Case Study #1 – Cardiovascular: Vioxx

CS6440 Intro Health Informatics, 2020 Spring

Xia, Hui

903459648

Georgia Institute of Technology

1. **What is Vioxx and why was it withdrawn?**

   Vioxx is the commercial name of nonsteroidal anti-inflammatory drug rofecoxib, which was approved by the Food and Drug Administration (FDA) in 1999 and widely promoted as a pain reliever (Findlay, 2015). However, since then, studies and analyses confirmed that Vioxx raised the risk of developing a confirmed adjudicated thrombotic cardiovascular event, including myocardial infarction, unstable angina, cardiac thrombus, etc., compared placebo (Mukherjee, Nissen, & Topol, 2001; Ray et al., 2002). Thus, Vioxx was withdrawn from the market in 2004 (Martinez, Mathews, Lublin, & Winslow, 2004).

2. **What types health care data would Vioxx researchers need to determine its effect on the risk of myocardial infarction? Why? How did you get to this conclusion? How could this data be used to determine its effect on the risk of myocardial infarction?**

   To determine Vioxx's effect on the risk of myocardial infarction (MI), we will need to perform randomized controlled trial (RCT) to compare the chance of developing MI using the patients that are treated with Vioxx, versus the patients that are treated with other anti-inflammatory drugs. Two major points in this trial: (1). The number of patient should be large enough to statistically expose the potential risk. (2). This clinical trial needs to be performed as double-blind and randomized to ensure no subjective effect to the result.

   I got such conclusion, as this conclusion is supported by actual randomized trials. Researchers performed several large-scale randomized trials: the smaller ones include ~1000 patients, while the larger ones included ~9000 patients. Patients are given either Rofecoxib (the chemical name of Vioxx) versus another kind of anti-inflammatory drug, or placebo (negative control) over 12 months. The percentage of patients developed MI events in both patient groups (i.e. treated with Rofecoxib or the control) is compared against each other to determine the effect of Rofecoxib on the risk of myocardial infarction (Mukherjee et al., 2001; Ray et al., 2002)

3. **How could Vioxx researchers go about getting these data for a patient like JM? What are the barriers to getting this type of data (privacy, lack of data standards, etc.)?**

   Back in early 2000s, the researchers performed clinical trials on Vioxx versus placebo by randomly assigning large number of patients that needs long-term anti-inflammatory drug treatment (e.g. have rheumatoid arthritis) and fit certain health conditions (e.g. at least 50 years of age, etc.) to receive either Vioxx, or another kind of anti-inflammatory drug every day. In the next 12 months, the number of patients who had potential clinical events that is associated with Vioxx were evaluated, and thus included in the statistical analysis (Bombardier et al., 2000).

   There are several barriers for researchers to perform similar drug-based clinical data and get similar data. First, such clinical study will need to be approved by an

institutional review board or ethics review committee at each participating clinical centers. For example, in the Vioxx clinical study mentioned above, the study was conducted at 301 clinical centers in 22 countries (Bombardier et al., 2000). Thus, performing revision on the clinical study in all participating centers requires heavy administrative work loads.

Secondly, performing such clinical trial need to prescribe a large number of treatments. As we have discussed above, a large Vioxx study included ~9000 patients to participate. This clinical study is feasible for Vioxx, an in-expensive drug, as a daily dose of 50 mg (Bombardier et al., 2000) tablet of Vioxx costs $3.07 in the year of 2000 ("Vioxx price increase," 2000). However, the financial expense for clinical studies on a more expensive drug will increase dramatically.

Furthermore, performing such clinical trial need to collect data from a large number of patients. Similarly, the Vioxx clinical study is capable to involve ~9000 patients, is because that Vioxx is used to perform a common medical treatment such as anti-inflammatory. For a drug that is used for a rarer treatment, performing similar clinical study will be much harder. In such scenario, it will be nearly impossible to find enough number of consent patients to obtain a statistically meaningful clinical study data.

4. **What types of technology or applications could be used to help inform providers about the emerging risks of medications they prescribe?**

The above-mentioned barriers can be potentially solved using big data. Researchers have been discussing the possibility of replacing specifically designed RCT with big data generated from measurements upon the patient's visits to clinics, and the treatments for them (Hernán & Robins, 2016; Raghupathi & Raghupathi, 2014; Wang, 2013).

