

# UNDERSTANDING DES RESEARCH

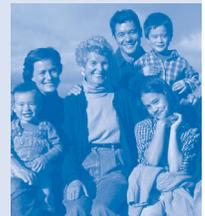
## Overview

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Researchers have been studying DES and its health effects for many years. However, sometimes the data and results are difficult for non-researchers to understand. It may also be difficult for people to figure out how research can be applied to their own health.

This section of CDC's DES Update will help you understand and use research about DES and includes the following information:

- **Understanding Scientific Research** – Tips for interpreting and understanding scientific research.
- **Deciding Whether a Source is Reliable** – Criteria for assessing whether a source is providing accurate and reliable information.
- **Role of Laboratory Animal Studies** – A basis for learning about human health risks from laboratory animal studies.
- **Role of DES Cohort Studies** – An explanation for understanding how studies of the DES cohorts (groups of DES-exposed persons who are included in follow-up research on DES-related health effects) fit into the DES research picture.



# UNDERSTANDING DES RESEARCH

## Understanding Scientific Research

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### Several journal article citations are provided in CDC's DES Update fact sheets. How do I read a citation?

Knowing how to read a citation for a journal article will help you find it either at the library or on a Web site. The following is an example citation for a journal article about DES:

Hatch EE, Palmer JR, Titus-Ernstoff L, Noller KL, Kaufman RH, et al. Cancer risk in women exposed to diethylstilbestrol in utero. *JAMA* 1998;280(7):630-4.

The authors who wrote the article are listed first. If there are several authors, only the first few authors' names will be listed, followed by "et al." The complete title comes next. The name of the journal where the study was published follows. Oftentimes, the name of the journal will be an acronym. For example, in this case, JAMA stands for *Journal of the American Medical Association*. The year the study was published is next. A new issue of this journal is printed each week, so the citation includes the volume (280) and issue number (7). The citation also includes the page numbers (630-4) of the article.

If you have difficulty reading a citation or finding an article, ask a librarian for help.

### Where can I find copies of scientific journal articles?

Community libraries often have copies of well-known scientific journals. Hospital or university libraries may have a wider range and older issues of these journals. Some journals also have articles available on their Web sites. Some Web sites offer the articles free of charge, but others may require you to register with the site and pay a nominal fee. You will need the citation for the article to find it either at the library or on a Web site. See the answer to the previous question for an example citation.

### What does it mean if an article or journal is "peer reviewed?"

Scientific journals require research articles to go through a process called "peer review." During peer review, scientific experts who were not connected to the study review the article and decide whether it was done properly and whether the findings have merit. Only studies that pass peer review get published.

### What does it mean when researchers say that results are "statistically significant?"

Because health problems occur for a variety of reasons, including chance, researchers must determine if a health effect they are studying may have occurred in study participants as a result of chance alone. Specifically, "statistical significance" refers to a finding in a research study that is larger or smaller than would be expected by chance alone.

Statistical significance is expressed in scientific journals by a probability value (p-value). P-values are calculated using a statistical formula that includes the number of people and health effects being studied and is designed to answer the question, “Could a group of this many people, who all experienced a common exposure, have had this health problem in common by chance alone?” A finding is considered statistically significant if there is less than a 5% probability (p=.05 or less) that the findings resulted from chance. Conversely, if there is greater than a 5% probability (p=.06 or greater) that a finding resulted from chance, the finding is not statistically significant.

### How do I interpret statistics in research about DES-related health risks?

Understanding research about DES-related health risks without knowing how to interpret statistics can be difficult. The following table offers some examples of how scientific studies present risk information.

Different Ways that Studies Describe Risks	Statistical Phrase	Risks Presented as Ratios	Risks Presented as Decimals or Percentages	Type of Risk
In the general population, a woman’s lifetime risk of developing breast cancer is about one in eight. That means that, over a lifetime, in a group of eight women, one of those women would be expected to be diagnosed with breast cancer.	One in eight	1:8	.13 or 13%	Absolute risk*
For women prescribed DES while pregnant, lifetime risk of developing breast cancer is one in six. That means that, over a lifetime, in a group of six women exposed to DES during pregnancy, one of those women would be expected to be diagnosed with breast cancer.	One in six	1:6	.16 or 16%	Absolute risk
For women prescribed DES while pregnant, the risk for breast cancer is approximately 30% higher than for women who were not exposed to DES during pregnancy.	Approximately 30%	From 1:8 to 1:6	.30 or 30%	Relative risk**

Source of risk information in this chart: Titus-Ernstoff L, et al. Long term cancer risk in women given diethylstilbestrol (DES) during pregnancy. Br J Cancer 2001;84:126-33.

\* The absolute risk is a number that represents the probability that an individual with a special risk factor (such as exposure to DES) will experience a health effect (e.g., breast cancer).

\*\* Relative risk is the comparison of disease rates (e.g., breast cancer) between persons with higher risks and those in the general population (who have no special exposure).

