HSC 335 -- Pharmaceutical Policy (Fall 2020)

Week 9 Questions

Deadline: October 22, 2020 at 2:45pm (submit via Slack DM)

Name:

Reasons and Traditional Strategies for Post-Approval Monitoring

A fundamental fact about testing of an investigational drug is that we'll never know the drug's full benefit-risk profile at the time that it is approved by a regulatory such as the FDA for widespread use. Information continues to emerge after the drug enters the market, so it is important for pharmaceutical manufacturers and regulators like the FDA to monitor a drug's use and outcomes from that use, which can help identify potential risks that the drug may pose to patients. In this module, we'll discuss the importance of post-market surveillance, and some of the tools that the FDA and other stakeholders use to identify potential emerging risks.

- What are limitations of clinical trials?
- What information would signal to regulators that post-market surveillance of a particular drug is necessary?
- What types of activities do regulators, manufacturers, and other researchers participate in after drugs have been approved?

Question 1

Which of the following are commonly used for post-market drug safety surveillance? (Select **all that apply**)

- ☐ Voluntary reporting of adverse events to FDA
- ☐ Patient outcomes in large insurance claims databases
- ☐ Observational studies of drug use and outcomes
- ☐ Randomized controlled trials

Question 2

Interviews and registries can be used to collect post-approval safety data on drugs.

- ☐ True
- ☐ False

Question 3

Questions and issues can arise about a drug's safety during the approval process that do not bar approval but may result in post-market requirements being applied by the FDA.

- [ ] True
- [ ] False

Reasons for Post-Approval Monitoring

(no video associated with this question)

Post-market surveillance is important because prospective clinical trials conducted before a drug is approved by the FDA have inherent limitations in their ability to detect all potential safety concerns.

Question 4

Is post-market surveillance more important for some drugs than for others? What are the characteristics of drugs or diseases that should signal for more intensive post-market surveillance? What particular types of post-market oversight do you think would be most appropriate in those circumstances?

Explain your answer here:

Please also cut and paste your answer to this question into the appropriate section of the #discussion channel on Slack and comment on at least one other student response.

- [ ] Click the checkbox to confirm you've posted and commented on Slack.

FAERS Surveillance

The FDA Adverse Event Reporting System (FAERS) is a long-standing program that collects voluntary reports of adverse events from manufacturers, physicians, and consumers. This information is used to monitor for new drug risks, including drug-drug interactions that may arise in patients who are taking multiple medications.

- What are the benefits and limitations of using a system like FAERS to perform drug safety surveillance?
- During what time frame do previously unknown risks of new drugs generally emerge?

Question 5

When drug manufacturers receive reports of adverse events related to the drugs they sell, they must pass them along to the FDA.

- ☐ True
- ☐ False

Question 6

Reports from the FDA Adverse Event Reporting System (FAERS) can provide sufficient basis for the FDA to recommend withdrawing a drug from the market.

- ☐ True
- ☐ False

Question 7

Which of the following is/are limitation(s) of FAERS? (Select **all that apply**)

- ☐ FAERS is a passive system that depends on individual physicians' and patients' willingness to submit adverse event reports.
- ☐ FAERS reports are individual anecdotes that may not describe a clear link between the drug and adverse event.
- ☐ FAERS reports are often missing key pieces of information.
- ☐ FAERS does not give physicians a means to communicate with the FDA.
- ☐ There are no reliable statistical approaches to aggregate FAERS reports that can generate hypotheses about potential drug safety risks.

Claims-Based Observational Analyses

While FAERS is a useful tool, it largely relies on voluntary reporting of these events by physicians and patients, so underreporting and selective reporting are common. To capture a fuller picture of potential risks and drug interactions, researchers can use data that are produced by the health care system during the course of routine clinical practice to monitor patients who initiate treatment with a particular drug. As you will see, these analyses can effectively uncover rare adverse events, but confounding can complicate the results.

- How do FAERS and observational studies using data from claims databases complement each other?
- What are the strengths and limitations of observational studies?

Question 8

FAERS may document adverse events not observed in pre-approval clinical trials.

- [ ] True
- [ ] False

Question 9

Which of the following are advantages of using post-approval drug prescribing databases to study prescription drug outcomes? (Select **all that apply**)

- [ ] They include more patient experiences than may be found in randomized trials.
- [ ] They provide evidence of a drug's use in a broader array of patient populations than may be included in a clinical trial.
- [ ] A drug can be compared against routine alternative treatments that may not have been tested in pre-approval clinical trials.
- [ ] Lack of randomization increases the likelihood of bias.

