## **Side Effects May Include Anything**

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A couple of days ago a patient said he'd become depressed after starting Xolair, a new asthma drug I know nothing about.

On the one hand, lots of things that mess with the immune system can cause depression. On the other, patients are notorious for blaming drugs for any random thing that happens around the same time they started taking them. So I did what any highly-trained competent medical professional would: I typed "does xolair cause depression?" into Google.

The results seemed promising. The first site was called "Can Xolair cause depression?". The second was "Is depression a side effect of Xolair?". Also on the front page were "Could Xolair cause major depression?" and "Xolair depression side effects". Clearly this is a well-researched topic that lots of people cared about, right?

Let's look closer at one of those sites, EHealthMe.com. It says: "Major depression is found among people who take Xolair, especially for people who are female, 40-49 old, also take medication Singulair, and have Asthma. We study 11,502 people who have side effects while taking Xolair from FDA and social media. Among them, 14 have Major depression. Find out below who they are,

when they have Major depression and more." Then it offers a link: "Join a support group for people who take Xolair and have Major depression".

First things first: if there were actually 11502 people taking Xolair, and only 14 of them had major depression, that would be a rate of 0.1%, compared to 6.9% in the general population. In other words, Xolair would be the most effective antidepressant on Earth. But of course nobody has ever done an n=11502 study on whether a random asthma medication causes depression, and EHealthMe is just scraping the FDA databases to see how many people reported depression as a side effect to the FDA. But only a tiny percent of people who get depression report it, and depression sometimes strikes at random times whether you're taking Xolair or not. So this tells us nothing.

And yet a patient who worries that Xolair might be causing their depression will Google "can xolair cause depression?", and she will end up on this site that says "major depression is found among people who take Xolair", which is one of the worst examples of weasel words I've ever heard. Then she will read that there are entire support groups for depressed Xolair sufferers. She will find all sorts of scary-looking information like that Xolair-related depression has been increasing since 2008. And this is above and beyond just the implications of somebody bothering to write an entire report about the Xolair-depression connection!

In case you haven't guessed the twist – no one's ever investigated whether Xolair causes depression. EHealthMe's business model is

to make an automated program that runs through every single drug and every possible side effect, scrapes the FDA database for examples, then autopublishes an ad-filled web page titled "COULD \$DRUG CAUSE \$SIDE\_EFFECT?". It populates the page by spewing random FDA data all over it, concludes "\$SIDE\_EFFECT is found among people who take \$DRUG", and offers a link to a support group for \$DRUG patients suffering from \$SIDE\_EFFECT. Needless to say, the support group is an automatically-generated forum with no posts in it.

And it's not just EHealthMe. This is a whole market, with competitors elbowing their way past one another to the top of the Google search results. Somebody who doubts EHealthMe and seeks an online second opinion will probably just end up at PatientsVille, whose page is called "Xolair Depression Side Effects", which contains the same FDA data, and which gets the Google description text "This opens a possibility that Xolair could cause Depression". Or Treato, whose page claims to contain 56 reader comments on Xolair and depression, but which has actually just searched the Web for every single paragraph that contains "Xolair" and "depression" together and then posted garbled excerpts in its comment section. For example, one of their comments – and this is not at all clear from Treato's garbled excerpt – is from a tennis forum, where a user with the handle Xolair talks about how his tennis serve is getting worse with age; another user replies "Xolair, I read this and get depressed, I just turned 49." But if you don't check whether it came from a tennis forum or not, 56 reports of a connection between a drug and a side effect sounds convincing!

This is *really scummy*. Maybe it's not the most devious of traps for you or me, but what about for your grandmother? What about for those people who send money to Nigerian princes? The law is usually pretty strict about who can and can't provide medical information – so much so that it <u>cracks down on 23andMe</u> just for reading off the genome in a way that uneducated people might misinterpret. Yet somehow sites like EHealthMe are allowed to continue, because they just *very strongly imply* fake medical information instead of saying it outright.

Remember, only about 50% of people who are prescribed medication take it. Sometimes it's personal choice or simple forgetfulness. But a lot of the time they stop because of side effects. I had a patient a few months ago who was really depressed. I started her on an antidepressant and she got much better. Then she stopped the medication cold turkey and got a lot worse again. I asked her why she'd stopped. She said her shoulder started hurting, she'd Googled whether antidepressants could cause shoulder pain, and read that they could. She couldn't remember what site she was reading, but I bet it was EHealthMe or Treato or some of the others just like them.

One day, somebody's going to Google "can penicillin cause cancer?", read a report with a link to a support group for penicillin-induced-cancer survivors, stop taking antibiotics, and die. And when that happens, I hope it's in America, so I can be sure their family will sue the company involved for more money than exists in the entire world.