THE ADVOCATE'S GUIDE TO

Understanding Breast Cancer Research

EUROPA DONNA
The European Breast Cancer Coalition

Mission

EUROPA DONNA – The European Breast Cancer Coalition – is an independent, non-profit organisation whose members are affiliated groups from throughout Europe. The Coalition works to raise awareness of breast cancer and to mobilise the support of European women in pressing for improved breast cancer education, appropriate screening, optimal treatment and care and increased funding for research. EUROPA DONNA represents the interests of European women regarding breast cancer to local and national authorities as well as to institutions of the European Union.

EUROPA DONNA's advocacy work is grounded on evidence-based practice, which involves the responsible use of the best current scientific evidence to make decisions about the care of individual patients.

CONTENTS

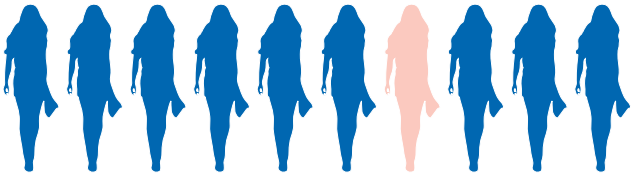
Epidemiology

Epidemiology is the study of patterns, determinants and control of a disease. Research in this field aims to prevent disease and improve health outcomes, and also provides the basis for performing clinical studies. In breast cancer, for example, it describes how many women are affected by the disease (incidence/prevalence), how many die from it (mortality/survival), according to geographical areas, and also measures the external factors that may influence the likelihood of a woman developing breast cancer.

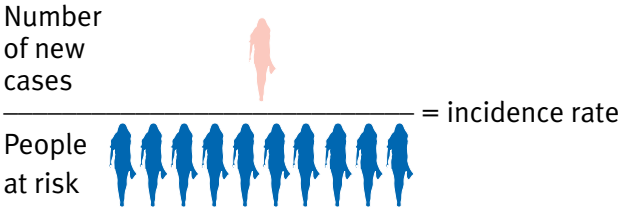
All of EUROPA DONNA's advocacy activities rely on **evidence-based** epidemiological studies, particularly those on population-based mammography screening programmes, as well as on the effects of lifestyle factors such as physical activity, obesity and alcohol consumption, as stressed in our Breast Health Day campaign.

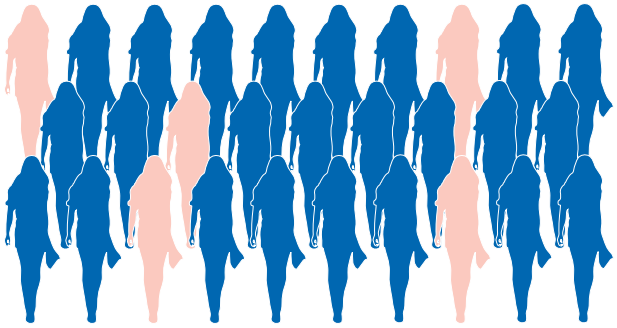
Incidence, prevalence, mortality and survival

Incidence vs. prevalence



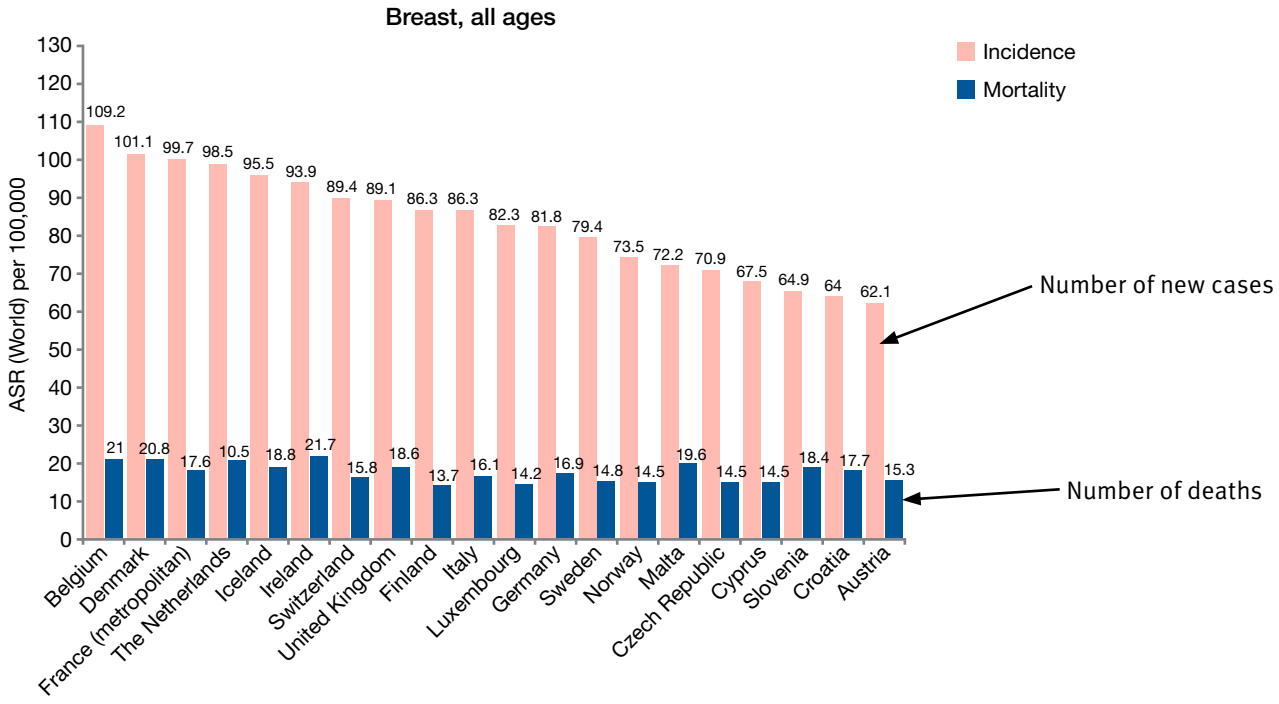
Incidence is the number of newly diagnosed cases of a disease that occur over a defined period of time within a specified population. Cancer registries record this information. Incidence numbers are used to measure risk, to compare the number of cases from one year to the next or to know if one group is more affected than another. Incidence rate is calculated by dividing the number of new cases by the number of people at risk of the disease.





