIJN COVID-19 RESOURCES

GIJN has [extensive resources](#) on investigative and data journalism techniques to help journalists working on the coronavirus crisis. GIJN's guide to covering the crisis is now in 13 languages, and there are tipsheets, webinars, and articles in multiple languages.

However, many unattended medical needs are part of the global public health picture. Billions of people worldwide lack access to basic hygiene, primary health care, and essential medicines, and in many fields affordable, safe, and effective treatments are not available. Some of these health issues have become worse as the focus has shifted to COVID-19. Also, lockdowns and other restrictions have produced an unprecedented disruption to health systems, many of them going from bad to worse; access to vaccines in developing countries is only one example. If the COVID-19 crisis has shifted the focus of journalists and editors to a single public health issue, it is important to look at other medical issues that are having a significant impact.

When Reporting about COVID-19 Vaccines and Drugs, Be Extra Cautious

First you need to get up to speed with the science relating to drugs and vaccines. Make sure you understand the fine balance between benefits and harms, and how regulatory authorities, scientific studies, and monitoring systems work; we've rounded up the necessary resources to support that understanding in this guide. For example, a very good resource is the [Brighton Collaboration](#), a network of vaccine safety specialists independent from the pharmaceutical industry. Also, these tips put together by [Journalist's Resource](#) are helpful when reporting on COVID-19 vaccines:

1. Reporters must understand what the various levels of clinical trials can – and can't – tell us. Be wary of announcements about scientific data made through press releases rather than academic journal articles.
2. Let your audience know now they could experience at least some mild side effects from COVID-19 vaccines.
3. Explain to audiences the demographics of the pools of patients used to test vaccines.

4. Help your audience understand the limits of what's known about vaccines.
5. Build a network of sources, especially the kind who can walk you through study data.

Learn from the Past

Although the dominant narrative in 2020 suggests that the world is facing a new and unprecedented medical emergency, lessons have been learned from hundreds of years of medicine, health care, and epidemiology. Get to know more about routines and protocols in health care: How are patients with respiratory diseases normally treated in intensive care units? Is it standard to use mechanical ventilation with elderly people? How often and for how long do complications from other viral infections affect a patient after hospital discharge? Get knowledgeable about guidelines and routines, and compare the usual standards of care with what is happening with COVID-19. Don't fall for the hype, and don't forget that media and government messages have been emotionally charged throughout this crisis; as investigative journalists we should try to keep a cool head.

ALSO WORTH A READ

- [Tip Sheet](#) for Journalists Covering COVID-19, from medical investigative journalist Jeanne Lenzer, for GIJN (2020).
- [Op-Ed: Covering Science at Dangerous Speeds](#), by Ivan Oransky, Columbia Journalism Review (2020).
- [Pandemic Science Out of Control](#), by Jeanne Lenzer and Shannon Brownlee, Issues in Science and Technology (2020).

Introduction



This guide focuses on medicines and medical devices. It aims to provide journalists with the tools and knowledge to independently assess the evidence, critically appraise the risk-benefit ratio of any given product or policy, and expose corruption and malpractice. It can be read as a textbook, one chapter at a time, or used selectively to support your work.

Investigating behind-the-scenes is consuming but rewarding. As we'll discuss in [Chapter 2](#), combining the methods and standards of muckraking and Evidence-Based Medicine (EBM) can be highly effective. EBM, [defined as](#) “the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients,” has been constantly revised to include a [wider public health approach](#). But as [Students 4 Best Evidence](#), a

network of students from around the world who are interested in learning more about evidence-based health care, put it: “It’s about asking the right questions and using the best research evidence to answer those questions.” EBM is an approach that matches the ethics and standards of investigative journalism.

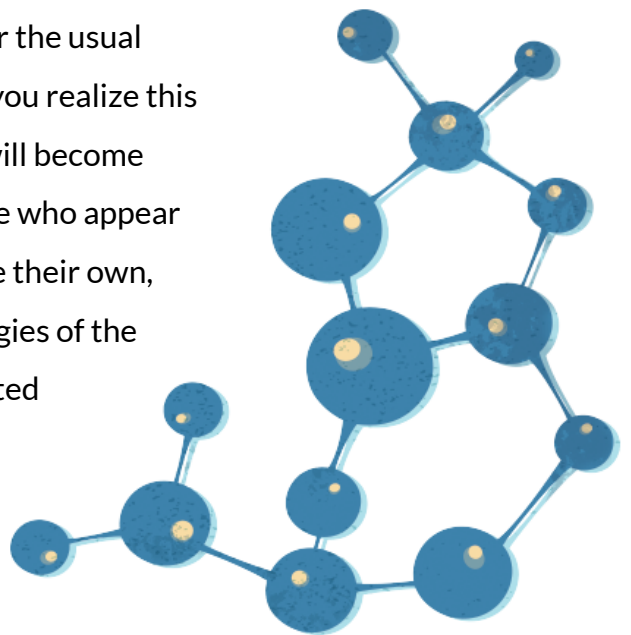
In his book “The Rise and Fall of Modern Medicine,” James Le Fanu identified 12 definitive moments of medical innovation: the discovery of penicillin, cortisone, streptomycin (an antibiotic), chlorpromazine (an antipsychotic drug), intensive care, open-heart surgery, hip replacement, kidney transplants, the control of hypertension (and the prevention of stroke), the treatment of childhood cancer, “test-tube” babies, and the clinical importance of Helicobacter, a type of bacteria. They are among medicine’s most remarkable successes of our modern times. But, as oncologist Vinay Prasad put it in his podcast “[Plenary Session](#)”: “Some of our interventions, some of our surgeries, some of our pills, some of our procedures are indisputably of benefit. They are the right pill at the right time,” but also, medicine is paved with myths, and it’s crucial to dispel them. Because, as John P. A. Ioannidis pointed out in the same podcast, “innovation is slow and infrequent, science is difficult... and the medicalization of society is becoming a major threat to humanity.”

In this field, you may end up misreading – and thus misrepresenting – reality if you are looking for the usual “bad guy.” As soon you gain experience in this field, you realize this view is too simplistic.

Health care and medicine, of course, affect each and every one of us. But contemporary public conversation is truly contradictory. On the one hand, medical triumphs are celebrated and even hyped; on the other hand, problems and conflicts of interest in healthcare and medicine have never been so obvious. Becoming knowledgeable about these critical issues is the first step to becoming a good medical investigative journalist.

The pharmaceutical industry's influence is pervasive and [medical marketing is skyrocketing](#). Around half of the world's population has to deal with limited access to essential medicines, such as antibiotics and vaccines, whose distribution depends on donor agendas. Counterfeit drugs and the black-market trade in pharmaceuticals are ubiquitous. In richer countries, over-diagnosis, over-detection, and over-treatment turn citizens into patients unnecessarily, and put health care budgets under pressure as states underwrite the costs of expensive new drugs with questionable efficacy. True breakthroughs remain extremely rare. The French independent drug bulletin Prescrire's [The Golden Pill](#), an award for therapeutic advances, can't be warranted most years. Notably missing in the list of award winners are new oncological drugs, even though they are routinely associated with the use of superlatives in [cancer research](#) and journalism. As Bloomberg reporter Peter Coy put it in this article: [Too Many Medicines Simply Don't Work](#). Also, consider that practices used sometimes for decades are, at a later point, shown to bring no benefit to patients and end up being dismissed, a phenomenon called "[medical reversal](#)" ("Ending Medical Reversal," Vinayak K. Prasad, Adam S. Cifu).

In this field, you may end up misreading – and thus misrepresenting – reality if you are looking for the usual “bad guy.” As soon you gain more experience, you realize this view is too simplistic. When you really dig, it will become apparent that many less obvious players, those who appear to be on the side of the patients, may also have their own, often complex, agendas. The marketing strategies of the pharmaceutical industry are highly sophisticated and go well beyond giving financial support to doctors or funding trips and other freebies. Although this continues on a smaller scale



than in the past, new strategies have been developed to influence prescribers and public health policies. Big Pharma knows, for instance, that giving generous funding to patient advocacy organizations can be highly rewarding. They will fight for a new drug to enter the market on an expedited basis, or for governments to pay for expensive medicine that is not necessarily effective. It is also known that the media will relay their message, focusing on the social justice angle and victims' stories. This is because journalists tend to look at "victims" and "patients" as the "good guys."

To dig deeper in this field you need to investigate the big picture. Many players in the global health market are keen to influence our work: health authorities, pharmaceutical manufacturers and medical devices companies, insurers, academic institutions, and nongovernmental organizations. They all have a message they want us to convey, and their actions can have a considerable impact on public health policies, sometimes ending up squarely complicit in furthering vested interests that have negative consequences for individuals and society.

CHAPTER 1

Regulating Drugs: Development and Approval



TIP 1: DIG DEEPER INTO DEVELOPMENT AND APPROVAL

If your story is about drugs, it is essential to delve into their development and approval history. There's a trove of valuable information. Although all countries have their own regulatory agency ([see Appendix](#)), the work by the US Food and Drug Administration (FDA) and European Medicines Agency (EMA) has great influence on the worldwide pharmaceutical market.

Evidence submitted by the industry to regulatory agencies to prove product safety and efficacy may be public and available on regulators' websites, even if

it often doesn't appear in post-approval marketing materials.

The drug development and approval process consists of five so-called phases shown in the illustration below. It is essential to dig deeper in all these stages, starting with randomized controlled trials (RCTs), the “gold standard,” which are conducted during Phase II and Phase III. This is often where you find the best available evidence – evidence that frequently is better than what is going to be collected when the product is on the market. However, even RCTs can be “gamed” in ways that mislead. So a good deal of investigative medical journalism should not just focus on financial corruption or adverse drugs or device effects, but on whether clinical trials are flawed, left unreported when negative, or misinterpreted. Indeed, even some of the most cited RCTs published in prestigious medical journals have been inaccurate; for more on this see the influential article by John P. A. Ioannidis: [Why Most Published Research Findings are False](#). In short, both the required methodologies and approval processes in these earlier phases are more rigorous and more revealing.

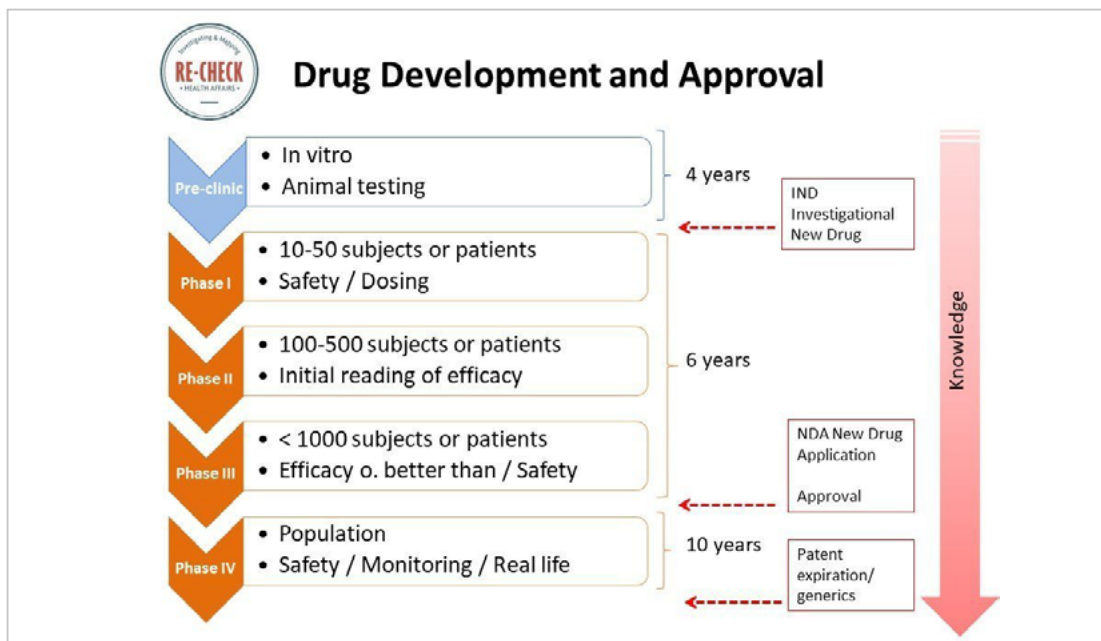


Illustration: Re-Check.ch

The approval stage creates major tension between public and commercial interests. The manufacturer will try to exert maximum influence on regulators, whose decision will determine not only whether the drug can be marketed but the uses for which it can be sold. Also, pharmaceutical companies notoriously flood regulators with a huge amount of documentation. Although that might sound like a good thing, in some cases it makes the agencies' work more difficult, as their capacities are notoriously limited.

The first step is to take a close look at all the details of the approval process. Assess if standards have been met and if the sponsor obtained exceptional flexibility like derogations or concessions. For instance, regulators may have allowed the company to show the drug's efficacy not based on its effectiveness

Randomized controlled trials – or RCTs – are the “gold standard,” but even they can be “gamed” in ways that mislead.

in addressing the main goal, but rather based on results in reaching a “surrogate endpoint” or “surrogate outcome.”

Surrogate endpoints are indicators (often bio-markers such as blood tests) chosen by researchers because they are considered important contributors in the mechanism of a disease. For example, blood pressure may be used as a surrogate endpoint in a trial on cardiovascular drugs, because it is a known risk factor for heart attacks and strokes. The hypothesis is that if the drug shows an effect on the surrogate endpoint (such as high blood pressure), it will also have an effect on the clinical outcome (such as heart attacks and strokes). Unfortunately, in many cases a drug's effect on a surrogate outcome won't bring the expected benefit to patients, and may even harm them. Also, surrogate markers only examine benefit without addressing harm. So a diabetes drug could be shown to be extremely effective at lowering blood sugar (another surrogate marker for diabetics who tend to die of heart attacks and strokes),

but that same drug could kill more patients by damaging their liver because other aspects of the mechanism of the disease have not been discovered or well-understood yet. That's why any results obtained in a study that was designed with a surrogate endpoint must be taken with caution.

The [Students 4 Best Evidence](#) (S4BE) website is a good resource to learn the basics in this field, as it is both accurate and understandable for non-scientists. S4BE explains the pitfalls of “surrogate endpoints” with a [classic example from the 1970s](#): “Patients suffering from arrhythmia (irregular heartbeat) are usually given anti-arrhythmic drugs to... ‘correct’ the heartbeat back to normal. Arrhythmia is a dangerous condition since it raises the risk of the patients suffering from sudden cardiac death. In the 1970s, a group of researchers were testing a new batch of anti-arrhythmic drugs and early results suggested that the new drugs were successful at normalizing the heart beat... Nevertheless, results later showed there was a greater mortality rate in the group receiving the anti-arrhythmic drugs compared to the group receiving the placebo. Therefore, heartbeat measurements were misleading and the drugs had actually been doing more harm than good.”

Once you have collected and analyzed evidence from clinical trials, it is crucial to compare data presented to the agencies with evidence published in the medical literature. Check for consistency and for discrepancies, and pay attention to every study submitted to the regulators. You might find out that a study that played a relevant role in the approval process was never published in a scientific journal, and that is often a red flag because not all results that agencies get have been or will be published. Manufacturers make sure favorable results are disseminated in scientific journals, but it is not always the case with unflattering results.



