# What's the denominator?

*Cesar G Victora*

## Floating numerator

Statements such as "most people with kidney stones drink less than six pints of liquid a day" and "most motor car accidents take place within a five-mile radius of the victim's home" lack a denominator, being based on a frequency count of a risk factor among affected individuals, and, whilst strictly true, they mislead by failing to measure relative risk. Obviously, most people drink less than six pints a day and spend more time travelling near than far from their homes. This does not mean, however, that such activities are riskier than their alternatives. This pitfall, "floating numerators",[1] can be solved by use of the appropriate denominator. Lack of a denominator is also behind the fallacy of drawing conclusions from statements such as "my grandfather smoked three packs a day and lived to be 90 years old". A proper denominator would show that the average life expectancy of a group of smoking adults is lower than that of a comparable group of non-smokers.

Floating numerators can also be more sophisticatedly disguised. For example, the entropy theory of ageing states that increasing human size is in conflict with a maximum lifespan. A report[2] attempted to support this theory by showing that adult weights and heights are inversely related to lifespan. By use of hospital records of 373 deceased men, the researchers showed that tall and heavy men had lower mean ages at death than short and light men. These findings were restricted to individuals who died, no proper population denominator being provided. The results may have been affected by the secular trend in growth as well as by loss of weight or height with ageing. For instance, men aged 90 or more who die today are likely to be shorter than those aged, say, under 40. Only population-based denominators allow study of longevity in a cohort of men of different heights and thereby avoid fallacious conclusions.

Choice of the appropriate denominator is therefore one of the most important tasks of an epidemiologist.[3-7] The most commonly used denominators are shown in the panel. These denominators are essential for measuring disease frequency. Before describing these measures, however, it is useful to recall some basic definitions. A ratio is the quotient of any two numbers. For example, the female to male ratio is greater than one in most communities. Ratios used in epidemiology range from 0 to $+\infty$. A proportion is a special type of ratio in which the denominator contains the numerator. For instance, 10% of the subjects examined in a survey may have a given disease. A proportion must range from 0 to 1, or 0% to 100%. Odds are the number of events divided by the number of non-events—eg, the number of patients in a population divided by the number of individuals without the disease. Odds, although common in betting, are harder to interpret than proportions. They vary from 0 to $+\infty$, often being expressed as 1:2 (that is, 1 case per 2 non-cases), 3:2, 7:4, and so forth. The main reason odds have become popular is because the ratio of two odds (odds ratio) is easy to calculate from case-control studies and via logistic regression, a common method of multivariate analysis.

**Mestrado em Epidemiologia, Universidade Federal de Pelotas, CP 464, Pelotas, RS 96001 Brazil** (Cesar G Victora PhD)

## Measures of disease frequency

Different types of epidemiological studies allow calculation of different measures of disease frequency. The figure represents a group under study. At time $t_0$, $a_0$ individuals already have the disease of interest and $c_0$ do not. Of $c_0$, $b_1$ will acquire the disease by $t_1$, while $c_1$ remain healthy. At the end of the study ($t_2$), $c_2$ will still be unaffected. Note that this simplified scheme assumes that the disease occurs only once in each individual and that there have been no further deaths or losses to follow-up.

### *Prevalence*

In cross-sectional studies, sampled subjects are examined once. The number of cases may then be divided by the total number of persons studied (denominator I in the panel). This is usually called the point prevalence, or sometimes the prevalence rate. At $t_0$, the prevalence is equal to $a_0/(a_0 + c_0)$, while at $t_1$ it equals $(a_1 + b_1)/(a_1 + b_1 + c_1)$. The point prevalence is in fact a proportion. For example, a survey may show that 12·7% of individuals aged 40 and over living in a city have chronic bronchitis.

Panel: **Commonly used denominators**

- The total number of persons under study at a given time (I).
- The number of persons who do not have the disease of interest at a given time (II).
- The number of persons at risk multiplied by the time for which each remains at risk (III).

The number of cases may also be divided by the number of people without the disease of interest (denominator II), resulting in the prevalence odds. At $t_1$, for instance, this equals $(a_1 + b_1)/c_1$. For the same data, the prevalence odds will always be larger than the prevalence rate since the prevalence rate's denominator will be greater. In our urban survey, the odds of chronic bronchitis would equal 0·154, or about 1:7.

A third, less common prevalence measure is period prevalence, or the proportion of individuals with a given condition in a whole period. In the figure, this would equal $(a_0 + b_2)/(a_0 + c_0)$.