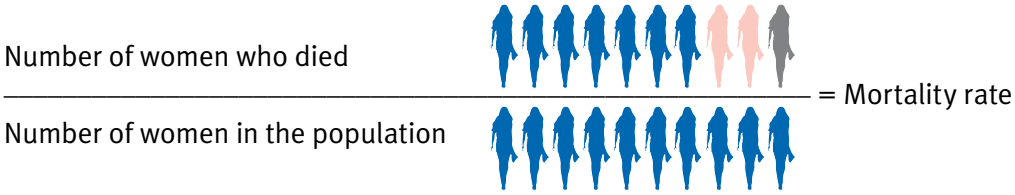
Prevalence is the number of existing cases of a disease in a population at a given point in time. In the case of breast cancer, it would be the number of women living with the disease, the survivors. *Complete prevalence* represents the number of people alive at a certain point in time who had a previous diagnosis of the disease, at any point in the trajectory, whether under treatment or considered cured. *Partial prevalence* is limited to those diagnosed during a fixed time in the past. Prevalence is the measure of disease burden and is useful for health care planning. Both incidence and prevalence figures could be relevant for the setting up of specialist breast units.

Mortality



Age-standardised rates (ASR) per 100,000 population, showing the number of new cases (incidence) and the number of deaths (mortality). From: Ferlay J, Shin HR, Bray F, Forman D, Mathers C and Parkin DM. GLOBOCAN 2008 v1.2, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10 [Internet]. Lyon, France: International Agency for Research on Cancer; 2010. Available from: http://globocan.iarc.fr, accessed on 27/04/2012.

Mortality is the number of people who die from a disease during a specified period of time within a specific population (see the Figure above). It is expressed as a rate per 100,000 population and is age adjusted. For breast cancer, the mortality rate is calculated as the number of women in a certain population who died from breast cancer in a given year, divided by the total number of women in that same population the same year:



Adjustment for age and population size: Since populations may not be of the same size and comprising people of the same age, the numbers are adjusted so that they can be compared between geographical areas. A computer programme adjusts the population being studied so that the age distribution is the same for the specific area or country being studied. For instance, the crude incidence rate (i.e., the raw numbers) may be 150 cases per 100,000 population. When adjusted for age, those incidence figures could be 100 per 100,000 (see Table on next page).

Breast cancer incidence in women older than 15 years. Crude and age-standardised rates per 100,000.			
POPULATION	Numbers	Crude rate	Age standardised rate (ASR) (world)
Western Europe	148,940	183.0	130.0
Northern Europe	70,515	169.6	123.3
European Union (EU-27)	332,670	154.4	111.8
Southern Europe	91,118	135.9	99.8
WHO Europe region	450,316	117.6	91.0
World	1,383,559	56.2	56.3

From: Ferlay J, Shin HR, Bray F, Forman D, Mathers C and Parkin DM. GLOBOCAN 2008 v1.2, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10 [Internet]. Lyon, France: International Agency for Research on Cancer; 2010. Available from: http://globocan.iarc.fr, accessed on 27/04/2012.

Survival

Survival is the percentage of people with a disease surviving to a specified time after diagnosis. Five-year survival is the most common measure and is calculated as the number of women alive 5 years after the first breast cancer diagnosis, divided by the number of women diagnosed with breast cancer at the beginning of the 5-year period.

Overall survival is the total, raw percentage of women who survived during a time period. Relative survival is when this percentage is corrected for other causes of death.

100 women first diagnosed — **70 women** are alive (**15 died** of breast cancer, **15 died** of other causes)

Day of diagnosis — 5 years later

Overall survival

$$\frac{\text{70 alive}}{\text{100 diagnosed}} \times 100 = \mathbf{70\%}$$

Relative survival

$$\frac{\text{70 alive + 15 dead of other causes}}{\text{100}} \times 100 = \mathbf{85\%}$$

Where do the figures come from?

Most statistics on prevalence, incidence and mortality come from national cancer registers. The data collection methods and validity of data may vary among cancer registers, which can sometimes make comparisons difficult. This underscores the importance of having accurate, standardised cancer registers within and between countries. Mortality figures often come from death certificates, in which case care must be taken to state not only the cause of death, but any underlying disease. For example, a woman may die from bone cancer, but this may have been a result of earlier breast cancer. The number of people in the population and those at risk usually come from census data.

Modifiable risk and protective factors

Epidemiological studies aim to determine factors that may increase or decrease our risk of acquiring a disease. While for breast cancer many of these have not been identified, it is known for example that a woman's alcohol consumption (i.e., **exposure**) can increase her chances of developing breast cancer (i.e., the **outcome**). On the other hand, regular moderate physical activity may decrease the risk of breast cancer, and is called a protective factor. Having evidence-based findings on the factors influencing a woman's future breast health are key to EUROPA DONNA's Breast Health Day campaign.

Modifiable risk and protective factors for breast cancer.

Modifiable protective factors	Modifiable risk factors
Moderate physical activity	Alcohol consumption
Prudent dietary pattern	Change in body weight
Vitamin D	Body fatness and obesity
Folate	Fast absorbed carbohydrates
Fibre	Trans fatty acids

Epidemiologists calculate a **risk ratio** to compare the risk of a disease or an outcome in one group compared to another.

$$\frac{\text{Risk of heat stroke in people running in a marathon (5 in 100 had heat stroke)}}{\text{Risk of heat stroke in people not running in the marathon (1 in 100 had heat stroke)}}$$

$$\text{Risk ratio: } \frac{5/100}{1/100} = 5.0$$

This means that people running in the marathon were **five times** more likely to get heat stroke than those not running the marathon. This would be considered a strong risk factor.

Risk factor	Risk ratio
Strong	> 4
Moderate	2-4
Weak	1-2
No risk	1
Protective	< 1

In epidemiological studies, such as **cohort studies**, as well as in clinical studies, the risk ratio is measured as **relative risk** (RR), i.e., the likelihood of developing an outcome/disease in the exposed group relative to those not exposed (e.g., risk of developing breast cancer in women who undertook regular physical activity and those who did not). These are measured against the **absolute risk**, which is the probability of a specified outcome/disease occurring in a specified population (e.g., breast cancer in all women in the EU).

