Aseem Malhotra: Evidence-Based Medicine Has Been Hijacked

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A real pleasure to be here for the second time. Second time in two months amongst friends, and I always find these sorts of events very interesting, because I always learn something new. I learned a lot of new stuff today from the previous speakers.

So this talk is slightly, not specifically, related to *Game Changers*, but to try and help explain and for us to understand what really is at the root of this health misinformation, which is sort of so prevalent across health care that it is, you know, it's an epidemic now, and we need to do something to cure it. Stephen Hawking, the late great Stephen Hawking said, "The greatest enemy of knowledge is not ignorance, it's the illusion of knowledge." And this next slide — and I know I mentioned this in my previous talk, which I did a month ago, but I promise there's a lot of new material for you coming up — I think this elegant concept really helps explain what we're all trying to achieve and why, you know, what areas of the system are creating barriers for people actually to have improved outcomes. For us, for our families, for our patients, you know, we use our clinical expertise, best available evidence, and last but not least, patient values and expectations. And I'm very much, you know, in the same thinking as Georgia, you know. I believe in patient choice, but our patients getting the full information — are the public getting full information to make those choices, and how far are we away from truly informed consent?

David Sackett, who is — was one of the founders of the evidence-based medicine movement, also said that, "Half of what you learn in medical school will be shown to be outdated or dead wrong within five years of graduation. The trouble is nobody can tell you which half. So you have to learn to learn on your own." Now, just coming back to this slide here, the best available clinical evidence unfortunately has been corrupted by commercial influence. And I think the one person in the world who's done more work than anyone to expose this is John Ioannidis, professor of medicine and statistics at Stanford, and he wrote this really interesting paper called "How to Survive the Medical Misinformation Mess," and he states these four major factors behind the fact that in his view, his analysis, most published research is false. And by the way, we're talking about research within, you know, the pharmaceutical and medical device industries as well. Where you have much more

money, you have much more in terms of randomized control trials. And I'm going to illustrate a little bit about how those trials are even unreliable or potentially unreliable. But most of the published research is not reliable, offers no benefit to patients. This is another barrier, you know: Don't assume your doctor knows this. Most health-care professionals are not aware of this problem. They're not aware of it. They're not gonna do anything about it, and they also lack the necessary skills to evaluate the reliability and usefulness of medical science. And then, you know, last of all, most importantly, the patients, then, also lack relevant accurate medical evidence and skill guidance at the time of making those decisions.

In his paper, "Why Most Published Research Findings are False," one of the factors behind it is, "The greater the financial and other interests and prejudices in a scientific field" — that includes intellectual prejudices as well — "the less likely the research findings are to be true." So in this epidemic of misinformed doctors and misinformed patients, there are seven sins put together by Gerd Gigerenzer from the Max Planck Institute in Berlin and Muir Gray, and they cite that we've got this biased funding of research issue, so researchers funded for profit — profit, not to benefit patients — the biased reporting in medical journals, biased patient pamphlets, biased reporting in the media — you know, I think *Game Changers* is one great example of that — commercial conflicts of interest, defensive medicine, and also an inability of a medical curricula that actually do not teach. We are not trained to actually understand and then communicate statistics very well. It's not something I learned in medical school. It's something I only came across probably in the last five to 10 years of my career.

Let's just pick a couple of examples. As a cardiologist, there's been a huge movement in the last 10-15 years where people with heart disease are managed by having heart stents put in. So the financial influence for individual — individual doctors to earn more based upon number of investigations and procedures can also put profits before patients. You know, from minority greed smothers the conscience. One U.S. cardiologist was jailed for ordering up to 19 million dollars worth of unnecessary investigations and procedures. We have this fee-for-service model in the U.S. as well, which also contributes to overuse and I would argue is actually unethical because it takes away true informed consent if there's a financial incentive to prescribe drugs or a particular diet. In the U.K., we have something similar, but not to the same degree. And just to give you an example so it's, you know — Independent analysis suggested up to half of all stents that were inserted

— coronary stents for heart disease in the U.S. — were inappropriate, which is costing U.S. health care about $2.4 billion per year, which is pretty — quite — which is quite extraordinary. Despite the fact there is still a lot, you know, despite the fact the evidence showed — the evidence shows that stenting does not improve prognosis, does not prevent heart attacks, does not prolong life — despite that evidence, though, why would cardiologists still be putting in so many stents? In fact, 88% of patients actually thought they're having the stent put in for the very purpose of preventing the heart attack, prolonging life even though the evidence did not suggest that would — that would be the case. And this is most extraordinary: When anonymously asked, 43% of cardiologists said they would still go ahead and do the procedure even if they felt it would not benefit the patient, and this is not a procedure that doesn't come without risk.