## What is a “cohort” study?

A “cohort” is a group of people who share common characteristics or experiences. By compiling and summarizing data from a cohort, scientists can observe whether disease conditions develop at higher rates in a cohort group than they would expect in the general population.

In this case, a DES cohort is a group of people who were exposed to DES. Scientists have been following DES cohorts for several years, to evaluate their medical conditions and disease rates. Researchers are trying to determine whether DES-exposed women and men are at an increased risk for certain health problems compared with the general population. For instance, one cohort study revealed that one in six women prescribed DES while pregnant can be expected to develop breast cancer in her lifetime, compared with an expected rate of one in eight women in the general population (Titus-Ernstoff, 2001).

## Deciding Whether a Source is Reliable

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Many sources of information about DES are available. Knowing if the information can be trusted can be difficult. The following are some criteria to help you consider the reliability of a source.

### Where was the research published?

Health care providers trust and use research published in credible, peer-reviewed scientific journals because experts have reviewed studies published in these journals to make sure they are of high quality. Some examples of credible, peer-reviewed journals are *JAMA*, the *Journal of the National Cancer Institute*, the *New England Journal of Medicine*, and *Science*. If you have any questions about whether a journal is peer-reviewed, ask a librarian or your health care provider.

### How does the new information fit with what is already known?

Each research study contributes to an existing body of knowledge. Usually, more weight can be given to study findings that support and build on the findings of other research. If the findings of one study contradict the findings of previous studies, months or several years may pass before more information becomes available to support the contradictory study. In other words, one study alone is never enough to make a case – it simply gives direction about what new research is needed.

### How does funding influence research?

Objectivity, the ability to report study results without personal bias, is an important consideration. The source of funding for a research project may bias the reporting of results. The funding source is usually included in the journal article. When reading an article from a funded research project, you must consider whether the funders of this research had anything to gain by the results. When research is paid for by a source that does not have an interest in the results, funders’ expectations or preferences were less likely to have influenced the results.

### Can I trust information from television, magazines, or brochures?

Many health reports in the media are based on articles published in peer-reviewed journals; however, some reports are not. When you see a report on television, in a magazine, or in a brochure, you must consider where this information came from, who provided the information, whether the source is credible, who did the study, and whether it is consistent with other research. If you are unsure, ask your health care provider.

Also remember that news stories focus on what is “new.” So when a new study is published in a scientific journal, reporters may highlight the results in their stories as being conclusive. However, a single study is never enough to make a case; new research requires other studies to support the results before a study’s findings are considered applicable to medical practice.

### **I get a lot of my information on the Internet. Is that okay?**

More and more, health-related Web sites and newsletters are available to people with Internet access. Use the preceding guidelines to think about the credibility, expertise, bias, and funding of the source of information. The most credible Internet sites come from recognized experts, like health agencies and reputable health and medical organizations. If you are unsure, ask your health care provider for credible Web sites. CDC’s DES Update has a Web site for health care providers and the public ([www.cdc.gov/DES](http://www.cdc.gov/DES)).

For a list of credible health information sources refer to the section of CDC’s DES Update titled **ADDITIONAL DES RESOURCES: Partner and Government Organizations**.

### **I’ve heard lots of stories about DES exposure that aren’t in the research. Why is that?**

Personal stories, sometimes called “anecdotal evidence,” refer to individual experiences. They may or may not be consistent with scientific research. An important element of studying large populations (like the DES cohort studies) is that individual experience is included in the reported data. Even though you may have heard details from persons that are not consistent with findings from scientific research, those experiences have been averaged into the population data. Scientific evidence from large studies (like the DES cohort studies) is reliable, because the studies are rigorous and better reflect the experiences of the population that is being studied.

## **Role of Laboratory Animal Studies**

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DES can no longer be prescribed to pregnant women, even for use in clinical studies. To project future health risks of DES exposure, scientists are conducting animal studies with laboratory mice. Scientists administer DES to pregnant female mice and then study the results. Because mice age more quickly than humans, these studies can be used to explore future health risks. Using laboratory animal models allows scientists to pursue hypotheses that are not possible to research in humans. Results from these animal studies can also guide them on the types of diseases and health effects to look for in humans. Although laboratory animal studies can often predict human health effects, because of differences between humans and mice, the results of laboratory animal studies are not always transferable to humans. In addition, studies of humans rely on tracking the outcomes of DES cohorts (women and men already exposed to DES).

## **Role of DES Cohort Studies**

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The National Cancer Institute’s (NCI) DES Combined Cohort Follow-up Study was formed in 1992. NCI researchers brought together a large group of mothers and their children who had been exposed to DES, as well as a group of similar (in age, medical history, etc.), but unexposed persons. NCI recruited for this study primarily from previously studied groups and their family members. These cohort groups were followed over a long period of time. For this reason, new people cannot be added to the study.