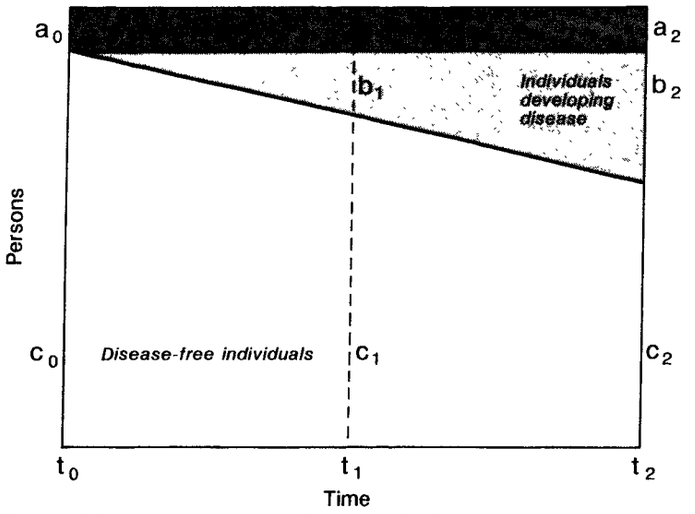


Figure: **Disease occurrence in a population**

### *Incidence*

The situation is more complex in cohort or incidence studies in which subjects are followed over time. When the disease is not recurrent, incidence studies usually exclude individuals who are already affected at the beginning ($a_0$). Others who are not at risk of the disease should also be excluded (eg, women who have had hysterectomies, in a study of endometrial cancer). A first choice of denominator is therefore II, the initial population at risk ($c_0$). If they are followed up until $t_2$, the number of new or incident cases ($b_2$) divided by $c_0$ gives the incidence risk, also known as cumulative incidence. An incidence risk is a proportion. As an example, the risk of developing breast cancer in a cohort of women aged 40, who are followed up over 30 years, may equal 4·2%

However, the numbers at risk change over time. Subjects who develop the disease, who die from other causes, or who are lost to follow-up can no longer be detected as incident cases. Recognition of this pitfall led to the development of the incidence rate, also known as incidence density or force of morbidity (or mortality). Its denominator is expressed as person-time units (III). Each person who is followed up for 1 time unit (say, a month or a year) represents 1 person-month or 1 person-year. 10 person-years, for example, may be accrued by following up 10 persons for a year, 5 persons for 2 years, or 1 person for 10 years. The number of person-time units is represented in the figure by the white area. In calculation of rates for a geographical area where the exact number of person-years is not known, the mid-year population provides a reasonable estimate.

An incidence rate is a ratio, ranging from 0 to $+\infty$, because the numerator (events) is not contained in the denominator (person-time). It reflects the velocity of change in some characteristic of the population. Oesophageal cancer, for example, may occur in a given community with an incidence rate of 10 per 100 000 person-years. For recurrent diseases, incidence rates may be greater than 1 per person-time unit. For example, in many developing countries there are around 3 diarrhoea episodes per child-year.

If the disease is rare—say, affecting less than 10% of the subjects over the duration of the study—and if deaths and losses to follow-up are few, the incidence risk and rate will be similar if expressed in the same time units. If these assumptions do not hold, the incidence rate will be larger than the risk, since the incidence risk's denominator will be greater.

A third possibility in a cohort study is to calculate incidence odds by dividing the number of cases by the number of subjects still disease-free at the end of study ($b_2/c_2$). This is less commonly done.

Incidence risks are usually more appropriate for presenting the prognosis of individual patients (say, a 50% chance of survival for 5 years). Incidence rates, on the other hand, are more appropriate for aetiological research, especially for chronic diseases in which the observation time for each subject is shorter than the incubation period of the disease.

### *Proportionate and case-fatality rates*

Even without population data a denominator can still be obtained. For instance, the number of deaths due to a particular cause may be related to the overall number of deaths in the same period. This denominator is analogous to II and allows calculation of a proportionate mortality rate, which is actually a proportion. A study may show, for example, that 12% of infant deaths in a given town were due to pneumonia. Similarly, if the total number of patients attending a clinic or being admitted is known, proportionate morbidity rates can be calculated for each type of disease. Such situations are akin to a cross-sectional study, each subject being considered once at the time of death, admission, or attendance.

Proportionate rates are not as useful as those based on the population at risk, because they may be artificially reduced if there are many deaths, attendances, or admissions due to other causes. The opposite may also happen, a large proportionate rate resulting from a deficit of other deaths, admissions, or attendances. Despite these pitfalls, such denominators are better than no denominator.

Finally, the proportion of deaths among new cases of disease in a given period (often unstated) is the case-fatility rate. This is often wrongly referred to as mortality (incidence) rate: "rabies is a disease with high mortality" is not true in most places, although its case-fatality is high everywhere. A case-fatality rate is in fact a proportion, ranging from 0 to 1.

Of the measures of disease frequency, the most commonly used are the prevalence rate, the incidence risk and rate, and the proportionate mortality and case-fatality rates. Odds are not often used for describing disease frequency but they have an important role in the calculation of measures of effect.