So, I wrote two consecutive editorials, one in the *BMJ* and then one in *JAMA Internal Medicine*, about this a few years ago, just to highlight that actually at a very basic evidence-based medicine level, we should just communicate that information to patients. I think they would want to know that, and it would probably change the decision making and, of course, this procedure does also carry a harm of 1% — harm of it causing a heart attack, stroke, or death. So, think about the stents being put in with no benefit to prevent a heart attack, but one in 100 people will either suffer a heart attack, a stroke, or die as a result of the procedure. And of course it could — They also detract some other things, like lifestyle changes that people can institute to improve their quality of life. So, anyway, the *BMJ* published my piece, and then *JAMA Internal Medicine*. It was press released, and then BBC News picks it up. I'm just giving an example about even when that information gets out there, you have to — there are challenges also coming from those vested interests that, you know, make money or have a culture of doing those procedures. So, this was you know, it came — it was in BBC News Online. I got some support from very — some very — a very eminent doctor in the U.K. called Terence Stephenson, actually now chair of the General Medical Council, and he said it's a legitimate debate that, you know, what I'd written, that we should be transparent with patients. But the British Cardiovascular Intervention Society said, “There was no evidence in the U.K. that patients had been treated inappropriately.” So, think about that wording: :No evidence that patients have been treated inappropriately.” I said, “It should be mandatory on the consent form.” I said, “Every patient, the default option should be on the consent form. When they're having stents, they should be told lack of prognostic benefit.” I trained as an interventional cardiologist. I did not need to tell

patients that, but I did. All I needed to tell them on the consent form was we are treating your heart disease, and there was a 1% risk of heart attack, stroke, and death. There was no mention at all that — of telling them there was no prognostic benefit.

And interestingly, so, they said there was no evidence of inappropriate treatment. Coincidentally, *JAMA Internal Medicine* then published a study a few months later where they gave this scenario to see, would it change the decision-making process? And it did. In fact, instead of 70% of patients that opted for a stent, it got reduced to 45%. And they calculated in U.S. health care, if this conversation was to take place in every consultation between a cardiologist and patient, which to be honest is not a long difficult conversation — it takes me about 30 seconds to explain this to a patient — it would save U.S. health care $864 million per year. This is just one part of a whole health-care system that can be improved just by being transparent with information.

Now, doctors' misunderstanding of health statistics is also a risk factor. Many doctors actually do not understand health statistics, which you may find very surprising, and therefore cannot evaluate the evidence for and against a treatment. So a study of 150 consultant, you know, attending gynaecologists, a third of them did not understand the meaning of 25% risk reduction created by breast cancer screening, by mammography. When asked, they actually thought you had to — if you screened a thousand women for breast cancer, that 25% risk reduction meant you would save 250 women from, you know, from breast cancer in terms of they'll be, you know, detected and operated on. But the actual data shows, from a Cochrane analysis of half a million women, that you would have to say you'd save one life for every 2,000 people screened. In other words, what should be said in that consultation if a patient asked, "Should I get breast cancer screening?" — In general, what doctor — I would argue the doctor should be saying to their patient is, "If we screen you, there's a 1 in 2,000 chance that it will save your life."

What was missed, though, later on in a smaller study is the harms of screening. The harms of screening were also not discussed. And it's interesting that you actually have 10 times more patients suffering a harm from an inappropriate treatment or an unnecessary operation because of a missed diagnosis of breast cancer. So actually, that transparent communication, conversation should be: "One in 2,000 chance it may, you know, save you — it will save your life, but you're 10 times more

likely, or a 10 in 2,000 chance, one in 200, you will suffer an unnecessary harm." And that should be how we should be communicating with patients.

I'm just going to very quickly just, you know — The relative risk, absolute risk issue is also still a big deal when it comes to how we communicate information to patients. As you know, in nutritional epidemiology and all these studies, we talked about relative risk. It sounds very exaggerated in terms of, you know, association of meat and cancer, or heart disease, etc. But relative risk communication exaggerates the benefits. And just one example, which I'm going to give you here is, if you look at a randomized trial of people taking statins with Type 2 diabetes, the relative risk reduction is 48% over four years from taking a statin. What does it actually mean? But if you look at the trial data instead of 28 in 1,000 people having a stroke on the placebo drug, 15 in 1,000 who took a statin suffered a stroke. Therefore, you saved 13 people out of 1,000 which is 1.3%, or one in 77. So the transparent, honest way, easy-to-understand way of communicating that information is to just tell the patient, "If you take the statin religiously and we trust the data completely, then there's a one in 77 chance you will be prevented from having a stroke."