Types of studies

Studies are set up to answer a specific question or set of questions. There are specific study designs that are accepted as the appropriate means of addressing the questions to be answered, and some study designs are considered to be stronger and thus more reliable than others. Depending on what is being measured, the hierarchy of the most reliable studies is as follows, from lowest to highest:

LOWEST

Expert opinion

This includes descriptive studies or reports of expert committees based on opinions of respected authorities, without explicit critical appraisal, or that are based on physiology, bench research or first principles.

Case report

This is a report on an individual case, the diagnosis, treatment and follow-up.

Case series

This is a group of case reports involving patients who were given a similar treatment or intervention.

Case-control study

This is an observational study of people with a disease such as breast cancer compared with a similar control group without the disease. It could retrospectively examine, for example, women with breast cancer and their level of physical activity compared to that of matched women without breast cancer. As the results may depend on a woman's recollection and reporting of her exposure, such studies can be open to what is termed **recall bias**. They may also have selection bias, when cases and controls do not reflect a similar population to each other; for example, if cases were drawn from a public hospital in a low income area and controls were recruited from a private hospital in an affluent area.

Case-control study

Retrospective

Measuring the effect of an exposure in women who already have the disease

Cohort study

Prospective

Measuring the effect of an exposure in women unaffected by the disease

Nested case-control study

This is a retrospective, observational study based on the population of a cohort study (see next page). Findings for subjects with a disease and controls without the disease are examined, helping to reduce any factor which may have influenced the results, i.e., **confounding factors**. For example, a nested case-control study from the French E3N cohort study examined the vitamin D levels in women with breast cancer versus those without. The findings supported a decreased risk of breast cancer associated with high vitamin D_3 serum concentrations, especially in younger women (Engel P. et al. Cancer Epidemiol Biomarkers Prev 2010, 19(9): 2341-50).

HIGHEST

Cohort studies

The European Prospective Investigation into Cancer and Nutrition (EPIC)
EPIC was designed to investigate the relationships between diet, nutritional status, lifestyle and environmental factors and the incidence of cancer and other chronic diseases. EPIC is a large study of diet and health having recruited over half a million (520,000) people in ten European countries: Denmark, France, Germany, Greece, Italy, The Netherlands, Norway, Spain, Sweden and the United Kingdom (http://epic.iarc.fr/index.php).

EPIC is an example of a **cohort study**, also known as a longitudinal, prospective or follow-up study, which is a study that compares a particular outcome (e.g., breast cancer) in groups of individuals who have many common characteristics but differ by a certain characteristic (e.g., menopausal women using hormone replacement therapy [HRT] versus those not using HRT). It is usually a prospective observational study, where the participants are disease-free and followed over time living their normal lives. They are not randomised to a group and receive no treatment or intervention. Another example of large cohort studies is the Nurses' Health Studies, which began in 1976 and have been following various groups of nurse participants to see who develops a particular disease (http://www.channing.harvard.edu/nhs/).

Randomised controlled studies

Randomised controlled studies are considered the gold standard for clinical research and testing new treatments, particularly when they are double-blind, placebo-controlled trials. The participants are assigned a treatment by chance (randomisation); in double-blind trials, both the trial participants and the research team are unaware of which treatment has been assigned to whom. Placebo-controlled trials test a treatment or intervention against a placebo (the same in appearance as the study drug but with no treatment effects). However, in cancer trials new treatments are tested against the standard treatment, and placebo would be given as part of a treatment combination.

Systematic reviews and meta-analyses

A systematic review is an overview of primary studies, such as randomised controlled trials in cases of therapy or treatment, or prospective cohort studies for prognosis-related factors, that used explicit and reproducible methods. A systematic review is done by searching for published studies that measured the same variables and outcomes in the same way. A meta-analysis is a mathematical synthesis of the results of two or more primary studies that addressed the same hypothesis in the same way. This is an effective method of extrapolating data, but it may be difficult for the studies being combined to be identical and therefore comparable. Studies in larger populations may be more valuable.

Example of a systematic review:
Aune D. et al. *Dietary fiber and breast cancer risk: a systematic review and meta-analysis of prospective studies*. Ann Oncol 2012;23(6):1394-402.
This study used a **PubMed database** search to identify 16 prospective studies on fibre intake and breast cancer risk. Applying a statistical model, the researchers combined the results of the 16 studies and found a relative risk of 0.95 for 10 g of dietary fibre consumed per day. This would mean that there is a 5% reduced risk of breast cancer for every 10 g of fibre consumed daily.

A detailed table of levels of evidence requirements from the Centre for Evidence Based Medicine at the University of Oxford is available from: www.cebm.net.

For more on clinical trials, see the EUROPA DONNA booklet *Clinical Trials and Breast Cancer*.

Understanding the study findings

The different types of studies use various methods to calculate what they are seeking to measure. In addition to the relative risk and mortality rates described earlier in this booklet, a number of important statistical measurements or factors are frequently employed.

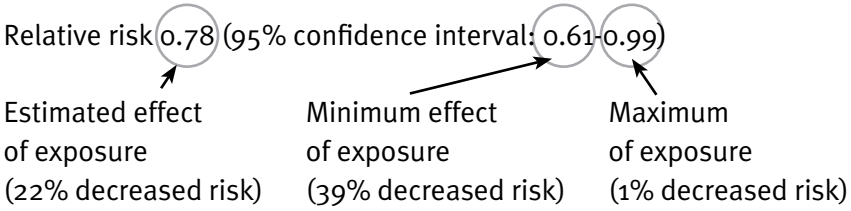
Confounding factor

This is a variable that is not being measured in the study but may influence the results. In a study measuring the effect of hormone replacement therapy (HRT) on breast cancer risk, obesity may be a confounding factor because it may influence a woman's risk of the disease regardless of whether or not she is taking HRT. Studies use a multivariable analysis to adjust the results for other confounding risk factors.

Confidence interval (CI)

This is a range used to calculate the possible degree of error between the population studied and the wider population it is expected to represent. It is based on the concept that if a study were repeated in a different set of participants, the results would vary slightly. It is usually expressed in a range referred to as the 95% confidence interval (CI), meaning that the findings are true 95% of the time, allowing for a 5% error. The shorter the range of the CI, the more reliable the results; a shorter range also usually reflects a higher number of subjects. If the CI range includes the number zero, it is possible that the association observed may be due to chance.