## Measures of effect

An effect relates to the association between an exposure (or risk factor) and a disease. Effects may be expressed in relative or absolute terms.

Relative effects are expressed as ratios, that is, quotients of two frequency measures. They are often referred to as relative risks although they can be relative prevalences, rates, or odds. Their general form is: ratio = (frequency among exposed)/(frequency among unexposed). Since both frequencies must be expressed in the same units, such a ratio is dimensionless, ranging from 0 to $+\infty$. For example, low birthweight children may have twice the risk of dying because of diarrhoea in infancy than those of appropriate birthweight. This relative risk of 2·0 corresponds to a 100% increase. If the disease is less common for the exposed than for the unexposed, the ratio will be below unity. For instance, children receiving a given vaccine may have a ratio of 0·4 relative to unvaccinated children. In this case, the protection would equal 60% (100% − 40%). Note that a

60% reduction does not correspond to a 60% increase for the unvaccinated, who would in fact have a 150% increase ([100% − 40%]/40%). Odds ratios are increasingly used. They may be calculated from case-control studies and are approximately equal to the rate ratio in a cohort study if the controls are properly chosen.[7]

Absolute effects are expressed through a difference between the prevalences, rates, risks, or odds of exposed and unexposed subjects. The form is: difference = (frequency among exposed) − (frequency among unexposed). A difference may range from $-\infty$ to $+\infty$. It is expressed in the same units as the frequency measures, such as percentage points or person-years. Negative differences imply that the exposure is protective.

Ratios imply a multiplicative relation between exposure and disease—eg, non-breastfed infants in a developing country may be three times more likely to die than breastfed ones. Differences, on the other hand, assume an additive relation—there will be an extra 120 deaths per 1000 infants who are not breastfed. For aetiological studies, ratios are most commonly used because they indicate the strength of the association. For the health administrator or planner, however, differences are more appropriate because they estimate the actual number of cases that might be prevented by a given intervention.

## Conclusion

Epidemiological terminology evolves. Different and sometimes conflicting terms may be used for describing the same measure, reflecting the intensity of progress in this field and rapid incorporation by other health sciences. Whichever terms are used, the denominator must be defined. The choice of the proper denominator is one of the most crucial aspects of describing disease occurrence and of evaluating risk factors.

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# Management of science

*Bruce G Charlton*

Another phase of the UK's National Health Service reforms is becoming visible, at least in outline—namely, the management of scientific knowledge in medicine. The strategy has several promising aspects but also contains serious threats, which require debate before new practices harden into dogma.

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Over the past ten years reforms have moved towards the goal of a managed NHS in which all areas of activity are accountable to a management structure (one including managerial clinicians as well as general managers).[1] The NHS is to be managed right through to the patient. Over the same time administrative regulation and internal competition have increased: the reforms have enhanced control from both bureaucratic and market mechanisms at the expense of professional influence.[2] The result has been a complex, contradictory, and probably unstable mixture of "purchaser/provider splits" in which self-governing NHS trust hospitals work alongside units directly managed by the purchasers, while traditional primary health-care teams live next door to fund-holding practices with both purchaser and provider functions. And into this state of evolving chaos, the NHS hierarchy is attempting to inject long-term planning, strategic thinking, and priorities, through *The Health of the Nation*.[3]

The management of science here is "top down", albeit after extensive consultation. *The Health of the Nation* and then *First Steps for the NHS*[4] set out priorities. These will be spelled out, in terms of service requirements, in purchaser-provider contracts; and the next logical step will presumably be to enforce these protocols at the level of individual practice. For the first time in the UK large areas of clinical decision-making will be subject to managerial accountability.

Purchasers will be contracting with service providers to adopt highly specific clinical management packages. For instance,[4] to "specify [a] protocol for beta-blocker and aspirin treatment post myocardial infarction"; to "ensure audit processes are in place to monitor treatment and follow-up [of skin cancers], particularly on stage and margin of excision"; and to "establish baseline data to monitor the prescription of benzodiazepines [in general practice], and encourage improved prescribing practice and the development of protocols for prescribing antidepressants and psychotropic drugs". District health authorities and family health service authorities will thus be managing the translation of scientifically established knowledge into NHS practice. What used to be decided at ground level by individual doctors will now be a contractual requirement. This extension of managerial control over clinical practice raises many issues.

The move is well-intentioned and commands support within medicine, and the desire to apply knowledge more rationally has a distinguished history. Unexplained variations in clinical practice are being unearthed by the increased level of data collection and publication; there is general dissatisfaction at the unpredictable speed of uptake of medical innovations; and there is also concern that some

**Epidemiology and Public Health, Medical School, University of Newcastle upon Tyne, Newcastle upon Tyne NE2 4HH, UK**
(B G Charlton MD)