There is one famous case where unpublished data submitted to a regulator was overlooked, with damaging consequences. The painkiller Vioxx (rofecoxib) had been a blockbuster for Merck until the shocking [findings in 2004 of David Graham, a scientist at the US Food and Drug Administration](#) (FDA). Vioxx considerably increased the risk of heart attacks, and Graham estimated that up to 140,000 heart attacks and 60,000 deaths occurred because of the drug's side effects. The company voluntarily recalled the drug from the market as Graham's disclosures were announced. [The Wall Street Journal reported](#) that at least since 2000, four years before pulling the drug from the market, Merck knew that Vioxx considerably increased the risk of heart attacks and deaths but chose not to disclose the data. Leaked company documents showed how Merck instructed its sales representatives to avoid initiating discussions on these side effects. A December 2004 study, published in *The Lancet* by Swiss epidemiologist Peter Jüni and his colleagues at the University of Berne, demonstrated that the FDA should have known of Vioxx's dangers, because at least part of the troubling and unpublished data had been actually submitted to the US regulator. [Jüni and his colleagues wrote](#): "Our findings indicate that rofecoxib should have been withdrawn several years earlier. The reasons why manufacturer and drug licensing authorities did not continuously monitor and summarise the accumulating evidence need to be clarified."

The Vioxx case made headlines worldwide and caused an avalanche of lawsuits, closed by Merck with record settlements. (See, among others, those reported in [this Nature article](#) and in [this Reuters piece](#).) It also became an example of how things can badly go wrong. Among the many available resources on the Vioxx saga worth checking out are NPR's special series [Vioxx: The Downfall of a Drug](#); [the transcript of David Graham's testimony before the US Senate](#); and the BMJ article [What Have We Learnt from Vioxx?](#)

Another example of selective publishing of relevant evidence by the pharmaceutical industry is the case of the painkiller OxyContin, marketed by Purdue Pharma, which has become emblematic of the US opioid crisis. The company knew about significant abuse of its drug in the early years that followed its marketing approval in 1995, and the company concealed information, as investigations by journalist

Barry Meier have shown.

Meier began covering the marketing of the painkiller OxyContin and the resulting epidemic of opioid addiction as early as 2001 for The New York Times. He dug for years,

writing a book on the topic which was first published in 2003, with a revised version in 2018: "[Pain Killer: An Empire of Deceit and the Origin of America's Opioid Epidemic](#)." In October 2020, the US Justice Department [announced](#) the resolution of its criminal and civil investigations into Purdue Pharma, resulting in criminal guilty pleas and a federal settlement of more than \$8 billion.

One paper pointed out that most new drugs approved by the FDA since the 1970s are no better for patients than previous drugs, and that the bar for "safe" is low, given that approved medicines have caused an undisputed epidemic of harmful side effects, even when properly prescribed.

Even though similar cases show the limits of the regulatory agencies' work, [the standards of the US federal regulator](#), the FDA, are among the most stringent and demanding in the world. The agency produces a lot of documentation, much of it published [on its website](#). It is a useful source if you want to understand how a product arrived on the market. On any specific drug page, you'll find a chronology with links to all relevant pieces of evidence that informed the long process of bringing a drug to market. To identify the studies considered during the approval process, pay particular attention to the [FDA's Approval Letters](#) and to clinical and statistical reviews. But keep in mind that FDA work is not flawless, and that the agency depends on the pharmaceutical industry for much of its

funding. As pointed out in a 2016 investigation by the Project On Government Oversight (POGO), [FDA Depends on Industry Funding: Money Comes with 'Strings Attached'](#), over the previous two decades “user fees” paid by the industry climbed from 35% to 71% of the FDA’s budget for “review of human drug applications” under the Prescription Drug User Fee Act. This dependency and clear conflict of interest enhances Big Pharma influence, POGO found, and there are signs that FDA work may be increasingly compromised, as evidenced by a trend to lower the bar for drug approval, for instance by widening the criteria for a product to be approved under the “Fast Track” process.

Originally, Fast Track was invented with a noble purpose: to quickly bring new treatments to patients that would address unmet needs. A special procedure was introduced that accelerates approval by reducing the amount and quality of evidence the industry must submit. However, in recent years Fast Track became a shortcut for pharmaceutical companies, allowing them to skip or shorten in-depth assessments by regulators.

Further issues that require our attention when investigating drugs are described by Donald W. Light, Joel Lexchin, and Jonathan J. Darrow in

ALSO WORTH A READ

- National Women’s Health Network’s [FDA Approvals: On a Fast-Track to Disaster](#) (2017).
- The Center for Public Integrity’s [Trump’s Praise Put Drug For Vets On Fast Track, But Experts Aren’t Sure It Works](#) (2019).
- The Wall Street Journal’s [Fast-Track Drug Approval, Designed for Emergencies, Is Now Routine](#) (2019).

[Institutional Corruption of Pharmaceuticals and the Myth of Safe and Effective Drugs](#), a paper published in 2013 in the Journal of Law, Medicine & Ethics.

Included in their list of issues is the fact that most new drugs approved by the FDA since the 1970s are no better for patients than previous drugs and that the bar for “safe” is low, given that approved medicines have caused an undisputed epidemic of harmful side effects, even when properly prescribed.

Combining in-depth research in both the [FDA](#) and [EMA](#) archives can bring real benefits to your journalism. If the FDA publishes many documents, the EMA can be a very interesting resource to access the clinical study report of a trial, typically a lengthy document that provides many details about the trial’s methods and its results. [As underscored by researchers Peter Doshi \(University of Maryland School of Pharmacy\) and Tom Jefferson \(Oxford University\)](#), the FDA “treats clinical study reports and other parts of the dossier submitted by sponsors as commercial confidential information and, therefore, not releasable under the US Freedom of Information Act. In contrast, the EMA interprets all documents, including clinical study reports, to be subject to its “reactive” freedom of information policy and is the only regulator in the world routinely releasing such data. However, the agency is dealing with a huge and growing number of requests.”

ALSO WORTH A READ

On EMA Work in General:

- The BMJ’s [Open Letter: European Medicines Agency Should Remove Barriers to Access Clinical Trial Data](#) (2014).
- Systematic Reviews’ [Access to Regulatory Data from the European Medicines Agency: The Times They Are a-Changing](#) (2012).

ALSO WORTH A READ

On the differences between the FDA and the EMA:

- Journal of Clinical Epidemiology's [The Food and Drug Administration Reports Provided More Data but Were More Difficult to Use Than the European Medicines Agency Reports](#) (2014).
- Tropical Medicine & International Health's [Registering Medicines for Low-Income Countries: How Suitable Are the Stringent Review Procedures of the World Health Organisation, the US Food and Drug Administration and the European Medicines Agency?](#) (2013).
- The BMJ's [The European Medicines Agency Is Still Too Close to Industry](#) (2016).
- The BMJ's [European Medicines Agency Is to Tighten up on Advisers' Conflicts of Interest](#) (2012).

Only citizens of the European Union and persons (natural or legal) residing or having their registered office in an EU Member State have the right of access to EMA documents. Details about the procedure to obtain documents are available on the [EMA website](#).

Doshi and Jefferson, who have substantial experience with the process, underline that the “release can take considerable time to occur and often only after a lengthy correspondence.” Also, pharmaceutical companies may object to the EMA releasing clinical trial data, and sometimes the conflict can end in court, as shown in a [2018 case involving the release by the EMA of clinical study reports on a drug for Duchenne muscular dystrophy](#).

Regulatory agencies are regularly criticized for their closeness to industry, and this applies to the EMA as well, even though the agency has recently made some efforts to increase communication about [its handling of competing interests](#).

In addition to national agencies, international organizations play a role in many aspects of drug and medical device regulation, including certification, manufacturing, distribution, pricing, marketing, research and development, and intellectual property rights. Digging deeper into their work is worthwhile if you want to fully understand regulation and approval of a drug. It may help you ask the right question regarding key issues such as:

- Why did regulatory authorities require some data and not others?
- How does the product's intellectual property affect its licenses and markets?
- Did the pharmaceutical industry try to influence the work of one of these organizations?

Here are some agencies to check out. Each of them has a wide range of competencies that cover different aspects of this market and that are described in detail on the agencies' websites:

- [International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use](#) (ICH)
- [World Health Organization](#) (WHO)
- [Pan American Health Organization](#) (PAHO)
- [World Trade Organization](#) (WTO)
- [World Intellectual Property Organization](#) (WIPO)

Investigating Medical Devices

Medical devices comprise a vast range of equipment, defined by Daniel B. Kramer and colleagues as “[health technologies that are not medicines, vaccines, or clinical procedures.](#)” Investigating them means dealing with an under-regulated environment. It is undeniable that in past decades new devices have offered better alternatives for some conditions. But they do not always deliver benefits to patients and have exposed some to substantial risks, as shown in recalls of breast and artificial hip implants.

Standards in this area are much lower than they are for pharmaceuticals.

In 2016, the review [Drugs and Devices: Comparison of European and US Approval Processes](#) found that only about 2% of medical devices approved in the previous 10 to 12 years went through Premarket Applications, the FDA’s most rigorous process for device approval. The review, published in JACC:

The Implant Files investigation by the ICIJ found that health authorities are failing to safeguard patients from medical devices that have been linked to more than 83,000 deaths and more than 1.7 million injuries in the past decade.

Basic to Translational Science, also reported that only 10% to 15% of FDA device submissions contained clinical data, and that 7% were exempted entirely from review. “When clinical trials are required for devices,

they frequently do not meet the same strict standards for clinical evidence that are required for drugs,” the review found. “They are often nonrandomized, nonblinded, do not have active control groups and lack hard endpoints.”

The approval processes for medical devices in the EU and the US share some similarities. But there are also critical differences, as the same review stated: “Before approval of a medical device in the United States, a device must not

only be shown to be safe, but efficacious. Medical devices approved in Europe need only to demonstrate safety and performance... A collateral effect of more 'commercially sensitive' regulations in Europe is that initial approval of US company-backed devices is increasingly being sought in the EU before application in the United States.”

The US and Europe lead the field, and although most national regulators have their own approval processes for medical devices, most countries tend to follow the FDA and EMA. In many countries, if a medical device has already been approved by the FDA and EMA it will benefit from a much shorter approval process.

Yet there are serious concerns about the appropriateness and effectiveness of both approval processes, as shown in Daniel B. Kramer, Shuai Xu, and Aaron S. Kesselheim’s 2012 review, [How Does Medical Device Regulation Perform in the United States and the European Union? A Systematic Review](#). The authors concluded: “Existing studies of US and EU device approval and post-market evaluation performance suggest that policy reforms are necessary for both systems, including improving classification of devices in the US and promoting transparency and post-market oversight in the EU.”

In 2014, Oxford scientist Carl Heneghan joined an undercover investigation to expose how the regulation was so lax that packaging for fruit could be approved as a medical device. [Jet Schouten, a journalist with Dutch public broadcaster AVROTROS, requested that Heneghan](#) produce a faulty scientific report based on repurposing the bags used in the sale of mandarins as a transvaginal mesh, which is normally used to enforce weakened tissue in the pelvic area. And the test worked: Regulators didn’t anticipate problems in the approval process, and no questions were asked about safety.

Five years later, far more people are familiar with medical devices because of the [Implant Files](#) investigation by the International Consortium of Investigative Journalists (ICIJ), inspired by the work of Schouten. The project found that health authorities are failing to safeguard patients from medical devices that have been linked to more than 83,000 deaths and more than 1.7 million injuries in the past decade. The ICIJ published a publicly searchable [International Medical Devices Database](#) which contains product recalls, safety alerts, and field safety notices, data drawn from public sources as well as responses to freedom of information requests.

The ICIJ collaboration involved 36 countries, more than 250 reporters, and data specialists from 58 media organizations. Since the Implant Files investigation was published, [regulators around the world have vowed to improve the oversight of medical devices](#).

To find out more about this ICIJ project and the tools the global team used and developed, see ICIJ's [Everything You Need to Know About the Implant Files](#) and [Lessons from Inside the Implant Files](#). The database and tools are good resources for journalists investigating related stories.

ALSO WORTH A READ

- [What Next for Transvaginal Mesh?](#) by Carl Heneghan, BMJ Opinion (2019).
- [The Danger Within Us: America's Untested, Unregulated Medical Device Industry and One Man's Battle to Survive It](#), by medical investigative journalist Jeanne Lenzer (2017).

TIP 2: SEARCH FOR RED FLAGS

During the approval process, pharmaceutical companies use a variety of techniques to achieve a favorable ruling. Marketing strategies and growing medicalization are used to interfere with the approval process. Here are three strategies they use:

- Enlarge the definition of the risks or sicknesses to be addressed in order to expand the potential value of the drug. See these classic examples on [cholesterol](#), [blood pressure](#), and [blood sugar](#).
- Intervene and detect earlier; the typical examples are cancer screenings, health checkups, and genetic testing. Good reads here include HealthNewsReview.org's [Screening: How Over-diagnosis and Other Harms Can Undermine the Benefits](#); Scientific American's [Putting Tests to the Test: Many Medical Procedures Prove Unnecessary – and Risky](#); PBS's [The \\$200 Billion Perils of Unnecessary Medical Tests](#); and [the Washington Health Alliance's First Do No Harm](#).
- Increase the number of conditions for which the drug can be prescribed or used, a strategy known as [disease mongering](#).

When taking a closer look at a drug approval process, focus on key aspects that will determine the market for the product, starting with its “indication.” The indication describes the condition for which a pharmaceutical product (drug, test, vaccine) should be used. If it is an approved indication, this means that regulatory authorities have reviewed the evidence submitted by the manufacturer for the treatment or prevention of a condition or a disease, and allowed the company to market the product for this specific use. Widening the indication is a common practice to expand a product’s market, and it often happens step by step, with the industry submitting new data to the regulators.

Keep digging and look at: the definition of the disease; how the risk for developing it is described and documented; the design of the clinical trials (outcomes, exclusion/inclusion criteria); the efficacy and safety data; and how study results are presented. If you are new to the health care beat, for a while you'll have to rely heavily on help from independent scientists to analyze the evidence. With time, though, as any senior medical investigative journalist can tell, you'll be increasingly able to spot red flags and independently assess the evidence. Your review may reveal that erroneous conclusions have been drawn about the risk-benefit ratio of a product and give you insight on how it happened.

Digging Even Deeper: Clinical Trials Databases

In 2005, the International Committee of Medical Journal Editors announced that in order for their studies to be published, “sponsors” who pay for the clinical trials would have to register clinical trials before they begin. Many journals will only publish the results of trials that have been pre-registered. Currently there are 24 registries (national, regional, and international; [here is the list](#)). WHO's [Clinical Trials Search Portal](#) provides access to a central database containing datasets provided by 17 registries, with links to the complete original records.

Some companies run their own registries, like [GlaxoSmithKline](#) and [Eli Lilly](#). [ClinicalTrials.gov](#) was the first online registry of this kind and remains the largest and most widely used. The US National Institutes of Health and the FDA worked together to develop the site, which was made available to

During the approval process, advisory committee meetings take place, and their minutes can be revealing, as regulators often see potential problems and ask the industry interesting and sometimes inconvenient questions. The FDA, EMA, and WHO websites are therefore a treasure trove of information and possible leads.

the public in February 2000. If you are considering an investigation into a specific class of drugs, or a medication that you came across, it is worth starting with [ClinicalTrials.gov](https://clinicaltrials.gov).