For example, for breast cancer risk in women consuming a certain high amount of dietary folate (there is a 95% chance that the correct answer falls between 0.61 and 0.99):



P-value

P-values are used to express statistical significance and represent the probability that the effect observed in a study could be the result of chance alone. Generally, a P-value ≤ 0.05 is considered statistically significant, meaning there is no more than a 5% probability of observing the result found in the study due to chance. If the P-value is > 0.05, then chance cannot be excluded as an explanation for the findings observed.

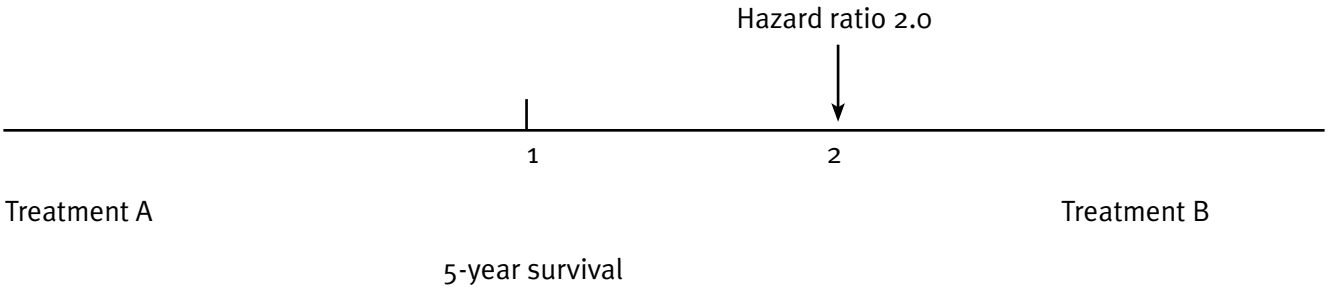
Odds ratio (OR)

This reflects the ratio of the probability of an event occurring in one population to the probability of the same event occurring in another population. It is often used in retrospective case-control studies to identify if a certain exposure increases the risk of breast cancer. An odds ratio of greater than one means that the exposure may increase the risk of cancer, and an odds ratio of less than one means that the exposure may reduce the risk of cancer. The opposite may be true if the exposure is actually a protective factor (e.g., physical activity). It is also referred to as relative odds and tends to be reported with confidence intervals.

OR > 1 Exposure (e.g., smoking) increases risk of disease (e.g., cancer)
OR < 1 Exposure decreases risk of disease
OR = 1 Exposure is not associated with the disease

Hazard ratio

This is a measure, used over time, of how often a particular event occurs in one group compared to how often it occurs in another group. In clinical trials, it is often used to measure survival at a point in time after a certain treatment compared with placebo or standard treatment. A hazard ratio of one indicates that there is no difference in survival between the two groups. If the hazard ratio is greater than one or less than one, this indicates that the survival was better in one of the groups. Hazard ratios are accumulative over the length of a study. In the example below, twice as many subjects on treatment B were alive at 5 years compared with treatment A.



Understanding the tables and figures

Below are some of the more commonly encountered and complex methods used to present data.

Tables

The table below shows the results from a case-control study of the Florence-European Prospective Investigation into Cancer and Nutrition (EPIC) cohort study, with patient cases and controls and odds ratios for risk of breast cancer (Petracci E. J Natl Cancer Inst 2011, 103: 1-12.). Which data are the strongest indicator of risk in this case?

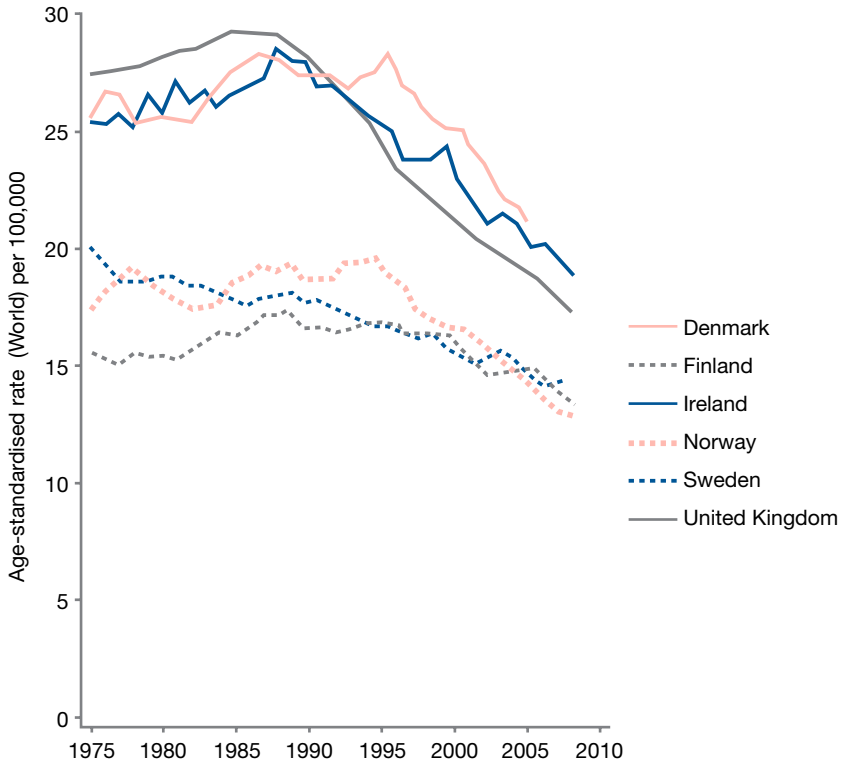
Risk factor	No. cases	No. controls	Odds ratio (95% CI)
Alcohol drinking habits			
Never drinker	748	860	1.0 (reference)
Current drinker	1632	1494	1.27 (1.12-1.43)
Former drinker	143	150	1.23 (0.95-1.59)

A 27% greater risk of breast cancer compared to never drinkers. Notice the confidence interval, indicating that it could be as low as 12% or as high as 43%, with a 95% degree of certainty

A 23% greater risk of breast cancer compared to never drinkers. However, notice the wider confidence interval in this case, with the lower limit < 1. In former drinkers the association is less certain.