Question 10

Claims databases can suffer from biases because patients are not randomly assigned to receive a drug treatment in the course of usual clinical practice.

- [ ] True
- [ ] False

Question 11

Which of the following is/are limitation(s) of using outcomes databases to evaluate drug safety? (Select **all that apply**)

- [ ] It may be unclear if any differences observed are due to underlying differences in patients being compared.
- [ ] Databases do not offer enough power to find statistically significant results.
- [ ] They cannot uncover rare adverse events.
- [ ] Such databases may not register patients' use of over-the-counter medical products.

Responding to New Risks

Through reports to FAERS and observational analyses, the FDA can uncover previously unknown risks of prescription drugs. Once such a risk has been identified, the FDA must decide what to do about it. In this video, we will look at what options for regulatory responses existed prior to 2007 as well as after the FDA Amendments Act of 2007 granted new authorities in this field to the FDA. As you watch, ask yourself:

- What actions can the FDA take to protect patients after a risk has been identified?
- What are some major limitations with the FDA's ability to request post-approval study commitments?
- What motivates pharmaceutical manufacturers to comply with FDA requests to complete post-approval studies or restrict the use of their drugs?

Question 12

Risk minimization plans (once called RiskMAPs, now called REMS) can require patients to take certain tests or attest to undertaking certain safety precautions as a condition for receiving a prescribed medication.

- [ ] True
- [ ] False

Question 13

"Dear Doctor" letters can be issued by manufacturers at the recommendation of the FDA to alert physicians to emerging safety issues related to a drug.

- [ ] True
- [ ] False

Question 14

"Post-market commitments" begun prior to 2007 were completed 90% of the time within 2 years after a drug's approval.

- [ ] True
- [ ] False

The Role of Litigation

So far, we have looked at the role of FDA reporting systems and observational analyses in uncovering the risks of particular drugs, but there is another often-overlooked source of information: lawsuits. Patients who experience severe side effects after taking a drug can sue the manufacturer for providing insufficient warnings about the potential for such side effects, and these lawsuits can uncover previously unreported information about the drug. The release of this information can influence decisions by regulators and the manufacturer regarding labeling language or even whether the drug should remain on the market.

- What information can litigation uncover?
- What might manufacturers and the FDA do in response to litigation?

Question 15

Litigation can do which of the following? (Select **all that apply**)

- [ ] Uncover previously unavailable data on adverse effects
- [ ] Undo a labeling change that the FDA has specifically recommended and approved
- [ ] Alter corporate marketing strategies
- [ ] Lead the FDA to recommend changes to the safety warnings on drug labeling.

Question 16

What is the legal practice that contributes to new safety information being uncovered during the course of litigation?

- [ ] Jury trials
- [ ] Pleadings
- [ ] Discovery
- [ ] Sealing motions
- [ ] Preliminary injunctions

Question 17

Litigation revealing unpublished clinical trials contributed to new laws in the US requiring public registration of clinical trials.

- [ ] True
- [ ] False

Who is accountable?

The outcomes of product liability lawsuits can differ based on who is responsible for updating a drug's labeling materials. In recent years, court cases against generic manufacturers alleging failure to warn have had a different outcome than product liability cases against brand-name drugs. Why is this? As you'll see, the Supreme Court has found that brand-name and generic manufacturers have differing responsibilities pertaining to maintaining a drug's labeling.

- What was the finding in Wyeth v. Levine?
- When must revisions to drug labeling be made? Who is responsible for making these revisions?
- Why do the labeling-related responsibilities of brand-name and generic drug manufacturers differ?

Question 18

Wyeth v. Levine held that which party has primary responsibility for maintaining the accuracy of the drug labeling?

- [ ] The FDA
- [ ] The manufacturer
- [ ] The American Medical Association
- [ ] Clinical trial investigators

Question 19

According to FDA rules, when must brand-name manufacturers revise their labeling to include warnings of new, clinically significant safety issues?

- [ ] As soon as reasonable evidence of a causal association with the drug exists
- [ ] When there is a statistically significant association between a drug and the safety issue
- [ ] If the safety issue concerns an increased risk of cancer

Question 20

Litigation can be used to force brand-name drug manufacturers to alter their drug labeling.

- [ ] True
- [ ] False