We'll be looking at this in more detail in the next section, but when searching clinical trials databases, take a closer look at:

- Study design.
- [Number of participants in the trial](#).
- Patients' inclusion/exclusion criteria from the study.
- Research centers involved.
- History of changes.
- If the trial is still ongoing.
- If results were published.
- Endpoints: primary, secondary, combined, surrogate. It is crucial to understand the concept of endpoint if you want to investigate health and medicine. According to the [Principles of Translational Science in Medicine](#), "Clinical endpoints are distinct measurements or analyses of disease characteristics observed in a study or a clinical trial that reflect the effect of a therapeutic intervention." Endpoints can be hard (objective) or soft (subjective). In some cases surrogate endpoints are used rather than clinically important outcomes ([see page 14](#)).

You can find changes in study design by comparing clinical studies as recorded in the registers with the same studies as they were later published in a scientific journal and/or submitted to regulatory agencies. As mentioned, studies do not always end up being published by academic journals. Lack of publication and changes in studies' design are often interesting red flags; it might indicate that problematic results have not been revealed.

During the approval process, advisory committee meetings take place, and their minutes can be revealing, as regulators often see potential problems and ask the industry interesting and sometimes inconvenient questions. Such minutes and related documents will give you valuable insights into issues and tensions. The [FDA](#), [EMA](#), and [WHO](#) websites are a treasure trove of information and possible leads.

To learn about the WHO's role in drug regulation worldwide, see [Drug Regulation: History, Present and Future](#). The WHO also manages the [Essential Medicines List](#) and the [List of Essential Diagnostics](#), defined by the agency as “core guidance documents that help countries prioritize critical health products that should be widely available and affordable throughout [health systems](#).” Both guidance documents have a big impact on the global pharmaceutical market.

TIP 3: GET UNPUBLISHED DATA

Not all documents may be part of the visible public record, but they can normally be obtained from the FDA and EMA through a freedom of information (FOI) request. Each time you make such a request you may be contributing to the common good because some requests may be made publicly available on the agency website.

With [iFOIA](#), developed by the [Reporters Committee for Freedom of the Press](#), registered users can create, send, maintain, and share US requests. You'll find plenty of FOI law tips and resources in GIJN's [Global Guide to Freedom of Information](#). Also consider using the



South African Promotion of Access to Information Act (PAIA) that interestingly applies to private bodies, too. Although the industry is resisting requests for full disclosure on the grounds this may damage intellectual property rights by exposing industrial secrets, if your investigation focuses on a company with headquarters in South Africa, a PAIA request is worth trying.

If you decide to file a FOI request with the FDA, consider asking for access to email correspondence and technical documents like the statistical Data Analysis Plans (DAP) of clinical studies. In 2011 we obtained the DAP document Merck submitted in order to get approval for the HPV vaccine Gardasil. As we noted in the journal *BMJ Evidence-Based Medicine*, the document showed a significant methodological adjustment was introduced during the Phase III trials, where a [pre-specified analysis was replaced by a lower value indicator](#). This so-called “outcome switching” is a controversial practice and is a potential problem in clinical studies reporting, as it can distort the evidence.

An example of the potential consequences of outcome switching is discussed in [this](#) 2018 brief from Enago Academy about the antidepressant Paroxetine, with links back to the original studies. The New York Times also addressed the issue in a [2015 piece by Benedict Carey](#).

To learn more about this problematic, though relatively common, practice, have a look at the [COMPARE](#) project that was done by a team of academics, medical students, and programmers based at the Oxford University's [CEBM](#).

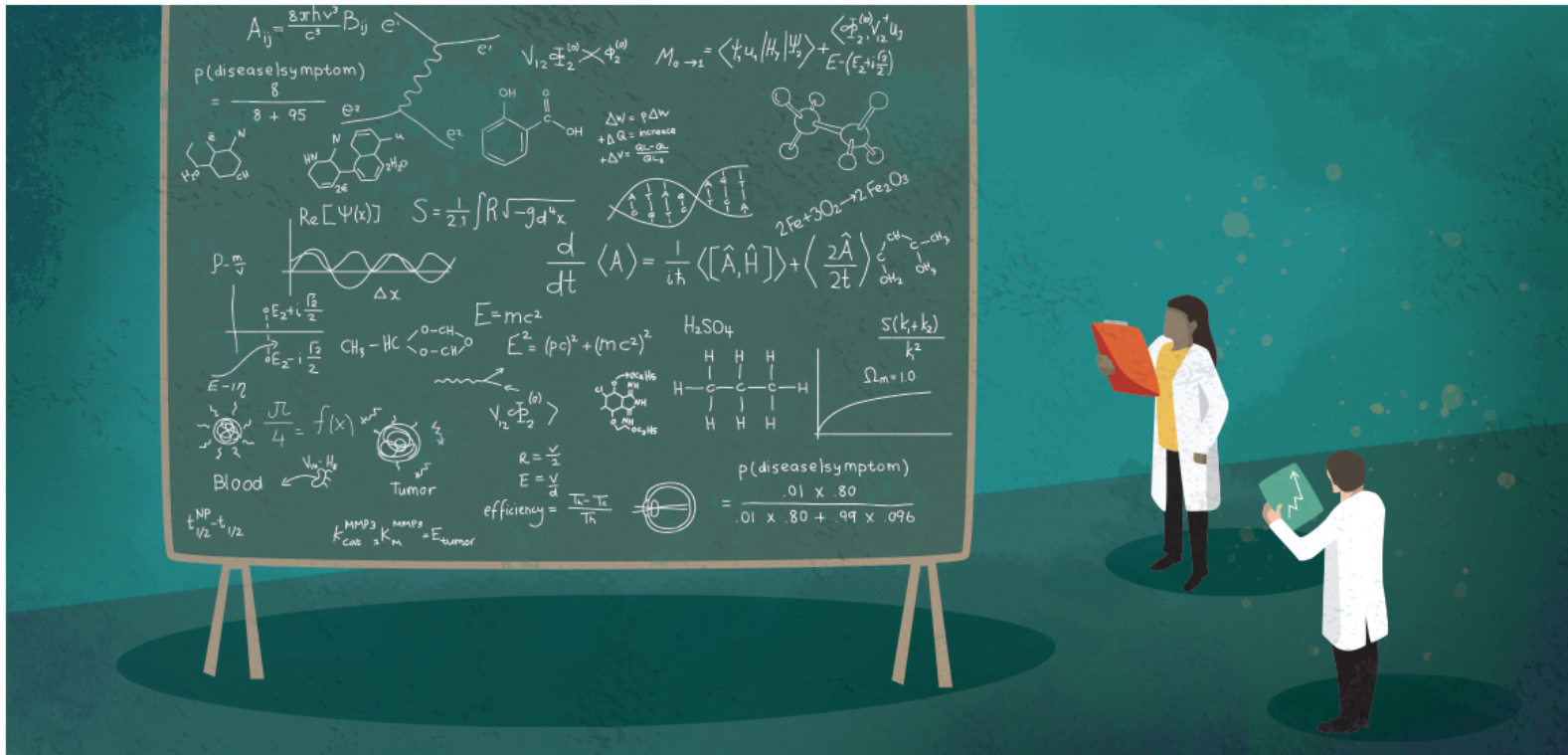
Unpublished clinical studies data can be important when assessing the real risk-benefit profile of a drug. But obtaining the data and performing an assessment can be difficult, even for experienced scientists. See, for instance, [Strategies for Obtaining Unpublished Drug Trial Data: A Qualitative Interview](#)

[Study](#). Note, for example, that the FDA is legally allowed to neither confirm nor deny the existence of a study in response to a FOI request. Recently, academics and investigative reporters have joined forces to locate missing or incomplete datasets.

One example is the [Tamiflu campaign](#) by the British Medical Journal, aimed at pressuring drug companies to release the underlying trial data for two globally stockpiled anti-influenza drugs. For further understanding of why the lack of transparency matters and also great resources for underreported stories see: [Restoring Invisible & Abandoned Trials Initiative](#), [AllTrials](#) and [TranspariMED](#).

CHAPTER 2

A Study Is Not Just a Study. Get Your Numbers Straight



TIP 1: STICK TO EBM AND USE PICO

As we stated in our introduction, using Evidence-Based Medicine (EBM), [defined as](#) "the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients," as a method of investigation can be time-consuming, but highly effective.

EBM methods are a great fit with good muckraking: keep questioning what you hear and read, look for the best available evidence, and independently assess its quality. Sounds familiar, doesn't it? Some EBM principles will be highly effective in your investigation like applying the [Critical Appraisal](#) method and adapting

[PICO criteria](#) to your journalism.

EBM states that to carry out research of the literature and analyze the risk-benefit ratio, a clinical question can be broken down into four dimensions, or PICO criteria. PICO helps us to see if data is missing or flawed, for instance if an [inadequate comparator](#) or an aforementioned surrogate outcome was applied.



PICO criteria	Meaning	Explanation & example
P	Patient or health issue	Patient's profile (age, sex) and/or the medical intervention supposed to fit in
I	Intervention	Treatment or test
C	Comparator	Placebo, treatment or test
O	"Outcome" (measured result, clinical claim, assessing criteria)	Survival rate after 5 years

Illustration: Re-Check.ch

TIP 2: A STUDY IS NOT JUST A STUDY

"A study has shown" ... but what kind of a study was it? As neatly put by [Gary Schwitzer](#) in his essential guide [Covering Medical Research](#): "Not all studies are equal. And they shouldn't be reported as if they were." Being aware of this will make a big difference to your investigation. If your work is based on weak scientific evidence, you won't have a strong story, and there's a good chance some of it will be wrong.

In order to work as an investigative journalist in the area of health and medicine, remember that flaws in scientific methodology often indicate that

further digging is needed. The learning curve can be steep, but you can start by checking out the wide range of studies as discussed in [Types of Study in Medical Research: Part 3 of a Series on Evaluation of Scientific Publications](#), a 2009 article in the journal *Deutsches Ärzteblatt International*.

Understanding the differences among types of studies will help you avoid many mistakes. In short, you have to start by asking two major questions. First, was the study conducted on humans? Or was it conducted on animals or on cells? The research on humans is called clinical research. When it comes to assess the effect of a drug or another health measure, the only truly significant results are those obtained on humans, in short, because humans are so different from mice.

Methods associated with Evidence-Based Medicine are a great fit with good muckraking: keep questioning what you hear and read, look for the best available evidence, and independently assess its quality.

A result on mice may be interesting, but any conclusions about a treatment's efficacy on humans drawn from animal studies are speculative.

Such studies are in the so-called “pre-clinical” development stage of a new drug. One should remember that in the story of medicine there have been many drugs that seemed very promising when tested on animals but had to be pulled when it became clear they were ineffective or even toxic for humans.

If the study was conducted on humans, you then have to ask the second relevant question: Was the trial an experimental (also called interventional) study or an epidemiologic (also called observational) study?

This is essential, as pointed out by [HealthNewsReview.org](#): “Epidemiologic – or observational – studies examine the association between what’s known in

epidemiologic jargon as an exposure (a food, something in the environment, or a behavior) and an outcome (often a disease or death). Because of all the other exposures occurring simultaneously in the complex lives of free-living humans that can never be completely accounted for, such studies cannot provide evidence of cause and effect; they can only provide evidence of some relationship (between exposure and outcome) that a stronger design could explore further.”

By doing an experimental study, researchers test if intervention A (e.g., a drug or vaccine) does actually lead to outcome B (e.g., a cure or disease prevention). Among experimental studies, the only design that can demonstrate a cause and effect relationship is the randomized controlled trial (RCT), where the study subjects are assigned at

random to the intervention (such as a drug or vaccine) or to a control (such as a placebo or another drug).

Randomization makes both

groups truly comparable: the only difference between the intervention group and the control group is whether their subjects receive the intervention under study or the control. This experimental setting is the only one that allows us to conclude that the outcome difference between the intervention group and the control group is attributable to the tested drug or vaccine.

When it comes to assessing the effect of a drug or another health measure, the only truly significant results are those obtained on humans, in short, because humans are so different from mice.

“Because observational studies are not randomized, they cannot control for all of the other inevitable, often unmeasurable, exposures or factors that may actually be causing the results,” concludes HealthNewsReview.org. Thus, any “link between cause and effect in observational studies is speculative at best.”

So beware: Observational studies cannot, in any circumstances, lead to a conclusion about the effectiveness of a measure, even when a statistically significant association seems to be established. Only an experimental study involving RCT can establish whether there is a causal relationship between the intervention tested and the observed effect.

Also, consider that observational and retrospective studies are more prone to the potential limits of statistical analysis. Sometimes statistics can be used by

*"Statistics can pull out of the bag almost anything that may be wanted."
– Darrell Huff, "How to Lie with Statistics"*

researchers or sponsors to tweak the results. So when analyzing numbers, keep in mind what Darrell Huff, best known for his book "How to Lie with Statistics," said in 1954: "Statistics can pull out of the bag almost anything that may be wanted." Nobel-winning economist Ronald H. Coase echoed this, saying: "If you torture the data long enough, nature will always confess."

Multicentric, double-blind RCTs are considered the gold standard in determining the efficacy of an intervention. Their design is superior in controlling the parameters likely to distort the results (so-called confounding factors and bias). Two valuable resources to learn these basics: [Students 4 Best Evidence](#) and [Types of Clinical Study Designs](#) from Georgia State University.

The illustration below describes best practice in evaluating the strength of the evidence. Note that experts' opinions are at the bottom of the pyramid.