Line graphs

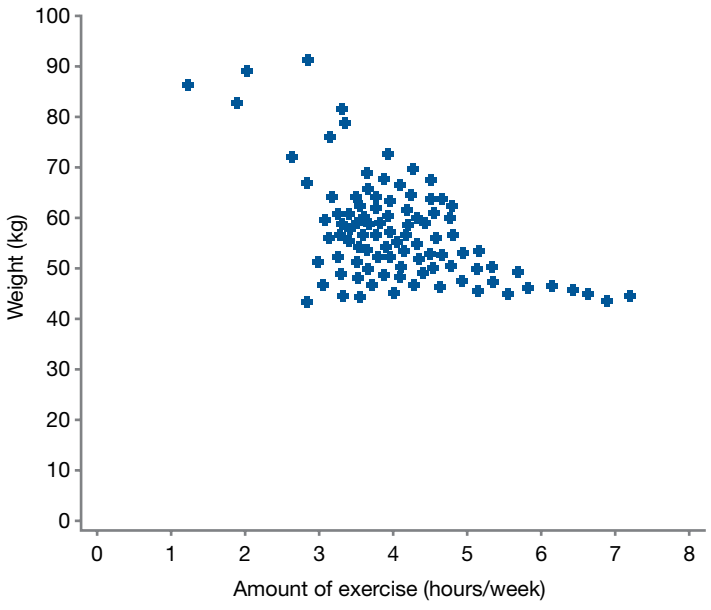
These can be used to show trends over time and compare populations. The graph below shows trends in mortality from breast cancer in selected countries: age-standardised rate (World) per 100,000 population.



(From: Ferlay J, Shin HR, Bray F, Forman D, Mathers C and Parkin DM. GLOBOCAN 2008 v1.2, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10 [Internet]. Lyon, France: International Agency for Research on Cancer; 2010. Available from: http://globocan.iarc.fr, accessed on 14/05/2012.)

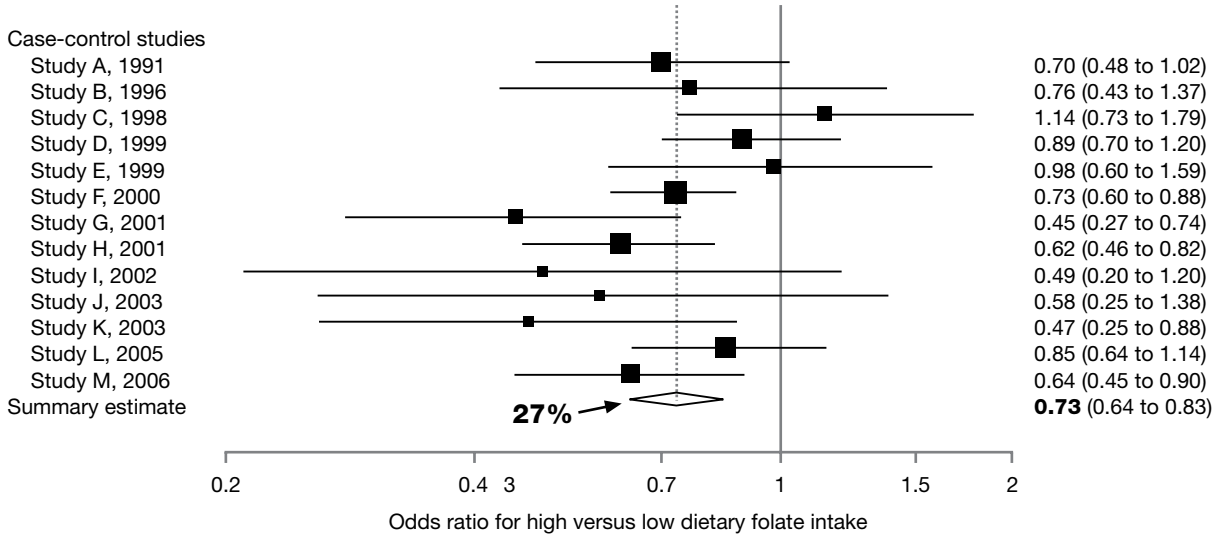
Scatterplots

These are used to show how two variables relate to each other. The horizontal (x-axis) is usually the independent variable and the vertical axis (y-axis) shows the dependent variable. The independent variable, in this case the amount of physical activity, may influence the dependent variable, in this case, weight.



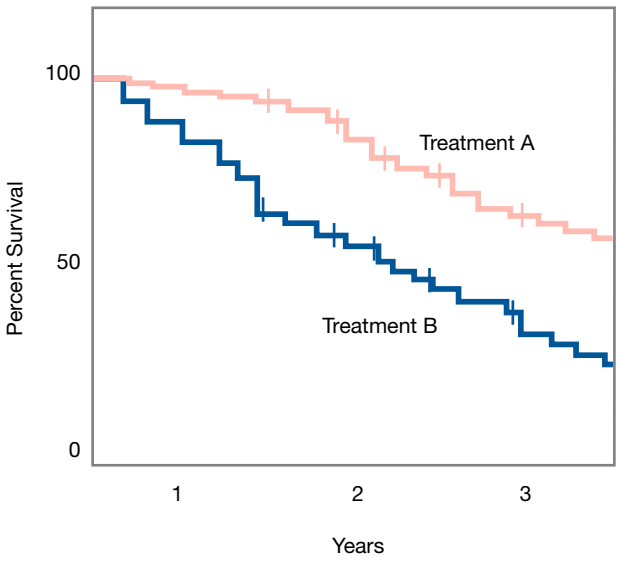
Meta-analyses

The figure below shows the results of a **meta-analysis** (a pooling of results of different studies) for the effects of folate consumption on breast cancer risk. The study references are on the left, while the right-hand side of the graph shows the values for the relative risk (in prospective studies) or odds ratio (in case-control studies) and the 95% confidence intervals. The horizontal axis indicates the relative risk or odds ratio with a vertical line marking the value 1, at which point the effect is null. In the graph, the squares indicate the risk estimate in each study and their size reflects how statistically significant the finding was in each study. The horizontal lines indicate the range of the confidence interval (the range within which the results are 95% certain they are not due to chance). The dotted lines indicate an overall finding for all the studies combined and the diamond indicates the confidence interval of the summary estimate. Notice that there was a statistically significant 27% reduced risk of breast cancer between the group of women with high versus low folate intake (From Larsson SC, Giovannucci E, Wolk A. J Natl Cancer Inst 2007;99(1):64-76.)