Following is a list and brief description of the DES Cohort Studies.

- **Diethylstilbestrol Adenosis Project (DESAD)** – The DESAD began in 1974 at Baylor College of Medicine, Gundersen Clinic, Massachusetts General Hospital, the Mayo Clinic, and the University of Southern California. The DESAD, the largest DES cohort, included 4,014 DES Daughters and 1,033 unexposed women. Exposed women had documented evidence of DES exposure through review of prenatal records or by physician referral. The DESAD was assembled to conduct studies to determine if DES Daughters were at an increased risk for health problems related associated with their exposure to DES (Labarthe, 1978).
- **DES Mothers Study** – The DES Mothers Study began in 1980. The participant group (cohort) included approximately 3,000 women exposed to DES while pregnant and 3,000 unexposed women. These participants had delivered babies during 1940–1960 at Boston Lying-In Hospital, the Mayo Clinic, Dartmouth Medical School, and a private practice in Portland, Maine. Exposure status was determined through review of medical records. The cohort was created to determine if women exposed to DES during pregnancy were at increased risk for cancer (Greenberg, 1984).
- **Mayo Clinic Sons Study** – The Sons Study included approximately 800 men exposed to DES before birth (in the womb) and 600 unexposed men. This cohort was identified by review of medical records of women who gave birth at Mayo Clinic hospitals (Leary, 1984).
- **Connecticut Mothers Study** – The participants included women who delivered babies during 1946–1965 at medical offices in Fairfield and New Haven Counties, Connecticut. The participants included 1,706 DES-exposed mothers and 1,405 unexposed mothers. The participants are now included in the DES Combined Cohort Studies (Hadjimichael, 1984).
- **Dieckmann Cohort** – Participants in the group, assembled in 1974 to study DES-related health risks, included approximately 800 women exposed to DES while pregnant and 800 unexposed mothers; approximately 400 women exposed to DES before birth (in the womb) and 400 women in a control group; and approximately 400 men exposed to DES before birth and 400 unexposed men. The 1974 group comprised the second Dieckmann cohort; the first included mothers who were participants in a study at the University of Chicago in the early 1950s. Results based on the initial study indicated that DES was not effective in preventing miscarriages (Dieckmann, 1953).
- **British Research Medical Council (BRMC) Study** – Participants included pregnant diabetic women enrolled in clinical trial and DES Daughters and DES Sons identified through follow-up study, for a total of 151 participants (79 DES-exposed and 72 unexposed people) (Reid, 1955).
- **British Randomized Trial** – A group assembled to study DES-related health effects. Participants included women exposed to DES during pregnancy and men and women exposed before birth (in the womb). The DES-exposed group included 379 mothers, 144 daughters, and 177 sons. A control group of unexposed included 371 mothers, 170 daughters, and 163 sons (Guisti, 1995).

- **Registry for Research on Hormonal Transplacental Carcinogenesis** – The Registry was established at Massachusetts General Hospital in 1971 to track the incidence of clear cell adenocarcinoma (CCA) of the vagina or cervix. The registry originally numbered 21 cases; however, by 2002, approximately 750 cases had been recorded at the registry. Most of the information on treatment outcome and recurrence rates of CCA has come from the study of patients in the registry. The registry is now located at the University of Chicago (Department of Obstetrics and Gynecology, The University of Chicago, 5841 South Maryland Avenue, Mail Code 2050, Chicago, IL, 60637. Phone: 773-702-6671. Fax: 773-702-5161) (Herbst, 1972).

### What kinds of research are still going on?

Researchers continue to monitor the health status of 15,000 members of the combined cohort study. Many of the health problems being monitored are health problems that may be influenced by exposure to DES before birth (in the womb). These health problems include breast cancer in women, testicular cancer in men, and the potential interaction of hormone replacement therapy with DES exposure.

Researchers also are monitoring rates of health problems that appear to have no relationship to DES exposure (such as heart disease and diabetes). Scientists have no hypothetical or other reason to believe there is any link between DES and these diseases. These studies are being done to evaluate the overall health of DES-exposed persons.

### Why don't we have final answers about DES health risks?

The health risks associated with DES exposure change over a person's lifetime. Consequently, research is ongoing to learn how health risks change as DES-exposed persons age.

For instance, DES Daughters who are still in their 30s may not have yet faced their risk for infertility, ectopic pregnancy, or other pregnancy complications. Older DES Daughters and their mothers could be just reaching the stage of life where they must make an informed decision about estrogen replacement therapy. Age of DES-exposed persons is particularly relevant when thinking about DES exposure and cancer risk. Most cancer diagnoses do not begin to emerge until people are well into their fifth decade of life. Men and women who were exposed to DES before birth (in the womb) are just beginning to reach that age. Only continued research will show whether people who were exposed to DES before birth are at an increased risk for breast cancer, prostate cancer, and other diseases.