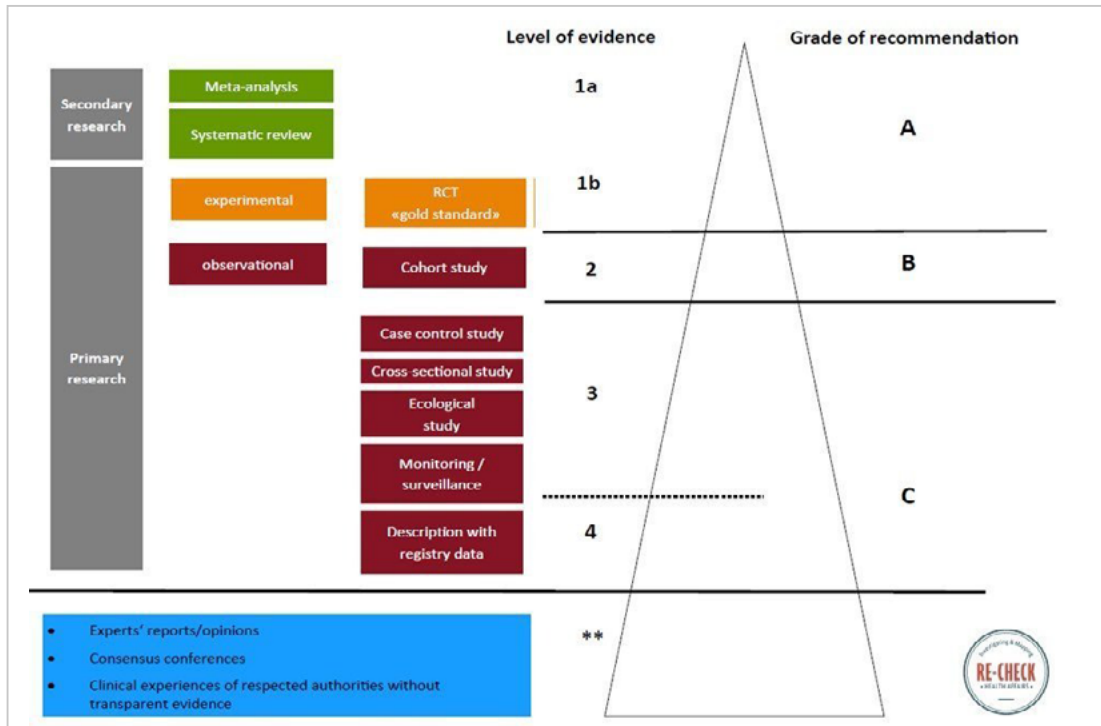


Illustration: Re-Check.ch

A simpler version can be found here:

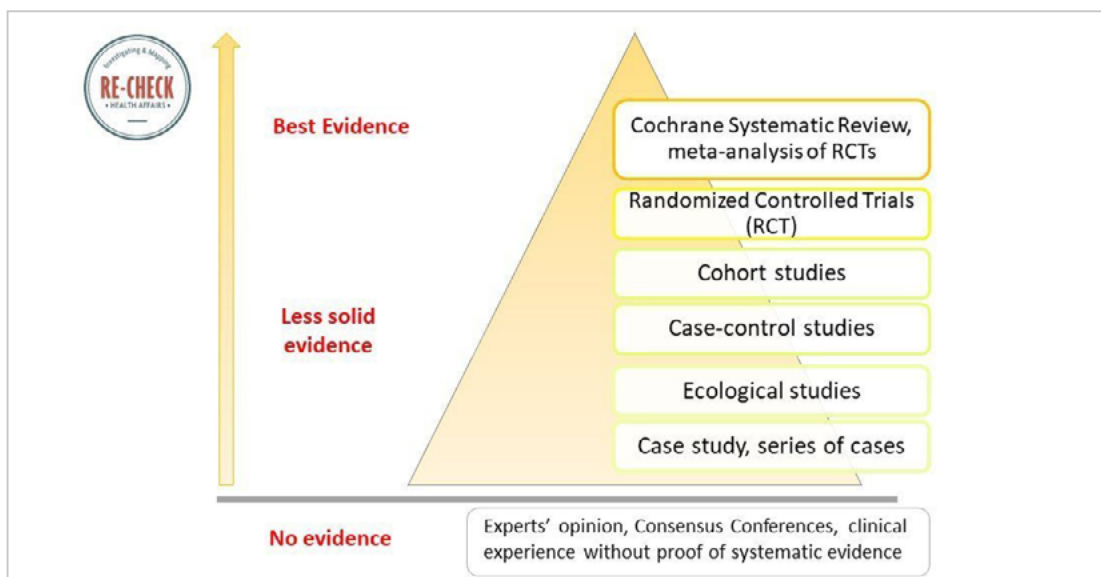


Illustration: Re-Check.ch

Be aware that the EBM pyramid concept should be questioned too. Whereas RCTs are the reference standard for studying causal relationships, a meta-analysis of RCTs – a systematic analysis and review of different studies and results – is considered the best source of evidence. Bear in mind, however, that if the studies in the meta-analysis are defective, its results won't be reliable, either. Furthermore, often meta-analyses (for instance those published by [Cochrane](#)) conclude there isn't enough evidence to answer a research question, which is not what journalists typically want to hear.

Reporting on health also means becoming knowledgeable about many flaws in clinical research. Trials showing a significant “positive” result are published, whereas “negative” studies most often are not. Some types of studies are more subject than others to bias, defined by the [Cochrane Handbook](#) as “systematic error, or deviation from the truth.” Another resource is the [Catalogue of Bias](#), a collaborative project mapping all the biases that affect health evidence.

In your reporting it's vital that all numbers are expressed in the same way, that is, in either percentages or absolute numbers. This is the only way the risks, benefits, and alternatives (for instance: do nothing) can be understood properly.

A typical mistake journalists make is to confuse [correlation and causation](#). It is tempting to see a link between two phenomena, but first you must ask if there really is a causal relationship. Mathematician Robert Matthews gives an amusing example of this: he shows a [highly statistically significant correlation between stork populations and human birth rates](#) across Europe.

Few are aware of the sometimes fraudulent practices that take place in the field of health research. There are studies based on imaginary patients, or written by ghostwriters. There is a lot of literature on such practices, and it is worth

getting familiar with it. See, for instance, Retraction Watch's [Study by Deceased Award-Winning Cancer Researcher Retracted Because Some Patients Were 'Invented,'](#) and Ivan Oransky's examples in his interview with The Irish Times, [The Shady Backstreets of Scientific Publishing.](#)

The most common mistake most reporters make is drawing the wrong conclusions from weak scientific evidence. Consider taking this free online course on [Epidemiological Research Methods](#) from the Eberly College of Science at Penn State University.

ALSO WORTH A READ

- HealthNewsReview.org's [Toolkit and Tutorials.](#)
- HealthNewsReview.org's [Tips For Analyzing Studies, Medical Evidence and Health Care Claims.](#)
- HealthNewsReview.org's [Just For Journalists: Tips and Case Studies For Writing About Health Care.](#)

TIP 3: ABSOLUTE VALUES AND NATURAL FREQUENCIES

Not everyone is a crack statistician. However, to investigate health the numbers are key. Don't be afraid to [Test Your Risk Literacy](#) (English, German, French, Dutch, and Spanish) and keep in mind that when a new drug or a new health policy or regulation is launched and/or promoted, the focus is on its benefits. Unfortunately, it's not enough simply to add risks to the picture.

It's necessary to understand the relationship between benefits and risks. This isn't easy. Our ability to reason is governed by so-called judgmental heuristics or cognitive shortcuts, resulting in limited rationality. Because of these well-studied phenomena, we tend to struggle with probabilities, especially percentages.

Confused? Have a look at [the illustration](#) below. Same numbers. Which one is easier to grab?

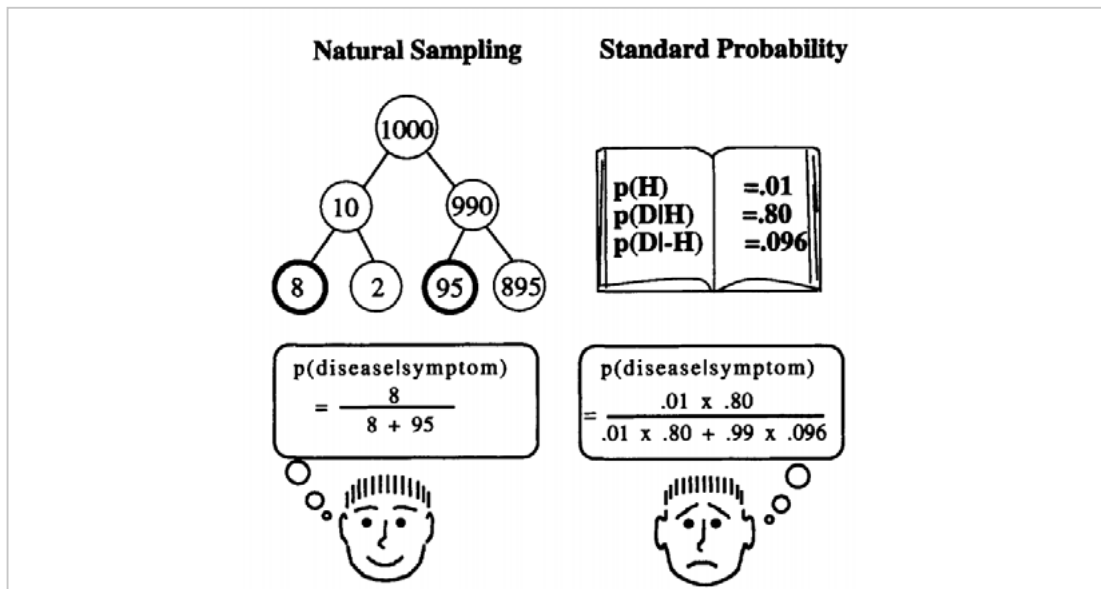


Illustration: Gerd Gigerenzer, Ulrich Hoffrage.

How to Improve Bayesian Reasoning Without Instruction: Frequency Formats.

Psychological Review, 1995, VoT102, No. 4,684-704

Advocates of a particular outcome may present the information they want to emphasize as a percentage, while communicating the information they want to make less prominent in absolute numbers. So, pay attention to the way the data is presented. Absolute numbers are more clearly representative than percentages.

The following example by [Gerd Gigerenzer and co-authors](#) from the Harding Center for Risk Literacy starkly shows how misleading this can be:

“In 1996 a review of mammography screening reported in its abstract a 24% reduction of breast cancer mortality; a review in 2002 claimed a 21% reduction. Accordingly, health pamphlets, websites, and invitations broadcast a 20% (or 25%) benefit. Did the public know that this impressive number corresponds to a reduction from about five to four in every 1,000 women, that is, 0.1%? The answer is, no. In a representative quota sample in nine European countries, 92% of about 5,000 women overestimated the benefit 10-fold, 100-fold, and more, or they did not know. For example, 27% of women in the United Kingdom believed that out of every 1,000 women who were screened, 200 fewer would die of breast cancer. But it is not only patients who are misled. When asked what the ‘25% mortality reduction from breast cancer’ means, 31% of 150 gynecologists answered that for every 1000 women who were screened, 25 or 250 fewer would die.”

The percentage exposure (relative risk) is often more spectacular, therefore more convincing or favorable from the point of view of companies and promoters of a public health campaign, than the exposure in absolute values (absolute risk). Read the HealthNewsReview.org [feature on why this matters](#) and check the simple example they propose in this illustration.

It sounds complex but the example below should help.

WHY THE NUMBERS MATTER

RELATIVE RISK "New wonder drug reduces heart attack risk 50%"	ABSOLUTE RISK "New wonder drug reduced heart attacks from from 2 per 100 to 1 per 100"
---	---

The **absolute risk** is more useful at conveying the true impact of an intervention, yet is often under-reported in the research and the news.



Illustration: HealthNewsReview.org – Your Health News Watchdog

In your reporting it's vital that all numbers are expressed in the same way, that is, in either percentages or absolute numbers. This is the only way the risks, benefits, and alternatives (for instance: do nothing) can be understood properly. Also, consider using absolute numbers in your reporting because more people will be able to understand them.

The [Harding Center for Risk Literacy](#) fact boxes and icon arrays on [breast](#) and [prostate cancer](#) screening are examples of best practice: benefits and harms are expressed in absolute values and immediately comparable; data is RCTs meta-analyses.

Early detection of breast cancer

by mammography screening



The numbers below refer to women aged 50 years and older* who either did or did not participate in mammography screening for approximately 11 years.

	1,000 women who did not participate in mammography screening	1,000 women who participated in mammography screening
Benefits		
How many women died from breast cancer?	5	4
How many women died of any type of cancer?	22	22
Harms		
How many women experienced false alarms and unnecessarily had additional testing or tissue removed (biopsy)?	-	100
How many women with non-progressive breast cancer unnecessarily had partial or complete removal of a breast?	-	5

*A few of the studies looked at women aged 40 years and older; these data are also included.

Short summary: Mammography screening reduced the number of women who died from breast cancer by 1 out of every 1,000 women. However, it had no effect on the number of women who died of any type of cancer. Among all women taking part in screening, some women with non-progressive cancer were overdiagnosed and received unnecessary treatment.

Source: [1] Gøtzsche & Jørgensen. Cochrane Database Syst Rev 2013(6):CD001877.

Last Update: October 2019

<https://www.hardingcenter.de/en/fact-boxes>

Illustration: [Harding Center for Risk Literacy](#)

Early detection of breast cancer by mammography screening



Numbers for women aged 50 years and older* who either did or did not participate in mammography screening for approximately 11 years.

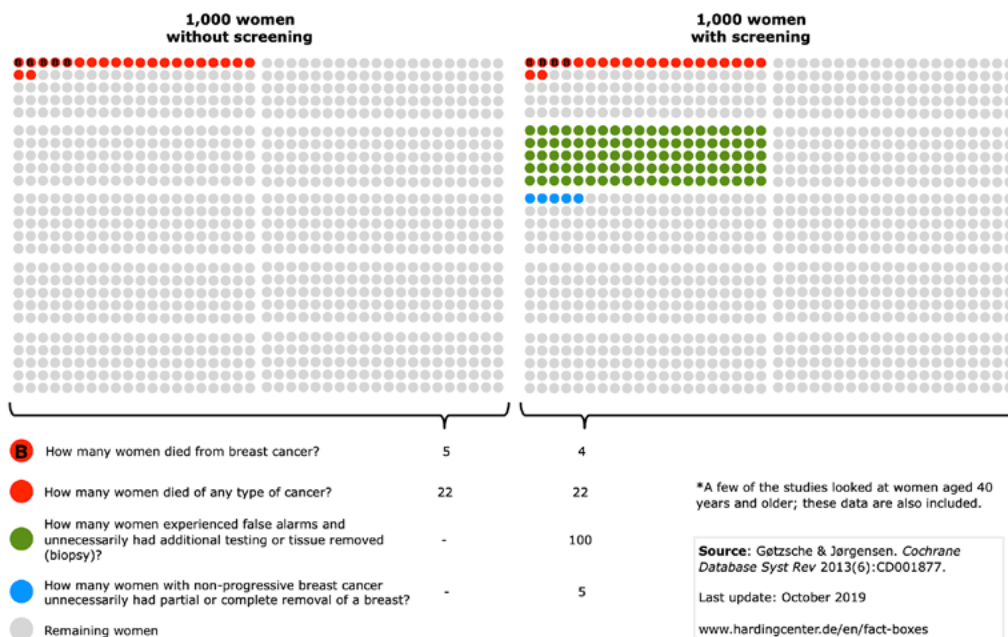


Illustration: [Harding Center for Risk Literacy](#)

TIP 4: BE AWARE OF FLAWS. AND READ THE PAPER

“A groundbreaking study published by prestigious journal X...” You definitely want to avoid putting this line in your story. Biomedical journals are affected by so many issues that even the most prestigious journals have to be scrutinized and cannot per se be considered reliable.

A quick way to understand this is to watch a recording of a seminar at the Liverpool School of Tropical Medicine by British Medical Journal Editor in Chief [Fiona Godlee: Why You Shouldn't Believe What You Read in Medical Journals](#). Godlee discusses the flaws of the peer-review system. She also is frank about how the business model of scientific journals, and particularly advertising, affects their content. Journals also rely on "reprints," bulk printed copies of published studies that are paid for by the industry and used for marketing purposes.

There is plenty of literature about commercial influence on the content of medical journals. Also, it's important to be aware that researchers' careers are determined by well-studied phenomena like “publish or perish” and by what is called the “impact factor” (how widely cited a journal is). Scientists also have to attract funding to their institutions, which can create conflicts of interests that have nothing to do with science or with the common good. A must-read is an evergreen paper by [John P. A. Ioannidis: Why Most Published Research Findings Are False](#).