Kaplan-Meier curves

These are used to estimate the survival function, often to measure the fraction of patients living for a specific amount of time after treatment. For example, patients may be grouped into categories, such as those receiving treatment A and those receiving treatment B. In the sample graph, those on treatment B have a shorter survival than those on treatment A.



Recognising reputable studies and publications

In addition to the design of the study, a number of factors can help to indicate if they are providing reliable information. The study should have a clear hypothesis and endpoint or outcome (what it is aiming to measure). **Sample size** (the number of people included in the study) also greatly determines the degree to which chance affects the findings. The **control group** also must be adequately matched to the patient group. For example, measuring the average weight of a population will be more accurate if 1000 people are included as opposed to 500. Also, one should consider the number of patients who withdrew from the study, for what reasons, and how many were lost to follow-up (stopped participating in a long-term study). Results should be described clearly, be clinically relevant and be reproducible. Any data that are not original should be fully referenced. An acknowledgements section may indicate the source of funding for the study and many journals now require that authors disclose conflicts of interest and ethical approval.

Below is an example of information that should be included in an article on an original research study.

Introduction/Background/Aim: An original article presenting the results of a study should begin with a background stating what is known prior to the study and what the study proposes to investigate (aim).

Materials/Patients and Methods: This section states the process for recruiting patients (inclusion and exclusion criteria), signing of informed consent and the randomization/treatment schedule assigned (if a treatment trial). The primary and secondary endpoints of the study should be stated (what the study will use to determine whether or not its aim has been met). This section usually ends with a subsection on statistical analysis and how statistical significance is calculated in the study (see P-values).

Results: This section states how many patients were finally included in the study and their baseline characteristics (age, gender, weight, etc. at the beginning of the study) and the findings of the study. These should reflect the aim of the study. If a safety study, any adverse events and side effects should be presented here, what they were and in what proportion of patients.

Discussion: Here the authors put their findings into context with what is already known. They should present any limitations to their study (e.g., small sample size – i.e., small number of patients, concurrent diseases) and allow for the influence of confounding factors (e.g., age, weight, smoking status) in their results.

Conclusion: The article should conclude with a general finding and often calls for further research on the topic.

References: This section should be complete (author names, article title, journal title, year, volume and page numbers), referring to past and recent studies and each should correspond numerically to the citation in the text. This is an important section.

Original study article check list:

- ☐ Clear aim/hypothesis
- ☐ High number of patients included
- ☐ Clear criteria for patient inclusion and exclusion
- ☐ Statistical analysis clear
- ☐ Confounding factors suggested
- ☐ Study limitations presented
- ☐ Full, up-to-date reference section
- ☐ Ethical approval
- ☐ Conflict of interest statement

There are many different types of scientific journals. The most highly regarded are peer reviewed, meaning that articles undergo strict assessment by other scientists before they are published. Journals are ranked by "impact factor", which is a measure of how often the articles in a journal have been cited in a particular year or period. The higher the number, the greater the impact or prestige of the journal.

Publication check list:
- ☐ The study is published in a reputable **peer-review** journal (N Engl J Med, JAMA, J Oncol, Oncology, The Breast, Nature, etc.)
- ☐ Source of funding would not influence study results
- ☐ Authors' affiliations are reputable
- ☐ Authors disclose no relevant conflicts of interest

How to find scientific studies

PubMed® is a freely accessible database of journal citations and abstracts created by the US National Library of Medicine. PubMed draws a large component of its content from the US National Library of Medicine's MEDLINE® database. It includes abstracts, often with links to the website of the publisher. Sometimes the articles can be accessed for free. Articles can be searched for using various criteria, such as author, journal, subject and are interlinked. Here, for example, it is possible to see how many articles an author has published and on what topics.
http://www.ncbi.nlm.nih.gov/pubmed

The EU clinical trials register provides information on protocols of clinical trials of medicines and can be used to access information included in EudraCT, a database of clinical trials in Europe. See the EUROPA DONNA booklet *Clinical Trials and Breast Cancer* for more information.
https://www.clinicaltrialsregister.eu

The National Cancer Institute, which is part of the United States Department of Health and Human Services, provides a comprehensive online database of cancer clinical trials from around the world. It can be searched according to type of cancer, stage/subtype, type of trial, trial location, type of treatment, drug name, trial phase, or a combination of these and other criteria. See the EUROPA DONNA booklet *Clinical Trials and Breast Cancer* for more information.
www.cancer.gov/clinicaltrials

The Cochrane Library publishes online Cochrane Reviews, which are systematic reviews (the highest level of evidence, see page 6) of primary research in health care and policy. They investigate the effects of interventions for prevention, treatment and rehabilitation, as well as diagnostic tests. For breast cancer, there are systematic reviews on screening methods, management and other topics. Although membership is required to access the full review article, the abstracts are accessible and in two languages.
http://www.thecochranelibrary.com

HONcode (Health on the Net Foundation Code of Conduct) certification is a seal of approval for online health and medical websites indicating that the website complies with a set of standards and is a reliable source of health information. For certification, websites are thoroughly evaluated according to HONcode guidelines. There is a continuous surveillance through the year and certified websites must undergo a biennial review.
http://www.hon.ch

Sources for further information

Centre for Evidence-Based Medicine
www.cebm.net

Google Scholar
http://scholar.google.com

International Agency for Research on Cancer. GLOBOCAN 2008.
Cancer Incidence, Mortality and Prevalence Worldwide in 2008.
http://globocan.iarc.fr/

Journal Citation Reports®, Impact Factor
http://thomsonreuters.com/products_services/science/free/essays/impact_factor/

National Cancer Institute, Dictionary of Cancer Terms
http://www.cancer.gov/dictionary/

National Cancer Institute, Glossary of Statistical Terms
http://www.cancer.gov/statistics/glossary

National Cancer Institute, Levels of Evidence for Adult and Pediatric Cancer Treatment Studies
http://www.cancer.gov/cancertopics/pdq/levels-evidence-adult-treatment/HealthProfessional/allpages

Glossary

Baseline: An initial measurement that is taken, such as tumour size, and that is used as a comparison over time to look for changes. It is often used in treatment trials.

