This module is going to present the different study designs used in epidemiology. There is an order and process by which study designs are chosen so before I go into the details of each study design, I want to present an overview of these different designs. This overview will discuss both descriptive and analytic epidemiology designs because it is important to see how they fit together.

We need to start by thinking about why we are doing any particular epidemiological study. The goal is usually to answer a research question or test a hypothesis. These usually fall into three areas (1) to identify significant associations that can be used to identify the causes of disease, and ultimately prevent disease; (2) to evaluate an intervention program, or (3) to determine the effectiveness of medical treatments or procedures.

As I said previously, there are two overall types of epidemiological study designs: Descriptive and Analytic. Descriptive studies are generally observational while analytic studies can be both observational and interventional. An observational study is one in which we observe behavior but do not do anything to change the behavior. For example, we ask people if they smoke cigarettes. An interventional study is one in which the researcher changes behavior, for example, by giving people with hepatitis C a treatment to see if it improves their health, or setting up an exercise program to see if it prevents obesity. As you will see there is a logical reason for choosing certain study designs.
To give you an overall sense of study design, I am going to tell you a story of an epidemic of vaginal cancer among young women in the 1960s. When we hear the word epidemic, we think of ebola or HIV. But essentially epidemic simply means more cases of disease than expected. So if a disease is very rare in a certain population, and you find you have more cases than expected that would be described as an epidemic.

First let me give you some background on vaginal cancer. This is a relatively rare disease, accounting for less than 3% of all gynecological cancers. Previous research has identified risk factors for this disease, which include smoking, age older than 50, history of cervical cancer or genital warts, a past hysterectomy, and past pelvic radiation. As you can imagine, young women would be extremely unlikely to develop this disease. If you would like more information on vaginal cancer there is a link to the CDC webpage.

When physicians see patients with unusual illnesses, they want to communicate this finding to other physicians in case the problem is more widespread than they expected. They do this by publishing the results of a single case (case study) or several cases (case series). In this descriptive study design, physicians simply describe their patient or patients and say why this is unusual. Physicians caring for these young women published their findings as a case series in the journal Cancer. This is not unusual at the start of an epidemic. These case series serve to alert the community to a medical problem or potential epidemic. Place your mouse over the purple box to find a link to the first report of HIA among 5 gay men in New York.

This case series was published in the MMWR (Morbidity and Mortality Weekly Report), a journal put out by the Centers for Disease Control. This journal differs from many of the others as it is published weekly and the time to press is much shorter. It can take more than 6 months and often longer than that to have an article published in the
usual medical journals. The reason for the short turnaround is so that if unusual diseases occur, physicians and researchers can get the information out to the public and other medical personnel relatively quickly. Not long after this report was published a second paper describing a rare cancer, Karposi’s sarcoma among gay men in San Francisco was published. Early publication of these case series was crucial in identifying that start of the AIDS epidemic. You can easily search for the MMWR online and look at recent articles to see what the current issues are in the health of our nation and the world. I have added an article from the MMWR to the class readings that presents these early reports of HIV/AIDS, long before either of these were identified.

Once we know there is a problem, one of the first things that needs to be done was to identify the cause of the disease. No one knew why these young women had cancer, so to understand that, we needed to compare young women with vaginal cancer to young women without vaginal cancer and see if there are any differences between the two groups of women. This is called a case-control study. Case-control studies are those in which participants are selected based on whether or not they have a certain disease. They are good at identifying possible risk factors as you can ask about many different exposures, and you look back in time to see what happened in the past.

So this is exactly what the researchers did. They identified 8 women with vaginal cancer and asked the young women and their mothers about past exposures. These are the cases. They also interviewed 32 young women and their mothers and asked them about their past exposures. These are the controls. The reason they chose more women without cancer is they needed a larger number to attain statistical significance and they could not find any additional women with cancer at that time. In a case-control study you do not need the same number of cases as controls. So what they found was very striking. The mothers of seven of the right girls with vaginal cancer had been given a drug called diethylstilbestrol (DES for short) during pregnancy compared to none of the other mothers.
who were in their late teens and early twenties thought to ask about exposure during pregnancy. This was not a time where many researchers would think about the possibility of a long term impact from something that occurred during pregnancy.

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<th>PHC 6000 - Historical Development of Epidemiology Handout</th>
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<td>So what is DES? In the 1940s, DES was used off-label to prevent adverse pregnancy outcomes in women with a history of miscarriage. On July 1, 1947, the FDA approved the use of DES for this indication. DES was originally considered effective and safe for both the pregnant woman and the developing baby. It was aggressively marketed and routinely prescribed. Sales peaked in 1953. In the early 1950s, a double-blind clinical trial at the University of Chicago showed no benefit of taking DES during pregnancy; adverse pregnancy outcomes were not reduced in the women who were given DES. By the late 1960s, six of seven leading textbooks of obstetrics said DES was ineffective at preventing miscarriage. We will learn more about clinical trials in the next module but basically they can provide excellent information on the effectiveness of treatments. Despite an absence of evidence supporting the use of DES to prevent adverse pregnancy outcomes, DES continued to be given to pregnant women through the 1960s. Very often the practice of medicine does not actually follow current research findings. The publication of the studies of young women with vaginal cancer and DES likely resulted in the change in practice. I think we should be very impressed that the researchers thought to ask about pregnancy exposures. This was not a common concept in the 1970s. I also hope you appreciate my wonderful artwork. As you can see there is a reason I am an epidemiologist and not an artist. There are a number of reasons for this, physicians don’t read all the studies, and they believe what they are doing works, drugs are heavily marketed. It takes time for things to change. Click on the purple button to see an example of a DES ad from the 1950s. The information in this ad is basically inaccurate but ads are one of the ways in which physicians obtain information. Note that it says DES is recommended</td>
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for use in all pregnancies. That is a scary thought. Hit return to go back to the main slide.