Unfortunately there are few mechanisms in place to address these issues. One of them is retraction — a study is withdrawn from publication when major flaws are exposed. However, this rarely happens. Check [Retraction Watch](#), a great resource to find stories.

So how do we manage this complexity as journalists? One shortcut is to search

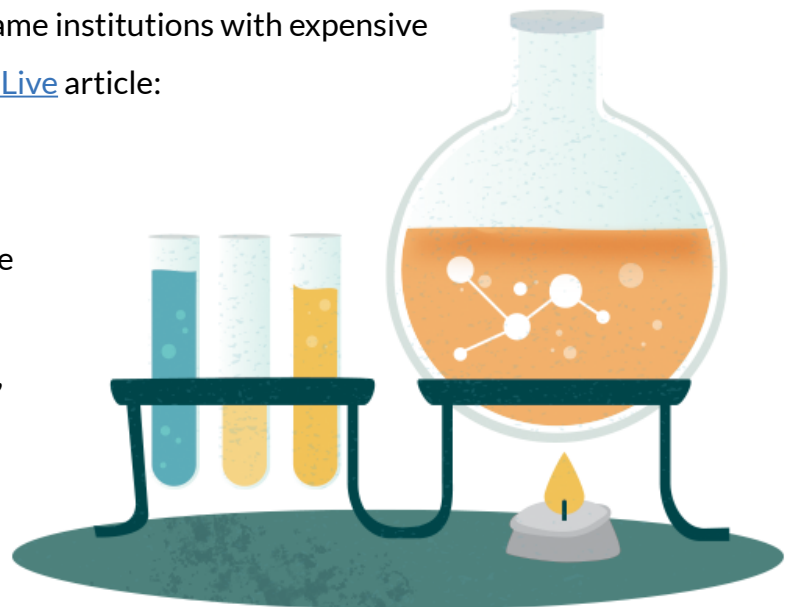
journals which are truly independent from the pharmaceutical industry. There are many worldwide, all members of the [International Society of Drug Bulletins](#).

It is even better to seek out the best available evidence yourself, much as you would do as a journalist in any other field. Which means: search, search, search. Also don't just read the study's abstract. Always read the full text, regardless of the journal, the author, or what an expert told you. But of course this is demanding work that will require time, patience, and having already acquired more than some basic knowledge in relevant methodologies and critical appraisal strategies.

Where do you find scientific studies? PubMed, from the US National Library of Medicine (NLM), is a free, searchable database of more than 30 million citations and abstracts of biomedical literature. MEDLINE, also from NLM, is a bibliographic database with more than 26 million references to journal articles in life science, with a concentration on biomedicine. However, many studies are not open access, which puts barriers in the way of those who wish to research and investigate. Most scientists work for publicly funded institutions, and journals don't pay the researchers when they publish their studies. Yet the journals charge the same institutions with expensive subscriptions. Read more in this [EBMLive](#) article:

[Research without Journals](#).

Paywalled papers might sometimes be available on the internet, or you can email the authors, or their institution, asking for a review copy. Such strategies may not be enough if you want to dig deeper, as



you'll need to retrieve and read many studies. If you can count on a generous budget, of course you can simply buy yourself access to the studies you want to read. On PubMed, you'll get a link to access the publisher page where payments can be made.

As most scientists and investigative medical reporters can't possibly pay for the large number of studies normally needed to research an issue, the portal by Kazakhstani scientist and computer programmer Alexandra Elbakyan is here to help: [Sci-Hub: To Remove all Barriers in the Way of Science](#). Elbakyan's website provides access to a huge number of scientific studies which are normally behind paywalls. On her personal website she describes [herself and her project](#); see also the feature on her [in the journal Science](#). Lawsuits by publishers force Elbakyan to continuously migrate Sci-Hub to different domains, which are regularly posted on Twitter.



Screenshot

CHAPTER 3

The Scientific Basis of Influence



TIP 1: YOU ARE BEING INFLUENCED

“We are pattern seekers, believers in a coherent world.”

– Nobel-prize winning psychologist *Daniel Kahneman*

One of the first things you learn as an investigative reporter is to beware of unconscious biases, including what is known as “anchoring” or “cognitive tunneling.” Neuroscience has shown that we tend to give more value to confirming, and less value to invalidating information. An example is [The Invisible Gorilla Strikes Again](#) experiment. Asked to identify lung nodules in CT scans, 20 out of 24 radiologists missed an image outlined in white of a gorilla

that researchers inserted in the images, although it was more than 48 times the size of the nodules doctors were asked to identify.

In some situations, the stronger the expectation, advantage, or threat of loss, the stronger the impact is on our thought processes – despite the fact that we are convinced of our own objectivity. In the field of health journalism, the risk of falling for appealing though flawed connections is substantial, and its consequences are significant.

Also, the science of influence underpins conflicts of interest, which are pervasive in science and medicine and whose impact on studies outcomes and practitioners' attitudes have been studied at length. There is a vast amount of literature on the topic, but a good read to start with is the systematic review [Scope and Impact of Financial Conflicts of Interest in Biomedical Research](#). The negative impact of these conflicts is undisputed, and that's why their disclosure is mostly compulsory, even if this is not always or consistently enforced.

It is also important to understand cognitive tunneling because the protagonists in your investigation may tell you they are “able to manage” conflicts of interest.

In fact, research has shown

this is not feasible, as influence acts at an unconscious level. As behavioral economist [George Loewenstein](#) put it: “Conflicts of interest will inevitably bias physician behavior, however honorable and well-intentioned specific physicians may be. Bias may distort their choices, or they may look for and unconsciously emphasize data that support their personal interests.”

In an experiment called The Invisible Gorilla Strikes Again, 20 out of 24 radiologists asked to identify lung nodules in CT scans missed an image of a gorilla that researchers had inserted, although it was more than 48 times the size of the nodules doctors were asked to identify.

TIP 2: BEWARE OF KEY OPINION LEADERS

Despite the gains made by Evidence-Based Medicine, Eminence-Based Medicine still exists. The difference between the two terms, which are largely known in the medical-scientific community, is duly explained in this [Students 4 Best Evidence tutorial](#). Basically, we tend to believe “the experts.” The longer their résumés, the more credibility we attach to their statements. Moreover, our relation to medical doctors is determined by a phenomenon known as the The White-Coat Effect. The industry relies on this in its marketing strategies where Key Opinion Leaders (KOLs) play a crucial role. KOLs are industry-designated doctors and scientists whose biographies and affiliations are perceived as prestigious. They are often, at the same time, consultants for industry, the government, and international organizations such as the WHO.

Companies engage them in every step of a product life cycle, and journalists tend to turn to them for quotes and advice, as they are considered “experts in the field.” KOLs populate the boards of medical societies, write guidelines, teach in medical schools, and give training in Continuing Medical Education systems.

Exposing conflicts of interest is worthwhile and a source of many good stories. Financial interests are not the only area to investigate; reputation, status, titles, and recognition play a role, too.

In several countries, pharmaceutical and medical devices manufacturers are required by law to release details of their payments to doctors and scientists. The data is available in databases like the US [Open Payments](#) or the French [Base Transparence Santé](#).

A recent increase in public awareness and media coverage of pharma money prompted the industry to launch “transparency” initiatives like the [Pharma](#)

[Cooperation Code](#) issued by the European Federation of Pharmaceutical Industries and Associations. Such datasets are typically difficult to analyze, as information is presented in various formats and published on single company websites. Projects like ProPublica's [Dollars for Docs](#) and CORRECTIV's [Euros for Doctors](#) try to go beyond these limitations. As the health market is global, it is worth searching extensively; a payment to a KOL could be made by a different office or branch of the company.

It is best practice to ask your expert about his or her conflicts of interest, and do your own research as well. You can start by checking what was declared in publications and advisory committees. Don't stop at that, though: KOLs tend to be selective in what they disclose. Search for abstracts and programs from medical conferences, industry press releases, and news stories. Don't forget to check the [Justia patents registry](#) and any organization sponsoring a research program being led by your expert.

Exposing conflicts of interest is worthwhile and a source of many good stories. Financial interests are not the only area to investigate; reputation, status, titles, and recognition play a role, too.

Conflict of interest disclosures have limitations and don't tell the full story. Many studies show that declarations provided by authors and advisory committee members are often [false and/or](#)

[incomplete](#). In addition, publications rarely apply the sanctions stated in their guidelines; medical journals and institutions don't routinely assess the accuracy of declarations of interest, nor impose sanctions for incomplete or inaccurate disclosure. In the end, conflict of interest disclosures are just not reliable.

As pointed out by the [Swiss Academy of Medical Sciences](#), transparency cannot constitute a goal in and of itself: "What is ethically problematic about conflicts

of interest is not primarily the fact that they are invisible, but that they can influence the behavior of medical researchers and other medical professionals at the treatment/research interface in a way that runs counter to patients' best interests."



Conflicts of interest also play a role in what is

called "[disease mongering](#)"— [defined by the Public](#)

[Library of Science](#) as the "selling of sickness in order to promote drug sales."

It is also a factor in [over-diagnosis](#), considered by some critics the biggest risk for the public health systems of richer countries. Read what over-diagnosis is, and isn't, [in this fact sheet by the Institute for Quality and Efficiency in Health Care](#). Other good reads are: The New York Times' [What's Making Us Sick Is an Epidemic of Diagnoses](#), the disease mongering [special edition of PLOS biomedical journal](#), and the British Medical Journal series [Too Much Medicine](#).

There is a global movement of doctors, starting in the 2000s with the No Free Lunch campaign, who have recognized the impact of conflicts of interest and [pledge to accept no industry gifts and to rely on non-promotional sources of prescribing information](#). Worldwide there are organizations of scientists and doctors working on the prevention of over-diagnosis; these people are also generally well-versed in both Evidence-Based Medicine and industry marketing strategies.

A list of [Industry-Independent Health Experts](#) is available at the Lown Institute website. The Lown List was first created by journalists Jeanne Lenzer and Shannon Brownlee who announced the project in a 2008 BMJ article entitled [Naming Names: Is There an \(Unbiased\) Doctor in the House?](#) The four List

coordinators, Jeanne Lenzer, Gary Schwitzer, Shannon Brownlee, and Adriane Fugh-Berman, were recently joined by the authors of this guide, Catherine Riva and Serena Tinari. The List is also posted at [HealthNewsReview.org](https://www.healthnewsreview.org) and on [Jeanne Lenzer's website](#).

Be aware of marketing strategies like disease awareness campaigns which aim to create a market for a certain drug (“Ask your doctor...”), and be cautious with industry-funded patients’ organizations. This hilarious [presentation](#) by Lisa Schwartz and Steven Woloshin at the 2018 Preventing Over-diagnosis Conference perfectly illustrates these methods. There is a lot of literature on this topic, as well as a database by Kaiser Health News: [Prescription for Power, Investigating the Relationships Between Patient Advocacy Groups and Big Pharma](#).

Examples of awareness campaigns and patients’ organizations that served industry agendas are Mother Jones’ [Unsealed Documents Show How Purdue Pharma Created a 'Pain Movement'](#), and The Guardian’s story from Australia, [Pharmaceutical Companies Spent \\$34m on Patient Advocacy Groups, Research Finds](#).

ALSO WORTH A READ

On marketing strategies:

- [How America Got Hooked on a Deadly Drug](#), by Fred Schulte, Kaiser Health News (2018).
- [The Man Who Sold America on Vitamin D – and Profited in the Process](#), by Liz Szabo, Kaiser Health News (2018).

ALSO WORTH A READ

On KOLs and conflicts of interest:

- [Prominent Doctors Aren't Disclosing Their Industry Ties in Medical Journal Studies. And Journals Are Doing Little to Enforce Their Rules](#), ProPublica (2018).
- [Top Cancer Doctor, Forced Out over Ties to Drug Makers, Joins Their Ranks](#), ProPublica (2019).

On industry influence:

- [From Twitter to Treatment Guidelines, Industry Influence Permeates Medicine](#), by Charles Ornstein, NPR (2017).
- [The Trail of Tainted Funding: Conflicts of Interest in Healthcare, Academics, Public Relations and Journalism](#), HealthNewsReview.org.

TIP 3: CONFLICTS OF INTEREST IN HEALTH JOURNALISM

Some media and health journalism organizations receive funding from the very industry they are reporting on, which raises important issues about conflicts of interest.

The 2019 World Conference of Science Journalists was [co-sponsored by Johnson & Johnson](#), with the company hosting a [luncheon](#) and pledging additional donations if the hashtag for its [#ChampionsofScience campaign was used on social media](#). At the same conference, Bayer offered a lunch called [“Raising the Bar on Sustainability and Transparency.”](#)

The Bill and Melinda Gates Foundation – by far the largest private foundation

in the United States – is especially active in funding health journalism. The foundation, whose stated goals include enhancing health care, has made huge donations to develop new drugs, vaccines, and health monitoring systems. It also has held corporate stocks and bonds in drug companies such as Merck, GlaxoSmithKline, Eli Lilly, Pfizer, Novartis, and Sanofi, according to a [2020 investigation in The Nation](#) by Tim Schwab. The main donor since 2015 of South Africa’s [Bhekisisa Centre for Health Journalism](#), the foundation contributes to the [Global Development section of the Guardian](#), the health reporting grants of the [European Journalism Center](#), and the [International Center for Journalists](#), [also supported by Johnson & Johnson](#). For more on the Gates Foundation’s involvement with journalism, see the Columbia Journalism Review’s two features by Robert Fortner, [How Ray Suarez Really Caught the Global Health Bug](#) and [The Web Grows Wider](#).

ALSO WORTH A READ

- [How Foundation Funding Is Shifting International News](#), by Martin Scott, GIJN (2019).

HealthNewsReview.org published a three-part investigation in 2017:

- [Conflicts of Interest in Health Care Journalism: Who’s Watching the Watchdogs? We Are.](#)
- [Conflicts of Interest: Time for World’s Top Health Journalism Organization to Reconsider Fundraising Practices.](#)
- [Conflicts of Interest in Health Care Journalism: An Unhealthy State of Things.](#)

TIP 4: CONNECT THE DOTS

It's tempting to focus on the “usual suspects” when you investigate health and medicine: manufacturers, insurers, and prominent players. However, the reality is much more complicated. Marketing strategies by players in the health industry have become increasingly sophisticated, and because they make decisions that affect public health, journalists need to dig deep and investigate the multiple players in the system.



At [Re-Check.ch](https://re-check.ch) we have come to realize that we have to include the “big picture” in our research. This means investigating as wide a range of institutions as possible, including nongovernmental organizations and the media. A practical example is our five-part investigation (in French) into the [interests surrounding mammography screening programs](#) — a complex maze with many lobbies at work. The investigation received an award from the Swiss Academy for Medical Sciences.