Cohort study: A study that compares a particular outcome (e.g., breast cancer) in groups of individuals who have many common characteristics but differ by a certain characteristic. Also known as a longitudinal, prospective or follow-up study.

Confounding factor: A variable in a study that is not being measured and that might influence the study results.

Epidemiology: The study of the patterns, causes and control of disease in different populations.

Exposure: A factor that may increase or decrease risk of a disease, such as smoking or physical activity.

Gold standard: The highest level of accepted treatment.

Impact factor: A measure of how often the articles in a scientific journal have been cited in a particular year or period, and an indication of the power of a journal.

Incidence: The number of new cases of a disease diagnosed in certain amount of time.

Kaplan-Meier estimator: A method whereby available data are used to estimate survival, plotted on what are referred to as Kaplan-Meier survival curves.

First-line therapy: The initial treatment used to reduce a cancer, such as surgery. It is also called induction therapy, primary therapy and primary treatment.

Morbidity: A disease or the incidence of disease within a group of people (e.g., breast cancer mortality is decreasing but morbidity is increasing). Morbidity also refers to adverse effects of a treatment (e.g., lymphoedema following breast cancer surgery).

Mortality: The number of people who die from a disease during a specified period of time within a specific population.

Primary prevention: Measures undertaken to prevent the development of a disease.

Outcome: A specific result or effect that can be measured in a study, such as developing breast cancer or reduced tumour size.

Prevalence: The number of people who had been previously diagnosed with the disease and are alive at a certain point in time in a specific population.

Primary and secondary endpoints: In clinical trials, an outcome or event that can be measured and that is the objective that the study is seeking to determine.

PubMed database: A freely accessible database of journal citations and abstracts created by the US National Library of Medicine (www.ncbi.nlm.nih.gov/pubmed).

Peer-review: A process through which original articles written by scientists are assessed for technical and scientific quality and correctness by other experts in their field.

Recall bias: Lack of balanced results due to answers being based on memory of events or exposure.

Sample size: Number of participants included in a study.

Secondary prevention: In public health, actions taken to prevent disease or injury when other risk factors are known to be present but before symptoms or other adverse consequences have become evident (under this definition screening would be secondary prevention). In epidemiology, measures undertaken to prevent the development of a disease or a recurrence in a person already affected by the disease.

Second-line: A treatment approach that is used after the primary therapy, such as chemotherapy, radiation therapy and hormone therapy.

Statistical significance: A mathematical measure of difference between the groups being compared. The difference is statistically significant if it is greater than what might be expected to occur by chance alone.

Test your understanding

1. If the incidence of breast cancer in country A is 10 and the prevalence of breast cancer is 40, this means:

a) There have been 10 new cases of breast cancer and 40 people are living with the disease
b) Ten people are living with the disease and there have been 40 new cases
c) Four people have survived the disease
d) None of the above

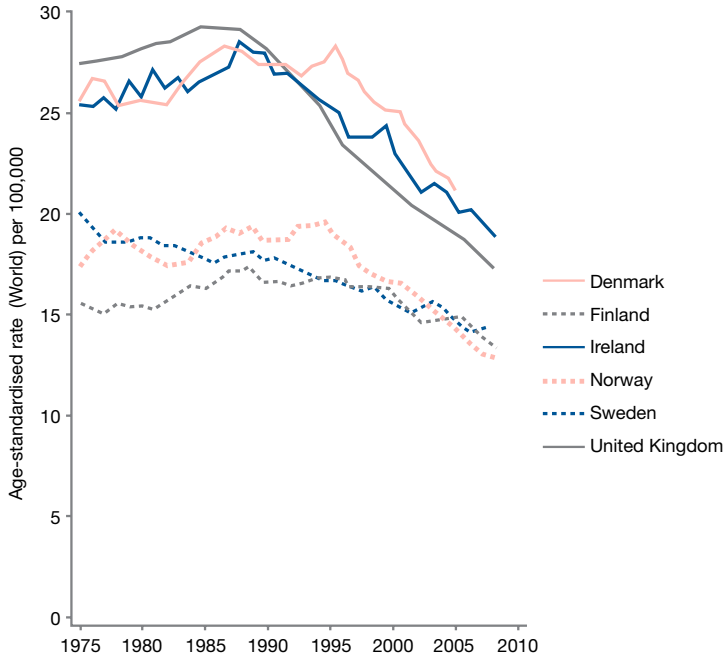
2. Taking into account the need to adjust for population size and that incidence rates are usually based on 100,000 population, we will compare the breast cancer incidence in two cities with a different population. City A has 15 new cases per 100,000 population. City B has 75 new cases per 300,000 population. Which city has a higher incidence rate?

a) City A
b) City B
c) The incidence is the same between city A and city B
d) This is a measure of prevalence not incidence

3. If the crude incidence rate in EU-27 is 154.4 and the age-standardised rate is 111.8, which rate better reflects the actual incidence of the disease?

a) The crude incidence rate (154.4)
b) There is no difference between the rates
c) The age-standardised rate (111.8)
d) Neither rate reflects the incidence

4. The graph below shows the trends in mortality from breast cancer in selected countries (age-standardised rate per 100,000 population). In the year 2002, which two countries had a similar mortality rate?



a) Norway and Finland
b) Denmark and Ireland
c) Sweden and Norway
d) Finland and Sweden

From: Ferlay J, Shin HR, Bray F, Forman D, Mathers C and Parkin DM. GLOBOCAN 2008 v1.2, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10 [Internet]. Lyon, France: International Agency for Research on Cancer; 2010. Available from: http://globocan.iarc.fr, accessed on 27/04/2012.