And then medical journals unfortunately missed, have mismatched framing. So, a third of medical journal articles published between 2004 and 2006 in the *JAMA*, *BMJ*, and the *Lancet* actually use relative risk when they were showing the benefits of a drug and use absolute risk in the harms, which is just absolutely ridiculous. And of course this then biases, you know, in favor of prescription versus not prescribing medications. And then, you know, don't just take my word for it. This is a World Health Organization bulletin from Gerg Gigerenzera in 2009. He said, "It's an ethical imperative that every patient and doctor understand the difference to protect patients from unnecessary anxiety manipulation" between relative and absolute risk, but this is not part of regular clinical practice.

Now, let's just take a step back a second. We're talking about, you know, nutritional epidemiology, lack of funding for, you know, lack of independent funding for good-quality randomized trials, although, as you know, Sarah has already said, I think in food — in food studies, even, that is going to be challenging to some degree. So, Peter Wilmshurst is a cardiologist, has done a lot of work over the years investigating medical fraud, looking at research, exposing research misconduct, and in a lecture he gave at the Centre of Evidence-Based Medicine in Oxford in 2014, he makes this very crucial point that we need to all acknowledge when it comes to how

we think about what's going on in the health-care system. So pharmaceutical companies actually have a fiduciary obligation as businesses to sell — to make a profit, and therefore, you know, and sell their product. They are not required, although most of us would hope or believe this to be the case — they are not required actually to give you the best treatment. But the real scandal is that regulators fail to prevent misconduct by industry and that doctors, institutions, and medical journals collude with industry for financial gain. These are these are, you know they are responsible for scientific integrity and for patients, duty to patients, but what they're doing is colluding with industry for financial gain. Now, more recently, Peter Wilmshurst then submitted more evidence to Parliament because they did an inquiry into research misconduct. They wanted a review of it. And he makes, you know — what is the root of this issue with — with commercial influence over medical science?

So, academic institutions bear responsibility for the pressure to publish for career advancement, and that can result in research misconduct. If you get a prominent publication, you're more likely to attract future funding, which institutions demand, and good publicity, which institutions desire. Other pressures for misconduct come from associations with industry with these institutions when investigators, all the institutions hold patient patents or shares, and they receive payments from industry. So, also, financial pressure to publish research that will be profitable for the company and to suppress negative findings. He says, “Some publications are simply organized criminal activities when prominent academics have paid large sums of money to publish false data by industry, or a sponsor may be one of the victims when payments for conducting research are made to investigators who simply fabricate data.”

Medical journals also — we shouldn't, we should not forget this — Medical journals also have financial pressures to publish positive findings on drugs and medical devices, because their manufacturers buy reprints of those publications, which they can then go and market and use the marketing material in hospitals and give to doctors, which is used, you know, we believe as medical professionals all this time, “This is gospel truth. This is good science.” And in fact, you know, in some cases they can, you know, pay hundreds of thousands of pounds or dollars to a medical journal just for one publication, which may well be false, and therefore the medical journal also takes money, you know, and that keeps the medical journal running, etc. So this is a bias in the research interface as well.

To protect their reputations academic institutions will often conceal research misconduct, destroy evidence, and silenced whistleblowers. Journals are reluctant to admit they published flawed research, so they commonly refuse to publish failures to replicate.

Now this is where the law is also not in our favor. The law is on the side of the corporates, because fear of libel action contributes to the failure to expose research misconduct. So whistleblowers are more, you know, reluctant to come out because they are afraid of legal action that may be taken against them, even if what they're saying is absolutely correct. And because of these lenient sanctions, institutions believe that misconduct is not very serious, and research fraudsters are not deterred. And what Peter Wilmhurst concludes — and I think I agree with him that the best way to address these problems of research misconduct would be by making these serious forms of misconduct criminal offenses with meaningful sanctions.

Now, just to give you another example of how things can go very, very wrong, and this, I don't think was financially — you know, there wasn't a financial root cause behind this. This was basically about prestige, power of publication. One researcher in Holland, a cardiologist, was found guilty of fabricating research on the use of beta-blocker drugs in non-cardiac surgery. And once this was exposed and all these so-called “articles,” which took time to be retracted, he actually — his research influenced European Society Cardiology guidelines. An independent analysis then calculated that because of his research misconduct, there was probably 800,000 excess deaths in Europe across eight years. This is just one level of research misconduct that's been exposed that is absolutely extraordinary. Now, this is not — this was not widely publicized. And why does everybody not know this? If everybody knew this, people would not be — They would want to know what is at the root of it, and then we try and correct the system failures that we've got.