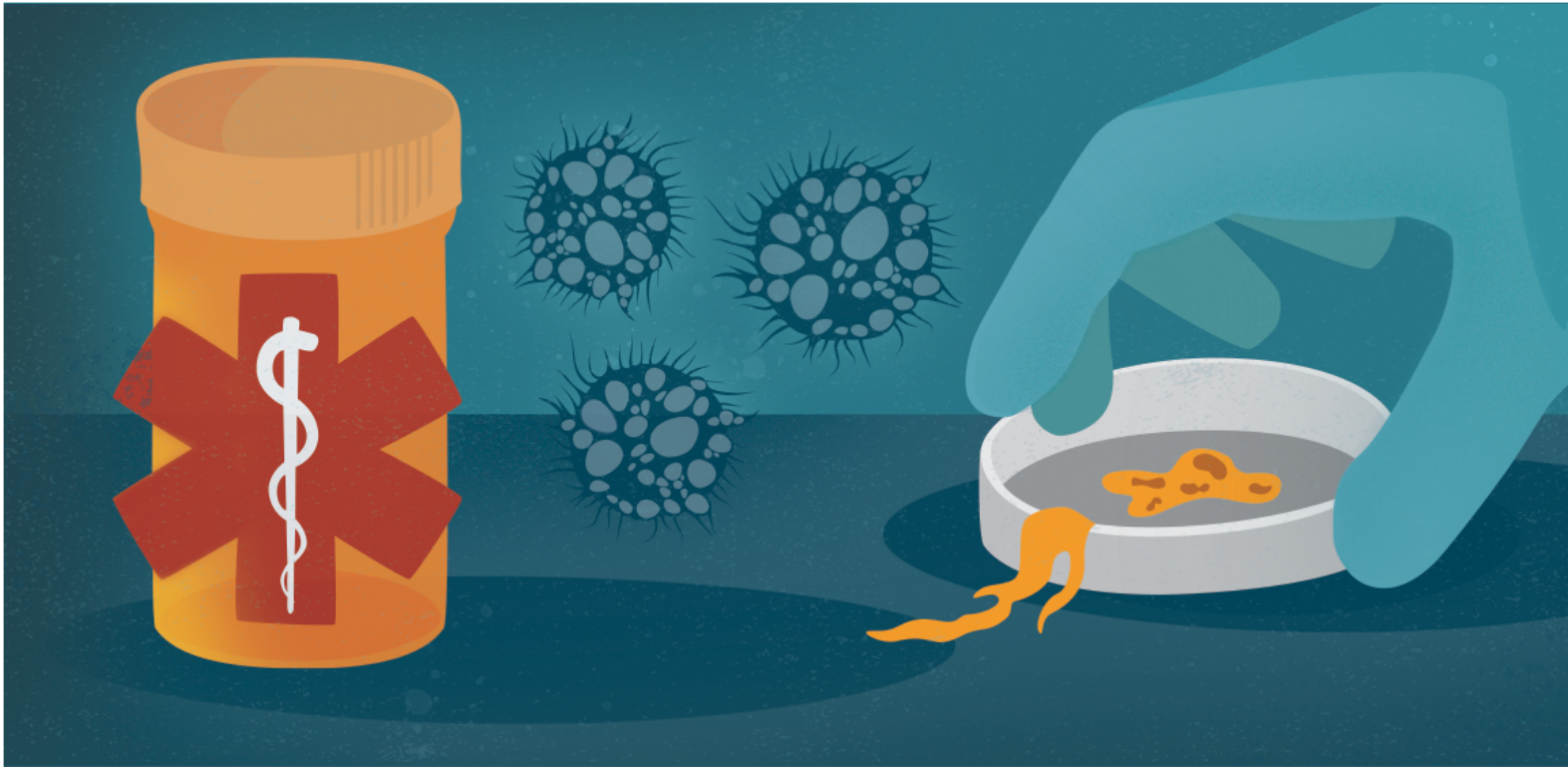
Two Canadian researchers, Sergio Sismondo and Marc-André Gagnon, have been developing this “big picture” angle, calling it [Ghost Management](#). It postulates that because of current business models, rather than producing innovative treatments, pharmaceutical firms focus more on influencing medical knowledge, shaping scientific narratives, influencing experts by nurturing conflicts of interest, capturing regulation and policymakers, and shaping media and culture in ways that allows maximizing profits. This means, [as Gagnon put it](#), that the “dominant business model of the pharmaceutical sector is based on the massive promotion of drugs that often do not represent any significant therapeutic advance. Clinical research is therefore run like a promotional

campaign. The data obtained from clinical research are primarily used to boost and support sales rather than to improve prescribing behaviour.” (Note: The authors of this guide, Catherine Riva and Serena Tinari, are working together with the two scholars on [a research project on Ghost Management.](#))

These marketing efforts are intended not only to shape doctors’ knowledge of the condition and their prescription habits (medical knowledge), but also to shape the political debate and people’s habits of thought. Ghost Management includes an effective methodology to dig deeper, and the practical application of these theories produce amazing visualizations [like these](#).

CHAPTER 4

First, Do No Harm. Reporting About Safety



Once a pharmaceutical product – a drug, vaccine, or medical device – has gone through the different testing phases, and the approval process with regulatory agencies, it hits the market and can be prescribed and sold. Serious adverse events can appear when the product is widely used for the first time by real patients. This relates not only to potential flaws in scientific research and problems related to regulatory approval and reporting in scientific journals. It is also sometimes a matter of numbers: If you test safety on 5,000 patients, an adverse event arising in one of 20,000 will become apparent when many more patients use the product. Therefore, the first 10 years after a drug is approved are considered especially important to spot harms.

TIP 1: ASSESS THE EVIDENCE

Editors love stories about the damage caused by drugs, vaccines, and medical devices because they are popular with audiences. There are a plethora of potentially good stories, but many pitfalls await and careful reporting is required.

First, one needs a systematic understanding of drug development and testing, including a review of the related literature and data. As we have seen in the [first chapter](#), a few thousand people or so will have tested a medical product in a controlled environment before it goes to market. That's why, although there are exceptions, "new drugs"

are generally considered less safe than older ones; they just aren't as well understood medically.

Beware of relying on a single report of an adverse reaction. These are called "signals" that tell experts to do further research into causality. Many other factors may have contributed.

What is defined as "post-marketing surveillance" by regulatory agencies is important. This includes pharmacovigilance, a type of monitoring which the [WHO defines as](#) "the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problem."

When pharmacovigilance is based on voluntary reporting, this can be a major issue. There are several ways for doctors, nurses, pharmacists, and patients to report suspected side effects, including by reporting them directly to regulators. If such reports are considered credible, national regulatory bodies may forward them to the [WHO Programme for International Drug Monitoring](#) in Uppsala, Sweden. The reports are not public; as a journalist you can have access to them if a patient or a doctor shares them with you. Regulators may

provide statistics from the reports, but even though personal identities are masked, the full reports are still considered highly confidential.

Underreporting of the adverse reactions to medical products is perhaps the most troubling weakness of this system. Only a tiny fraction of adverse events are reported, according to a [comprehensive study](#) from 2006.

Beware of relying on a single report of an adverse reaction. These are called “signals” that tell experts to do further research into causality. Many other factors may have contributed. A single report needs to be evaluated along with other evidence.

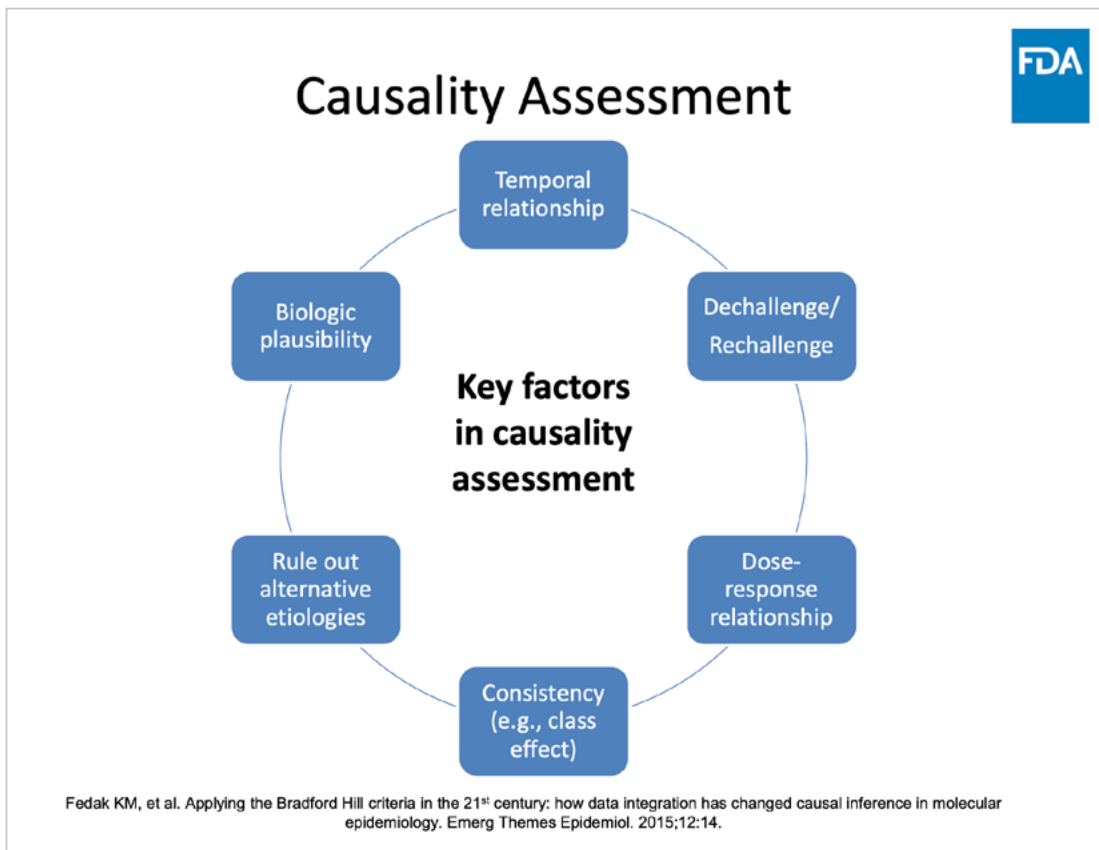


Illustration: US Food and Drug Administration

Typically, news stories affect the reporting of adverse event reporting (called AER). If there is media reporting of a drug's alleged dangers, in the weeks that follow regulatory agencies will record a significant increase in reports. Events reported by patients, although considered of lower quality than those filed by medical professionals, have real potential to improve the system, as pointed out in the article [Patient Reporting Is the Future of Pharmacovigilance](#) by Sten Olsson, then-president of the [International Society of Pharmacovigilance](#). Keep in mind that exposing evidence will not necessarily lead to a drug being pulled off the market. Regulatory procedures are often more complicated. Your reporting may push regulators to modify the drug label, a process where extensive negotiations with the marketing company will take place.

TIP 2: RETRIEVE DATA AND TALK TO THE VICTIMS

There is a [big difference between](#) the safety data collected during development and approval and the data that emerges post-marketing.

All reports on the side effects of a drug from a WHO member country from 1968 onwards are stored in [VigiBase](#) and remain available, even if the products are no longer on the market. You can request access to the data available by filing a request with national regulatory agencies.

The data come with many caveats and are truly hard to analyze, as a single case can be recorded under several different codes. However, health stories need real humans speaking about the harms or damages they have experienced. "Case reports" are always anonymized, so when you receive data from pharmacovigilance officers, you need strategies to find such alleged victims. One is through doctors: They may have a patient who is willing to talk to journalists. Or they may know another doctor whose patient experienced that side effect.

Social media sites offer many possibilities via crowdsourcing, as do websites and newsletters of your media outlet. Posting an open call that states clearly that you are investigating the potential harm, or patients' experience with a pharmaceutical product, will expose your ongoing project but will give you the greatest chance of getting in touch with potential protagonists.

So, let's imagine you came across a potential harmful product and even identified potential characters for your story, patients that allegedly were harmed by that product. What do you do next? The key is to independently assess the evidence and compare your findings with studies published in the literature.

Often victims' stories have not been reported at all. Telling their stories may provoke responses from patients or families contacting your newsroom.

Collect all the cases, complete with medical details, and don't forget to ask

Health stories need real humans speaking about the harms or damages they have experienced.

them to sign a waiver of their physician-patient privileges.

Without this waiver, your investigation will be delayed,

as doctors and hospitals will refuse to respond to your requests until you have the waiver. Be aware that national laws protect the privacy of patient medical information, and some are quite strict.

When you have a complete picture of specific cases, present the evidence to the regulators. Experience has shown many times that it's useful to contact them before your investigation is concluded and well before publication. If your methods are solid, and you have discovered facts that are in the public interest, it's actually in the regulators' best interest to support your work as far they can. Of course, they won't give you the names of patients or information that puts them in a bad light. But they may point to aspects you might have

underestimated (say a study, or data, or a specific rule applying to the case), so they can help you avoid errors in your reporting. Sometimes, they may even hint at the pharmaceutical company or the doctors' organization that played a role in delaying or hindering regulators' work. At the same time, the industry often uses a strategy of information overload when responding to queries from investigative journalists. Expect lengthy statements and references to studies replete with scientific jargon.

Our [To Die for the Skin](#) investigation for the Swiss public broadcaster on acne drug Accutane's psychiatric side effects, led to a wave of patients and their families sending their testimonies. Out of over 300 reports we received, 61 cases were included by the Swiss regulatory agency Swissmedic in the national and global database on drug safety. The agency also issued an [update to prescribers](#) and patients on the drug's psychiatric risks.

Similarly, the medical devices investigation by [Jet Schouten, a journalist with Dutch public broadcaster AVROTROS](#) which inspired the [ICIJ Implant Files project](#) was sparked by the many testimonies the broadcaster received after publishing its first story.

Finding sources of all kinds for such an investigation can be complicated. Crowdsourcing and social media searches are key. Use advanced research tools like those listed in the [GIJN guide](#).



Court proceedings can be a trove of information, as well as a place to look for sources, particularly if you are investigating harmful effects and damage.

Getting too close to your sources is never a good idea; it certainly should be avoided when reporting about drug safety. When you are presented with injustice, patients who weren't properly informed, regulators who knew but didn't act, potential or real conflicts of interest, and highly knowledgeable experts with huge reputations, it is tempting to rely too much on one or two sources. Your duty is to assess the evidence and expose wrongdoings, not make new friends.

It's also important to use careful, accurate language, and not to hype your drug safety story. Inflammatory language simplifying the risk-benefit ratio and distorting the scientific evidence will leave space for the authorities to ignore the matter. Poor quality reporting could even inhibit intervention by regulatory authorities. Patients may stop taking a drug without talking to their doctor; this could be dangerous to a their health. Hyped stories may lead to actions which are not evidence-based, such as pulling a drug from the market instead of modifying prescription guidelines to make sure it is taken correctly.

TIP 3: EXPOSE FRAUD, SCIENTIFIC MISCONDUCT, AND MEDICAL MALPRACTICE

From nursing homes to research labs, from public hospitals to medical practices, health care is affected by fraud and misconduct. Many of the cases would not have come to light without the wrongdoing being exposed by victims, prosecutors, human rights advocates, and journalists. Some of this work is inspirational and instructive.