5. At the beginning of a time period, 150 women are diagnosed with breast cancer. Five years later, 120 are alive, 15 having died of breast cancer. What is the overall 5-year survival for this group of women?

a) 90%
b) 80%
c) 70%
d) 60%

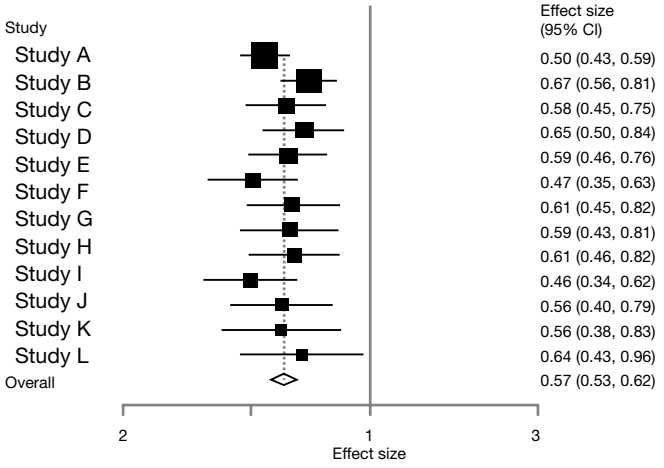
6. What is the relative 5-year survival for the group of women in question 5?

a) 90%
b) 80%
c) 70%
d) 60%

7. Two hundred women are experiencing menopausal symptoms. Of these, 100 women took hormone replacement therapy (HRT) and 100 did not. Of those who took HRT, two were diagnosed with breast cancer. Of those who did not take HRT, one was diagnosed with breast cancer. What is the risk ratio between the women who took HRT and those who did not?

a) 20
b) 2.0
c) 0.2
d) 0.05

8. The figure below shows the relative risk of breast cancer mortality for women at a time when mammography screening was in place compared with before screening implementation. What were the overall findings?



a) A 57% reduction in breast cancer mortality with screening compared to without screening
b) A 43% reduction in breast cancer mortality with screening compared to without screening
c) A 43% increase in breast cancer mortality among screened women
d) The figure does no show this information

From: Cancer Epidemiol Biomarkers Prev 2006;15(1):45–51

9. You would like to find out the effects of a certain treatment on the survival of women with breast cancer. Which study design would best measure this?

a) A case study
b) A randomised controlled trial
c) A cohort study
d) A systematic review

10. Researchers wish to determine the possible association between exercising for more than 5 hours a week and reduced risk of breast cancer. What would be the most reliable study design to measure this association?

a) A cohort study
b) Expert opinion
c) A case series
d) A case-control study

11. If in study A the 95% confidence interval is 0.41-0.99 and in study B it is 0.85-0.96, which study results are stronger?

a) Study B
b) Study A

12. According to the results in the following table, does overweight (having a body mass index of 25.0-29.9) increase or decrease the risk of breast cancer?

BMI at age ≥50 year, kg/m²	No. cases/No. controls	Odds ratio (95% CI)
<25.0	799 / 868	1.0 (referent)
25.0–29.9	639 / 652	1.13 (1.03-1.24)
≥30.0	283 / 291	1.28 (1.06-1.54)

Data from: Petracci E. J Natl Cancer Inst 2011, 103: 1-12.

a) It increases the risk of breast cancer
b) It decreases the risk of breast cancer
c) It has no effect on the risk of breast cancer

13. In the table in question 12, being obese (having a body mass index of ≥ 30) is associated with:

a) A 28% decreased risk of breast cancer
b) A 28% increased risk of breast cancer
c) A 28 times higher risk of breast cancer
d) A 6-54% risk of breast cancer

14. One study on the effects of physical activity on breast cancer risk recruits subjects from a health club and compares them to subjects from a weight loss clinic. What effect might this recruitment have on the results?

a) Bias
b) Recall bias
c) Selection bias
d) The results would be unbiased

Test your understanding: Answer key

Question 1, correct answer: a) Incidence refers to new cases diagnosed in a certain period of time, in this case 10; while prevalence refers to all the people living with the disease, in this case 40.

Question 2, correct answer: b) City B has a higher incidence rate. In order to compare the rates of the two cities, one needs both populations to be the same (i.e., 100,000). City B with 75 new cases/300,000 would therefore have 25 new cases/100,000 population. Given that city A has 15 new cases/100,000, city B has the higher incidence rate.

Question 3, correct answer: c) The age-standardised rate is a more reliable measure of the true incidence because the numbers are adjusted to compensate for differences in population size and age.

Question 4, correct answer: d) Finland and Sweden. In 2002 the lines for Finland and Sweden overlap.

Question 5, correct answer: b) 80%. The overall survival is the number of women who are alive (i.e., 120) at the end of the 5-year period, divided by the number of women diagnosed at the beginning of the 5-year period (i.e., 150):

$$\frac{\text{120 alive}}{\text{150 diagnosed at beginning}} = \text{x } 100 = 80\%$$

Question 6, correct answer: a) 90%. The relative survival is the number of women who are alive (i.e., 120) plus those who died from non-breast cancer-related causes (i.e., 15), divided by the number of women diagnosed at the beginning of the 5-year period (i.e., 150):

$$\frac{\text{120 alive + 15 dying of other causes}}{\text{150 diagnosed at beginning}} \text{ x } 100 = 90\%$$

Question 7, correct answer: b) 2.0. In this case, this would indicate that those who took HRT had a twofold greater chance of having breast cancer:

$$\text{Risk ratio} \quad \frac{2/100}{1/100} = 2.0$$

Question 8, correct answer: b) A 43% reduction in breast cancer mortality with screening compared to without screening. The bottom right-hand number in the list on the right shows a relative risk of 0.57 overall. This translates to a 43% reduction in breast cancer mortality.

Question 9, correct answer: d) A systematic review. A study analysing the results of various randomised controlled trials has the highest level of scientific evidence.

Question 10, correct answer: a) A cohort study. A study that prospectively measures the association between physical activity in women who are disease-free at the time of recruitment will provide stronger evidence-based data than the other studies mentioned. A case-control study could be used, but would be more subject to bias.

Question 11, correct answer: a) Study B. The shorter confidence interval indicates less probability of error.

Question 12, correct answer: a) It increases the risk of breast cancer. The odds ratio is greater than 1, indicating an increased risk.

Question 13, correct answer: b) A 28% increased risk of breast cancer. The odds ratio is 1.28 indicating a 28% increased risk of breast cancer. The range within which this is likely to be true 95% of the time is 6-54%.

Question 14, correct answer: c) Selection bias. When subjects are chosen based on a certain characteristic and may not be comparable to the control or patient group, there may be selection bias. Controls must be representative of the population being studied.

Notes

The data shown in this booklet are used for demonstrational purposes only and do not necessarily reflect actual scientific findings.

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