For those of you who like a pictorial representation, this slide represents the case control study with the eight unhappy women on the left (those with vaginal cancer) and the 32 happy women on the right (those without vaginal cancer). Again, note the great artwork. These two groups were compared to ask about past exposures that differed between them.

I always ask this question but seldom get the answer I am looking for. Think for a few minutes about the fact that you know vaginal cancer in young women is caused by their mother’s use of DES during pregnancy. If your mother had used DES, what might you want the researchers to study?

Well researchers wanted to know what other bad effects might occur from the use of DES. If this is the answer you came up with, congratulate yourself. So in order to do this, researchers needed to set up a study in a different manner. They needed to compare women whose mothers used DES during pregnancy with women whose mothers did not use DES and determine if there are other illnesses associated with maternal DES use. This is done is what is known as a cohort study. In a cohort study, women are picked on the basis of exposure. Exposed women are compared to non-exposed women and followed over time to identify the incidence of disease in the two groups.

Remember that incidence refers to new cases of disease.
Again for you who like pictures, this is a picture of the two groups. The numbers of people in the actual studies varied, and we will learn more about how to identify the right number of people in a study later. In this case the sad women have been exposed to DES and the happy ones have not. Again, we look for differences between the two groups. Only this time we are looking at differences in the outcome rather than the exposure. And indeed a number of cohort studies were done. Click on the study findings slide to see some of the results of cohort studies.

Cohort studies were conducted among both women and men whose mothers used DES. This slide shows some of the findings. For women, there was evidence that exposure to DES in utero can cause abnormalities in the reproductive tract, increased infertility, spontaneous abortion, pre-term delivery, ectopic pregnancy (which is when the baby grows in the fallopian tube which can be life threatening to the mother), early menopause and breast cancer. In men there was some evidence of increased risk of testicular cancer, infertility, and urogenital abnormalities. They are also conducting studies looking at prostate cancer. There are also some studies looking at the children of men and women exposed to DES so there will likely be findings for years to come.

If one wanted to learn more about the prevalence of DES exposure among a certain group, you could conduct what is known as a cross-sectional study. In this study, you enroll people who represent the group you are interested in, for example, women who were born in the 1950s. You would not pick them based upon having the exposure or any disease related to the exposure, but just because they were born at that time. You would then ask them about DES exposure or perhaps since they may not know, obtain a copy of their mother’s medical records during pregnancy. You could also ask about the prevalence of infertility which is one of the known side effects of DES exposure or you may ask about others factors that might be associated with DES exposure, race and ethnicity for example. The key components of a cross-sectional study is that people are selected because they represent a certain group, and information on exposure and outcome is collected at the same time. We will go into more detail on this later.
There is a type of study known as the ecological study in which rates of exposure and disease are compared across populations, as opposed to using individual data. I could not find an ecological study comparing vaginal cancer with DES so I chose to show one looking at a different but related issue, cervical cancer. This map shows variation in the rates of cervical cancer mortality across different countries. The authors indicated that the rates of cervical cancer deaths are highest in countries without screening programs. Ecological studies are a type of descriptive study and we will learn more about these in the next lecture.

The last study I want to introduce in this talk is the randomized clinical trial which is an experimental study, in which the investigator actively intervenes with the subjects, as opposed to merely observing which is what happened in the other studies I described. If we wanted to evaluate a treatment for vaginal cancer, for example, we may take a group of women with vaginal cancer and randomly (which means by chance) put them into two groups: those who get the treatment and those who do not. We will then compare the outcome (e.g., survival) between the two groups. Again, this is something, we will discuss in much greater details in future classes.

We talked about quite a few studies in this lecture and I am sure it is a challenge to keep all of them straight. We are actually going to spend some time on more of these with much more detail in this module and the following one. Understanding study design is central to your understanding of epidemiology. I am hoping that introducing these designs within the context of a research problem might make the different types of designs easier to understand. Remember the first difference is between descriptive and analytical studies. Descriptive studies focus on describing a population and looking at the relationship between exposure and disease but mostly these designs do not really try to determine causality. Descriptive studies are all observational. We do not actively intervene with the participants. Analytic studies are more concerned with testing a specific hypothesis. They can be observational such as the case-control and cohort studies I described. Or they can be analytic, such as a randomized clinical trial. There are other study designs as well but collectively these are the ones you will most likely encounter.
This graph shows the progression of research studies in terms of the ability to identify causation of a disease. As you move up the triangle, studies are more effective at determining the cause of a disease. We start with basic opinions and guesses, an occasional anecdote about a situation. From this early idea, one might do a case study or case series. There is no comparison group so people are merely describing what has occurred in a person or group experiencing an unusual health event. The next study in terms of identifying causation is the cross-sectional study in which a sample of some population is identified and then asked about exposure and disease at the same time. This type of study can give some early clues about what is happening as well as help identify the prevalence of disease or exposure. The ecological study is a type of cross-sectional study but data are collected on groups rather than individuals. The next study is the case control study in which people with the disease are compared to those without the disease to determine differences in exposure. This study is often done when there is a new disease and we do not know what caused it. The next study is the cohort study which compares people with and without exposure to determine what illnesses might result from an exposure. Then there are the randomized clinical trials in which the investigator actively assigns people to receive and not receive a medication or treatment to determine the effect of this medicine. This is an experimental study in which the researcher has control over the intervention. The last study which we did not mention is essentially a statistical analysis of multiple studies to identify the result of many studies evaluating the same exposure and disease.

To review any of the study designs you are not familiar with, move your mouse over the name of the study and a description will appear.
Drag and Drop Activity