In some cases, it was necessary to go undercover. In 1887, American journalist Nellie Bly pretended to be mentally ill to investigate reports of brutality and neglect at a New York psychiatric institution. Fast forward over 100 years, and Naziha Syed Ali also went undercover in Pakistan to dig deeper into organ trafficking for [Doctors, Police and Middlemen](#). So, too, did a BBC Africa Eye team led by Solomon Serwanjja for [Stealing from the Sick](#), an investigation exposing the black market of pharmaceuticals in Uganda.

In 1887, American journalist Nellie Bly pretended to be mentally ill to investigate reports of brutality and neglect at a New York psychiatric institution.

Victims' testimonies are key, as in Deborah Cohen's BBC story on [stem cell experiments](#), or in the Thomson Reuters Foundation investigation led by Roli Srivastava [Missing Wombs: The Health Scandal Enslaving Families in Rural India](#).

Medical malpractice can be analyzed by combining data with victims' testimonies, as Peruvian outlet [Ojo Público](#) is pursuing with the project [Cuidados Intensivos](#). Or see journalist and former molecular cell biologist [Leonid Schneider](#)'s investigation into an alleged case of scientific misconduct involving trachea transplants. The story is also featured in [Benita Alexander](#)'s documentary "He Lied About Everything" (Discovery) and Bosse Lindquist's three-part documentary "[The Experiments](#)" (SVT). Another good read is [Tide of Lies](#) by Kai Kupferschmidt about the long journey of researcher [Alison Avenell](#) in exposing a major case of scientific fraud that highlights the many problems affecting biomedical journals.

One disturbing example can be found in Sushma Subramanian's in-depth piece for Slate, [Worse Than Tuskegee](#), on how in the 1940s American researchers infected Guatemalans with syphilis and gonorrhea, then left without treating

them. The case emerged in 2003 thanks to Susan Reverby, a historian at Wellesley College. The Wall Street Journal's John Carreyrou, who won a 2015 Pulitzer Prize for his [Medicare Unmasked](#) series, began a groundbreaking investigation that same year on blood testing firm [Theranos](#) that resulted in a new series, indictments, and his book "[Bad Blood: Secrets and Lies in a Silicon Valley Startup](#)."

There is much to investigate in the area of so-called "corporate crime." Two references guaranteeing you sleepless nights: Peter C. Gøtzsche's book "Deadly Medicines and Organised Crime" (extract on BMJ: [Big Pharma Often Commits Corporate Crime, and this Must be Stopped](#)) and Public Citizen's [Twenty-Seven Years of Pharmaceutical Industry Criminal and Civil Penalties: 1991 through 2017](#).

CHAPTER 5

Tips on Traps, Hype, and Ethics



Although in parts of the world investigating pharmaceuticals can be physically dangerous, in others you risk your reputation rather than your life. Drug companies often hire effective and persistent public relations managers, some of them former journalists. Much less often, lawyers will be involved. They might send aggressive letters threatening legal action, for example.

Putting your editor and publisher under pressure is common practice, as this leads to delay while editors carry out further checks, often prompting you to provide additional evidence. In our experience, this exercise can be extremely time and energy consuming. What helps is being disciplined in archiving

correspondence and making sure all correspondence with the companies is in written form. Critical scientists, however, can pay a high price, as this example shows: [GlaxoSmithKline Tried to Silence the Scientist Who Exposed the Dangers of its Drug Avandia](#).

When reporting about alleged victims of a drug, you need to pay special attention to the language you use and make sure you seek comment from the company before publication – which is standard practice, of course. Media coverage and new or additional warnings on a drug’s label are known to affect

It may seem insensitive, but make sure to question the victims’ agendas, too. Get to the bottom of their medical histories and ask searching questions.

sales, so companies will go to great lengths and expense to try and minimize the potential damage.

Also, [Key Opinion Leaders](#) can be especially persistent. Their reputation is at stake. Many of them don’t see a problem in their close relationship to the industry; they can get aggressive and even sue media outlets and reporters if their name is associated with victims or malpractice.

Don’t expect a person representing the pharmaceutical industry to be forthcoming in a recorded or filmed interview. These are professionals who are well-trained in dealing with the media. Drug companies may avoid interview requests or put up their public relations officers.

Finding a whistleblower in the relevant medical or scientific community or within the industry rarely happens but can be extremely helpful. One example is the exemplary investigation into generic drugs by Katherine Eban that took many years to complete. Her book, “[The Bottle of Lies](#),” shows how Eban also collected a huge amount of data and documents during her investigation.

Sometimes honest public servants will help you if your methods are solid. Read the [GIJN guide on this topic](#) and make sure you protect the identity of your confidential sources.

Beside regulators, in every country there are public health authorities involved in health care. Don't forget to investigate their

conflicts of interest. They also produce extensive documentation about health interventions and assess risks, benefits, and economics. Their work is a trove of hints and facts. However, it is important to keep in mind that they are routinely under pressure by commercial entities with an interest in their decisions.

Although in parts of the world investigating pharmaceuticals can be physically dangerous, in others you risk your reputation rather than your life.

Build your own network of people whose knowledge you trust. Look for them among specialists that are strong in Evidence-Based Medicine and free of conflicts of interest with the industry and the regulators. Often emeritus professors, especially if they have strong skills in biostatistics, or in the specific field of medicine or science you need for your investigation, are very informative; they have reached the prime of their career, are not worried about how to fund their research, nor are they generally concerned with raising their profile. Make sure to do in-depth research on the background of any expert you turn to for advice, as you need to be sure you can trust her or him. Read two GIJN features on [collaborating with doctors](#), and on [turning them into muckrakers](#).

Medical and scientific conferences can be useful for your work. They are crammed with advertising and pharma representatives. Also, participants don't expect independent-minded journalists to join such events, so they can be pretty open to informal chats. Because medical societies' conferences are

routinely sponsored by the industry, the program itself provides valuable hints on where the manufacturers are going with a class of drugs. When a rather rare condition is suddenly presented as a major public health concern, that could be a red flag. Such a strategy could signal the imminent launch of a new product or a shift in industry strategy. When joining medical conferences, look for “satellite symposia” presented by drug companies. These may be promotional events presented as scientific sessions.

Make sure you don’t accept gifts or other benefits as you will have a conflict of interest which could jeopardize your credibility. Being too close to doctors and scientists is also a bad idea. It may seem insensitive, but make sure to question the victims’ agendas, too. Get to the bottom of their medical histories. As we have seen in the [first chapter](#), a few thousand people or so will have tested a medical product in a controlled environment before it goes to market and ask searching questions ([see page 60](#)).

Some of the bigger risks in investigating this area include getting the evidence wrong, relying on an expert who is conflicted or incompetent, and becoming a victim of the exaggerated claims made in medicine. “Red flags here are keywords like “personalized medicine,” “breakthrough,” “big data,” “life-saving drugs,” “hope,” “revolutionary treatment.”

ALSO WORTH A READ

- [Tweeting Oncologist Draws Ire and Admiration for Calling Out Hype](#), NPR (2018).
- [Death by 1,000 Clicks](#), by Fred Schulte and Erika Fry, Fortune, via Kaiser Health News (2019).

APPENDIX A

Glossary of Terms



Adverse Event Reporting (AER)

Reports filed by patients and medical professionals to national and international regulatory bodies regarding adverse reactions to medical drugs and devices. See, for example, [the US FDA's system here](#).

Bio-Markers

Biological markers refer to a broad subcategory of medical signs — that is, objective indications of the medical state of a patient, observed from outside the patient — and which can be accurately measured and the findings reproduced. For example, a blood test result. Medical signs stand in contrast to medical symptoms, which are limited to those indications of health or illness perceived by patients themselves.

Blinding

When study participants do not know if they are receiving an intervention. If a study is double-blinded, medical providers administering the treatment do not know either. Many studies have shown that if you know what treatment you are receiving, you'll eventually experience greater placebo effects than a subject who doesn't know what treatment s/he is having.

Confounding Factors and Bias

A confounding factor is an element that might influence the results of a study or analysis. For instance, comparing the epidemiological situation of two countries, without adjusting for population age; there are countries with a much older population than others, and this can greatly influence an analysis. In this example, population age is the confounding factor. When analyzing a dataset or a study result, researchers try to make adjustments to exclude any confounding factor, thus achieving a more reliable answer to the research question. Bias is defined as any “non-random error” that interferes with an accurate assessment of a study outcome. More: [Identifying and Avoiding Bias in Research](#).

Correlation and Causation

Correlation: when two phenomena are linked by a relationship. For instance, it's raining and at the same time, the lights go off in your apartment. These two events happen at the same time, so there is a sort of relationship, but you can't say if the lights went off because of the rain. Causation, conversely, indicates that two phenomena are linked by a cause and effect relationship. In the example, you call up a specialist to fix your electricity problem and he explains to you that clearly a leak in your building meant the rain shut the lights off. In scientific methodology, the difference between correlation and causation is key. Many phenomena can seem linked by a cause and effect relationship, but unless proven we must assume that they are instead connected because of

correlation. Attributing a causation value to a phenomenon is a very common and problematic bias.

Critical Appraisal

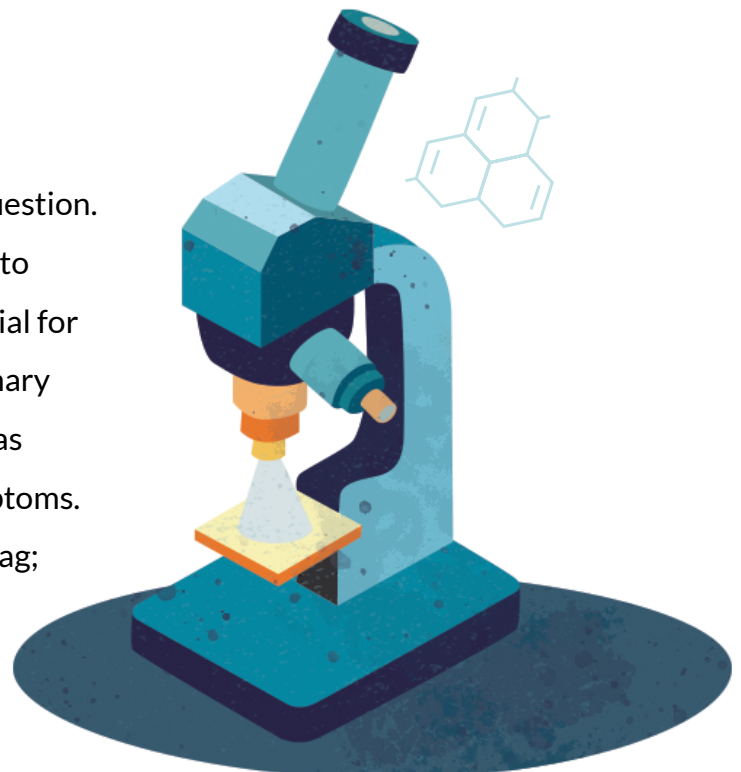
One definition in relatively plain language: “Critical appraisal is the process of carefully and systematically assessing the outcome of scientific research (evidence) to judge its trustworthiness, value, and relevance in a particular context.” Source: [What is Critical Appraisal?— Center for Evidence Based Management.](#)

Disease Mongering

One definition of disease mongering is the “[selling of sickness](#)” in order to promote drug sales. It is a strategy used by pharmaceutical companies to enlarge the potential market for their products, either by inventing new illnesses, or by framing a normal phenomenon as such. Common symptoms, though not pathological, can become the indication for a new drug, or a new indication for an already marketed product.

Endpoints: Primary, Secondary, Surrogate, Combined

A clinical trial aims to answer a research question. The “endpoints” are indicators established to measure the trial’s result. For instance, a trial for a new oncological drug could set as its primary endpoint prolonging the patient’s life, and as secondary endpoint the time without symptoms. Surrogate endpoints are inherently a red flag; in this example that could be the size of the tumor. Combined endpoints use



two or more outcomes as a single measure; beware of this as it might bias the study results.

European Medicines Agency (EMA)

The EMA is an agency of the European Union in charge of the evaluation and supervision of medicinal products. Along with the US Food and Drug Administration, the agency's decisions on drugs have great influence on the worldwide pharmaceutical market.

Evidence-Based Health Care

The term indicates an approach used by health care providers to decide on appropriate intervention to treat a condition, basing the decision-making process on the "best evidence available." More: [Evidence Based Health Care](#).

Experimental (also called Interventional) Study

A study where all the conditions are pre-determined and controlled by the person carrying out the experiment. More: [Experimental Study definition](#).

Exposure in Absolute Values (Absolute Risk)

Conversely to relative risk, the absolute risk gives an indication of the likelihood over time of an event happening. See this website for accurate but plain language definitions, and many examples: [Relative Risk and Absolute Risk: Definition and Examples](#).

Field Safety Notice

The notice a manufacturer releases to acknowledge that a serious safety concern regarding the use of its product has emerged.

Food and Drug Administration (FDA)

The FDA is a US regulatory agency responsible for supervision of pharmaceutical drugs, vaccines, and medical devices. Along with the European Medicines Agency, the FDA's decisions on drugs have great influence on the worldwide pharmaceutical market.

Indication

An indication describes the approved use of a pharmaceutical product (such as a drug, test, or vaccine). It means that regulatory authorities have reviewed the evidence submitted by the manufacturer for the treatment or test of a condition or a disease, and allowed the company to market the product for this specific use. Widening the indication is a common practice to expand a product's market, and it often happens step by step, with the industry submitting new data to the regulators.

Intervention

The WHO defines [a health intervention](#) as: "An act performed for, with or on behalf of a person or population whose purpose is to assess, improve, maintain, promote, or modify health, functioning, or health conditions."

Medical Devices

The full definition of a "medical device" by the WHO: "Any instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purpose(s) of diagnosis, prevention, monitoring, treatment, or alleviation of disease; diagnosis, monitoring, treatment, alleviation of or compensation for an injury; investigation, replacement, modification, or support of the anatomy or of a physiological process;

supporting or sustaining life; control of conception; disinfection of medical devices; providing information by means of in vitro examination of specimens derived from the human body; and does not achieve its primary intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its intended function by such means.”

More: [Medical Device – Full Definition](#).

Meta-Analysis

A meta-analysis is a statistical analysis that combines the results of several, comparable studies.

Multicentric Double-Blind Randomized Controlled Trials

Multicentric indicates that a trial is performed in several, different locations (hospitals, for instance). For double-blind and randomized controlled trial (RCT) see nonrandomized, nonblinded, below.

Nonrandomized, Nonblinded

Randomization is a key concept in scientific studies that aim at comparing two groups of subjects that are receiving different interventions (such as a tested drug and another drug for comparison). By randomly assigning patients to one of the two groups, bias and confounding factors are minimized so that the two groups are as much alike as possible at the onset of the study. Nonetheless, by chance alone, baseline imbalances, such as one group being older than the comparator group, do occur and can skew the outcome.

Observational Study

Observing phenomena as they take – or took – place and trying to draw conclusions on their underlying causes. Although observational studies can provide valuable hints, they can't provide solid and final evidence, as they are

especially prone to bias and confounding factors. The best course of action is normally to use observational studies to formulate hypotheses, to be confirmed with randomized controlled trials that allow firmer conclusions on the intervention's effect.