In terms of research, when actually the pharmaceutical industry or the medical device industry is found guilty of conducting, you know, illegal marketing of drugs, hiding data on harms, nothing really happens. Peter Gøtzsche wrote this article in the *BMJ*. He's one of the cofounders of Cochrane Collaboration. And between 2009 and 2014, most of the top-10 pharmaceutical companies paid fines close to $13 billion for fraud, basically. Now, what was interesting is, despite that, nothing seems

to have changed. No one got fired. No one lost their job. GSK is one company that were found guilty of — they payed the largest amount, I think $3 billion in that time period for illegally marketing and hiding data on harms and for drugs. But again, there were no real meaningful sanctions imposed, and they made $25 billion in profit during the period covered by the settlement. So, what Peter Gøtzsche says is, you know, if crime pays, you commit more crime.

We have this innovation crisis in drugs as well. So 667 new drugs approved by the FDA between 2000-2008. Only 11% were actually truly innovative. Most were basically copies of old ones. Drug companies changed a few molecules around, say, then marketed these drugs. By the time someone's worked out the new drug is no better than the old one, they've made their money, they're off patent, they go — the cycle continues. Marcia Angell, former editor of the *New England Journal of Medicine*, considered the highest-impact medical journal in the world, she herself says, “It's no longer possible to trust most of the published research or rely on the authority of medical guidelines.” And she really reached this conclusion very reluctantly after almost two decades as editor of the *New England Journal of Medicine.* Richard Horton, another editor, said, “Possibly half of the published research is untrue.” He wrote this in an online editorial for the *Lancet* in 2015. And Richard Smith wrote in the *BMJ* — he's former editor of the *BMJ* — he actually, talking about research misconduct, he actually gave a lecture somewhere to several academics and he asked the audience, he said — you know, this is all anonymized — but, “How many of you in your career are aware of research misconduct going on in your department or have witnessed it, manipulation, fabrication of data, whatever?” He said a third to a half of the audience put their hand up. He then said, “How many of you reported it?” Everybody put their hand down.

So what can we do about all of this? Well, I think one of the simple steps — I was involved in some of my private advocacy work with the Medical World Colleges and, you know, spent about a year with them explaining all of these issues. And we started something called a Choosing Wisely campaign in the U.K., basically to try and wind back the harms of too much medicine and essentially say that this is a big health-care system problem. We've only got finite resources where we need to use them better. It's more ethical to do so. And we talk about the fact that really increasing information and better data is crucial through medical education, through the system. Patients should be encouraged to ask questions when it comes — when they go to see the doctor about whether they really need a test or

procedure. What are the risks, are the simplest safe options? And that's where I think things like prescribing people walking, you know, doing more exercise, joining CrossFit, eating real food, that's where this comes in, and a lot of people's health improves when they do that. And of course, medical schools also too need to ensure that students develop a good understanding in medical literature and be able to critically evaluate research in a way that people here are able to do very effectively. This needs to be widespread. Everybody should be empowered. Every doctor should be empowered to be able to analyze research as good as Zoë or Georgia, you know, Sarah, you know, Gary. We need — we need that kind of — this needs to be, you know, a mainstream part of medical education.

I'll just quit, go forward very quickly. I'm almost finished in literally 30 seconds. There's also an environmental impact of too many drugs as well. We're now seeing that, you know, this is affecting, you know, wildlife. It's affecting sea life, because of all the drugs that's going into the water supply from all of the overconsumption. Now, my personal view, having been in this for, you know, a few years, this again, is a gross injustice being committed on the public, on doctors. And the way to change the system is make that injustice visible. Now, I think the best way, the only one of the ways to do this is really to have a full public inquiry, you know, involving, you know, Congress, in the U.K., Parliament, for example. This is what needs to be — needs to happen. I wrote this in The Guardian and made the case for that. And for me, when I, you know, when everybody knows of these system failures, when everybody knows that stent doesn't prevent a heart attack, you know, then we can really have better quality care for patients. So when I walk into a coffee shop, if the barista serving me says to me, “Do you know that most published research is false?” I know we're winning, right? I know we're winning then. We can change the system.

“The preservation of the means of knowledge amongst the lowest ranks is of more importance to the public than all the” — This is about real transparency. It's actually about democracy. Yesterday I spoke in L.A., and I said, and I'm gonna say this again today, and I said it yesterday. I took a bit of a risk: “The way the system is at the moment, the way the pharmaceutical and the food industry function, the way they've controlled information, they are enemies of democracy in my view.” And this should make people angry, and once it does, when they realize what's going on, we can really change the system. Thank you.