The essentials of applying big data in clinical trials is pattern recognizing. To determine that if any of the medications prescribed to the patients could be associated with health risks, we need to recognize patterns from the patent's medication and health history. That is, data on all the medication and illness of the patient should be stored in a database. Based on the database, patterns on whether any given prescriptions are associated with health risks should be brought up for notice. However, this is not easy task, as the size of health care data tend to be large, and the number of patients is also large. Thus, big data with machine learning technology could be used to recognize patterns from such large database.

5. **Do some research on either two privacy or medication solutions that are currently available and share them, with a brief description and a link with more details.**

There are various kinds of anti-inflammatory drugs available beyond Vioxx. After Vioxx is taken out of market, conventional and much less expensive anti-inflammatory drugs such as aspirin and ibuprofen are still available in the market ("Alternatives to Vioxx if Heart Disease Present," 2005).

Aspirin is also known as acetylsalicylic acid, is a well-used medication to reduce pain, fever, or inflammation:

https://en.wikipedia.org/wiki/Aspirin

Aspirin is known for the risk of causing internal bleeding when a large dosage is used (Kelly et al., 1996; Sanak, Simon, & Szczeklik, 1997).

Ibuprofen is also known as isobutylphenylpropionic acid, is a well-used medication to reduce pain, fever, or inflammation:

https://en.wikipedia.org/wiki/Ibuprofen

Ibuprofen is known for the risk of causing asthma in children (Lesko, Louik, Vezina, & Mitchell, 2002).

References

Alternatives to Vioxx if Heart Disease Present. (2005). Retrieved from https://www.health.harvard.edu/heart-health/alternatives-to-vioxx-if-heart-disease-present--thefamily-healthguide

Bombardier, C., Laine, L., Reicin, A., Shapiro, D., Burgos-Vargas, R., Davis, B., . . . Hochberg, M. C. (2000). Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. *New England Journal of Medicine, 343*(21), 1520-1528.

Findlay, S. (2015). *The FDA's Sentinel Initiative*: Project HOPE.

Hernán, M. A., & Robins, J. M. (2016). Using big data to emulate a target trial when a randomized trial is not available. *American journal of epidemiology, 183*(8), 758-764.

Kelly, J. P., Kaufman, D. W., Jurgelon, J. M., Sheehan, J., Koff, R. S., & Shapiro, S. (1996). Risk of aspirin-associated major upper-gastrointestinal bleeding with enteric-coated or buffered product. *The Lancet, 348*(9039), 1413-1416.

Lesko, S. M., Louik, C., Vezina, R. M., & Mitchell, A. A. (2002). Asthma morbidity after the short-term use of ibuprofen in children. *Pediatrics, 109*(2), e20-e20.

Martinez, B., Mathews, A. W., Lublin, J. S., & Winslow, R. (2004). Merck pulls Vioxx from market after link to heart problems. *Wall Street Journal*, A1.

Mukherjee, D., Nissen, S. E., & Topol, E. J. (2001). Risk of cardiovascular events associated with selective COX-2 inhibitors. *JAMA, 286*(8), 954-959.

Raghupathi, W., & Raghupathi, V. (2014). Big data analytics in healthcare: promise and potential. *Health information science systems, 2*(1), 3.

Ray, W. A., Stein, C. M., Daugherty, J. R., Hall, K., Arbogast, P. G., & Griffin, M. R. (2002). COX-2 selective non-steroidal anti-inflammatory drugs and risk of serious coronary heart disease. *The Lancet, 360*(9339), 1071-1073.

Sanak, M., Simon, H.-U., & Szczeklik, A. (1997). Leukotriene C4 synthase promoter polymorphism and risk of aspirin-induced asthma. *Lancet, 350*(9091), 1599-1599.

Vioxx price increase. (2000). Retrieved from https://pink.pharmaintelligence.informa.com/PS036997/Vioxx-price-increase

Wang, S. D. (2013). Opportunities and challenges of clinical research in the big-data era: from RCT to BCT. *Journal of thoracic disease, 5*(6), 721.