Outcome Switching

Outcome switching is a questionable practice in which researchers modify the aim of the study after it has started. Researchers are supposed to identify the expected outcome of the medical intervention being tested in a study protocol before the trial is launched. If that outcome is dropped part way through a study and another outcome is substituted, it could be because the researchers looked at the data and did not get the positive outcome they had hoped for.

Percentage Exposure (Relative Risk)

The US National Institutes of Health defines relative risk as “a ratio of the probability of an event occurring in the exposed group versus the probability of the event occurring in the non-exposed group. For example, the relative risk of developing lung cancer (event) in smokers (exposed group) versus non-smokers (non-exposed group) would be the probability of developing lung cancer for smokers divided by the probability of developing lung cancer for nonsmokers. The relative risk does not provide any information about the absolute risk of the event occurring, but rather the higher or lower likelihood of the event in the exposure versus the non-exposure group.” Source: [Relative Risk](#).

Pharmacovigilance

According to the [WHO](#), “the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problem.”

PICO Criteria

PICO is a tool to break down a research question. The acronym stands for Patient/Population; Intervention; Comparison; Outcomes. Using it allows for a well-structured search in the biomedical literature and it can also be extremely helpful to journalists who need to dig deeper on any medicine-related interventions. More: [PICO – Evidence Based Medicine](#).

Post-Marketing Surveillance

The monitoring of a drug or vaccine safety after it has been put on the market.

Pre-Identified Outcome Measures

See outcome switching.

Premarket Approval Application

In order for a drug or a vaccine to be approved for the market, the manufacturer must submit a Premarket Approval Application, whose aim is to give the regulators all relevant information about the product's expected effectiveness and safety, as measured in clinical trials.

Randomized Controlled Trials (RCTs)

A randomized controlled trial can be one of the most rigorous ways of determining whether a cause-effect relationship exists between treatment and outcome, and for assessing the cost effectiveness of a treatment. Comparable groups of subjects are randomly assigned to receive a new medical intervention, or an intervention that is already standard, a placebo, or no intervention at all. If they are single-blinded, the receiver doesn't know which group they are in, and if they are double-blinded, those administering the intervention do not know either. Such design allows for comparisons between interventions, and it is considered the gold standard among medical studies.

More here: [Understanding Controlled Trials: Why Are Randomised Controlled Trials Important?](#)

Retrospective Studies

These are performed looking back at previously collected data. Retrospective studies are observational studies prone to bias, because data was not collected to answer that specific research question.

Surrogate Endpoint or Surrogate Outcome

Surrogate endpoints are indicators (often bio-markers) chosen by researchers because they are considered important contributors in the mechanism of a disease. For example, blood pressure may be used as a surrogate endpoint in a trial on cardiovascular drugs, because it is a known risk factor for heart attacks and strokes. The hypothesis is that if the drug shows an effect on the surrogate endpoint, high blood pressure, it will also have an effect on the clinical outcome (heart attacks and strokes). Unfortunately, in many cases a drug's effect on a surrogate outcome won't bring the expected benefit to patients, and may even harm them, because other aspects of the mechanism of the disease have not been well understood yet. That's why any results obtained in a study that was designed with a surrogate endpoint must be taken with much caution.

World Health Organization (WHO)

The WHO operates under the United Nations to coordinate international responses to public health. Based in Geneva, Switzerland, the agency has six regional offices and 150 field offices worldwide.

APPENDIX B

Regulatory Agencies

North America

- USA: [Food and Drug Administration \(FDA\)](#)
- Canada: [Health Canada](#)

Latin America

- Argentina: [National Administration of Drugs, Food, and Medical Devices \(ANMAT\)](#)
- Belize: [Ministry of Health](#)
- Bolivia: [Ministry of Health and Social Welfare](#)
- Brazil: [Brazilian Health Surveillance Agency \(ANVISA\)](#)
- Chile: [Public Health Institute of Chile \(ISPCH\)](#) (ISPCH)
- Colombia: [Ministry of Health and Social Protection](#) / [INVIMA](#) Instituto Nacional de Vigilancia de Medicamentos y Alimentos
- Costa Rica: [Ministry of Health](#)
- Cuba: [CECMED](#)
- Ecuador: [National Agency for Regulation, Control, and Sanitary Surveillance \(ARCSA\)](#)
- El Salvador: [Ministry of Health](#)
- Guatemala: [Ministry of Health](#)
- Guyana: [Ministry of Health](#)
- Jamaica: [Ministry of Health](#)
- Mexico: [Federal Commission for the Protection Against Sanitary Risk \(COFEPRIS\)](#)
- Nicaragua: [Ministry of Health](#)
- Panama: [Ministry of Health](#)

- Paraguay: [Ministry of Public Health](#)
- Peru: [General Directorate of Medicines, Supplies, and Drugs](#) (DIGEMID)
- Trinidad and Tobago: [Ministry of Health](#) / [Bureau of Standards](#)
- Uruguay: [Ministry of Public Health](#)
- Venezuela: [National Institute of Hygiene “Rafael Rangel”](#) / [Autonomous Health Service Comptroller](#) (SACS)

EU and EU Member States

There are [several options for applying](#) for a marketing authorization within the EU.

- European Union: [European Medicines Agency](#) (EMA)
- Austria: [Bundesamt für Sicherheit im Gesundheitswesen](#) (BASG / AGES)
- Belgium: [Federal Agency for Medicines and Health Products](#)
- Bulgaria: [Bulgarian Drug Agency](#) (BDA)
- Croatia: [Agency for Medicinal Products and Medical Devices of Croatia](#)
- Cyprus: [Ministry of Health](#)
- Czech Republic: [State Institute for Drug Control](#) (SUKL)
- Denmark: [The Danish Medicines Agency](#)
- Estonia: [Agency of Medicines](#)
- Finland: [Finnish Medicines Agency](#) (FIMEA)
- France: [Agence nationale de sécurité du médicament et des produits de santé](#) (ANSM)
- Germany: [Bundesinstitut für Arzneimittel und Medizinprodukte](#) (BfArM)
- Greece: [National Organization for Medicines](#)
- Hungary: [National Institute for Pharmacy and Nutrition](#) (OGYEI)
- Ireland: [Health Products Regulatory Authority](#) (HPRA)
- Italy: [Agenzia Italiana del Farmaco](#) (AIFA)
- Latvia: [State Agency of Medicines](#)
- Lithuania: [State Medicines Control Agency](#) (SMCA)

- Malta: [Medicines Authority](#)
- Netherlands: [Medicines Evaluation Board](#) (MEB)
- Poland: [Office for Registration of Medicinal Products, Medical Devices, and Biocidal Products](#) (UPRL)
- Portugal: [National Authority of Medicines and Health Products](#) (INFARMED)
- Romania: [The National Agency for Medicines and Medical Devices](#) (NAMMD)
- Slovakia: [State Institute for Drug Control](#)
- Slovenia: [Agency for Medicinal Products and Medical](#)
- Spain: [Ministry of Health, Social Services, and Equality](#)
- Sweden: [Medical Products Agency](#) (MPA)

Non-EU Member States

- Albania: [National Agency on Drugs and Medical Devices](#)
- Andorra: [Ministry of Health and Welfare](#)
- Armenia: [Scientific Center of Drug and Medical Technologies Expertise](#) (SCDMTE)
- Azerbaijan: [Center of Drug Analytical Expertise of the Ministry of Health of Azerbaijan](#)
- Belarus: [Center for Examinations and Tests in Health](#)
- Bosnia and Herzegovina: [Agency for Medicinal Products and Medical Devices of Bosnia and Herzegovina](#)
- Georgia: [Ministry of Labor, Health, and Social Protection](#)
- Iceland: [Icelandic Medicines Agency](#)
- Kosovo: [Kosovo Medicines Agency](#)
- Macedonia: [Agency for Medicinal Products and Medical Devices](#)
- Montenegro: [Agency for Medicines and Medical Devices](#)
- Norway: [Norwegian Medicines Agency](#)
- Russia: [Federal Service on Surveillance in Healthcare and Social Development](#)

- San Marino: [Ministry of Health and Social Security](#)
- Serbia: [Medicines and Medical Devices Agency of Serbia](#)
- Switzerland: [Swissmedic](#)
- UK: [Medicines and Healthcare Products Regulatory Agency \(MHRA\)](#)
- Ukraine: [State Inspectorate for Quality Control of Medicines](#)

Asia and The Pacific

- Australia: [Therapeutic Goods Administration \(TGA\)](#)
- Bangladesh: [Directorate General of Drug Administration \(DGDA\)](#)
- Bhutan: [Drug Regulatory Authority](#)
- China: [China Food and Drug Administration \(SFDA\)](#)
- Hong Kong: [Department of Health / Central Drugs Standard Control Organization](#)
- India: [Central Drugs Standard Control Organization](#)
- Indonesia: [Ministry of Health Medical Device Regulatory & CRO](#)
- Japan: [Pharmaceuticals and Medical Devices Agency \(PMDA\)/Ministry of Health, Labour and Welfare \(MHLW\)](#)
- Kyrgyzstan: [Department of Medicines Supply and Medical Equipment of the Ministry of Health of the Republic of Kyrgyzstan](#)
- Laos: [Food and Drug Department](#)
- Maldives: [Ministry of Health](#)
- Malaysia: [National Pharmaceutical Regulatory Agency \(NPRA\)](#)
- Nepal: [Department of Drug Administration](#)
- New Zealand: [New Zealand Medicines and Medical Devices Safety Authority \(MEDSAFE\)](#)
- Pakistan: [Drug Regulatory Authority of Pakistan](#)
- Philippines: [Department of Health](#)
- Singapore: [Health Sciences Authority](#)
- South Korea: [South Korea Ministry of Food and Drug Safety](#)

- Sri Lanka: [Cosmetics, Devices, & Drugs Regulatory Authority](#)
- Taiwan: [Taiwan Food and Drug Administration](#)
- Thailand: [Thailand Food and Drug Administration](#)
- Vietnam: [Drug Administration of Vietnam](#) / [Medical Devices Department](#),
[Ministry of Health](#)

Middle East

- Bahrain: [National Health Regulatory Authority](#)
- Iran: [Ministry of Health](#)
- Iraq: [Ministry of Health](#)
- Israel: [Ministry of Health](#)
- Jordan: [Jordan Food and Drug Administration](#) (JFDA)
- Kuwait: [Kuwait Institute for Medical Specialization](#)
- Lebanon: [Ministry of Public Health](#)
- Morocco: [Ministry of Health](#)
- Oman: [Ministry of Health Sultanate of Oman](#)
- Qatar: [MOH Pharmacy and Drug Control Department](#)
- Saudi Arabia: [Saudi Food and Drug Authority](#) (SFDA)
- Syria: [Directorate of Drug Control](#)
- Turkey: [Turkish Medicines and Medical Devices Agency](#)
- United Arab Emirates: [Ministry of Health](#)
- Yemen: [Supreme Commission for Drugs and Medical Appliances](#)

Africa

- Algeria: [Ministry of Health, Population, and Hospitals](#)
- Angola: Direcção Nacional de Medicamentos e Equipamentos / [Ministry of Health](#)
- Benin: [Direction de la Pharmacie et des explorations diagnostics](#)
- Botswana: [Drug Regulatory Services / Ministry of Health](#)

- Burkina Faso: [Direction Générale de la Pharmacie, du Médicament et des Laboratoires](#) (DPMED)
- Burundi: [Direction de la pharmacie, du médicament et des laboratoires](#) / Ministry of Health
- Cabo Verde: [Entidade Reguladora Independente da Saúde](#) (ERIS)
- Cameroon: [Direction de la Pharmacie, du Médicament et des Laboratoire](#) / Ministry of Health
- Chad: [Direction de la pharmacie, du médicament et de la pharmacopée](#) / Ministry of Health
- Congo: Direction des pharmacies, du médicament et des laboratoires / [Ministry of Health](#)
- Côte d'Ivoire: [Direction de la pharmacie, du médicament et des laboratoires](#) (DPML) / Ministry of Health
- DR Congo: [Direction de la pharmacie et du médicament](#) (DPM) / Ministry of Health
- Djibouti: [Direction du médicament, de la pharmacie et des laboratoires](#) (DMPL) / [Ministry of Health](#)
- Egypt: [Egyptian Drug Authority](#) (EDA)
- Equatorial Guinea: Direction générale de pharmacie et médecine traditionnelle / [Ministry of Health](#)
- Eritrea: National Medicine and Food Administration / [Ministry of Health](#)
- Ethiopia: [Ethiopian Food and Drug Authority](#) (EFDA)
- Gabon: Direction du médicament et de la pharmacie / [Ministry of Health](#)
- Gambia: [Medicine Control Agency](#) (MCA) / Ministry of Health
- Ghana: [Food and Drugs Authority](#)
- Republic of Guinea: Direction nationale de la pharmacie et du laboratoire / [Ministry of Health](#)
- Guinea Bissau: [Ministry of Health](#)
- Kenya: [Pharmacy and Poisons Board](#) (PBD)

- Lesotho: [Ministry of Health](#)
- Liberia: Liberia Medicines and Health Products Regulatory Authority / Ministry of Health
- Libya: Pharmacy Management Department / Ministry of Health
- Madagascar: Direction de la pharmacie, des laboratoires et de la médecine traditionnelle / [Ministry of Health](#)
- Malawi: Pharmacy, Medicines, and Poisons Board / [Ministry of Health](#)
- Mali: Direction de la pharmacie et des médicaments / [Ministry of Health](#)
- Mauritania: [Direction des médicaments et de la pharmacie](#) / Ministry of Health
- Mauritius: Pharmacy Board / [Ministry of Health](#)
- Morocco: [Direction du médicament et de la pharmacie](#) / Ministry of Health
- Mozambique: [Direcção Nacional de Farmácia](#) / Ministry of Health
- Namibia: [Namibia Medicines Regulatory Council](#) / Ministry of Health
- Niger: Direction de la pharmacie, des laboratoires et de la pharmacopée traditionnelle / [Ministry of Health](#)
- Nigeria: [National Agency for Food and Drug Administration and Control](#) (NAFDAC)
- Rwanda: Department of Pharmaceutical Services / [Ministry of Health](#)
- São Tomé and Príncipe: Direction de la pharmacie et du médicament / [Ministry of Health](#)
- Senegal: [Direction de la pharmacie et du médicament](#) / Ministry of Health
- Seychelles: Medicines Regulation Unit / [Ministry of Health](#)
- Sierra Leone: Pharmacy Board of Sierra Leone / [Ministry of Health](#)
- Somalia: Pharmaceutical and Medical Department / [Ministry of Health](#)
- South Africa: [South African Health Products Regulatory Authority](#) (SAHPRA)
- South Sudan: Food and Drugs Control Authority, South Sudan / [Ministry of Health](#)
- Sudan: [National Medicine and Poisons Board](#)

- Swaziland: Pharmaceutical Services Department / [Ministry of Health](#)
- Togo: [Direction de la pharmacie, du médicament et des laboratoires](#) / Ministry of Health
- Tanzania: Tanzania Food and Drug Authority (TFDA) / [Ministry of Health](#)
- Tunisia: [Direction de la pharmacie et du médicament](#) (DPM)
- Uganda: [National Drug Authority](#)
- Zambia: [Zambia Medicines Regulatory Authority](#) (ZAMRA)
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APPENDIX C

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