

2002 02

Descriptive studies: what they can and cannot do

Notice: This Material May Be
Protected by Copyright Law
(Title 17 U.S. Code).

David A Grimes, Kenneth F Schulz

Descriptive studies often represent the first scientific toe in the water in new areas of inquiry. A fundamental element of descriptive reporting is a clear, specific, and measurable definition of the disease or condition in question. Like newspapers, good descriptive reporting answers the five basic W questions: who, what, why, when, where . . . and a sixth: so what? Case reports, case-series reports, cross-sectional studies, and surveillance studies deal with individuals, whereas ecological correlational studies examine populations. The case report is the least-publishable unit in medical literature. Case-series reports aggregate individual cases in one publication. Clustering of unusual cases in a short period often heralds a new epidemic, as happened with AIDS. Cross-sectional (prevalence) studies describe the health of populations. Surveillance can be thought of as watchfulness over a community; feedback to those who need to know is an integral component of surveillance. Ecological correlational studies look for associations between exposures and outcomes in populations—eg, per capita cigarette sales and rates of coronary artery disease—rather than in individuals. Three important uses of descriptive studies include trend analysis, health-care planning, and hypothesis generation. A frequent error in reports of descriptive studies is overstepping the data: studies without a comparison group allow no inferences to be drawn about associations, causal or otherwise. Hypotheses about causation from descriptive studies are often tested in rigorous analytical studies.

Descriptive studies have several important roles in medical research. They are often the first foray into a new disease or area of inquiry—the first scientific “toe in the water.”¹ They document the health of populations and often prompt more rigorous studies. Since descriptive studies are often reported,² clinicians need to know their uses, strengths, and weaknesses.

A descriptive study is “concerned with and designed only to describe the existing distribution of variables, without regard to causal or other hypotheses.”³ The key qualifier about causal hypotheses is sometimes forgotten by investigators, resulting in erroneous conclusions. Here, we provide an overview of the advantages and disadvantages of descriptive studies, provide examples of several types of descriptive study, examine their clinical uses, and show how they can be misinterpreted.

The descriptive triad—or pentad?

Five “W” questions

Traditional descriptive epidemiology has focused on three key features: person, place, and time,⁴ or agent, host, and environment.⁵ An alternative approach is that of newspaper coverage. Good descriptive research, like good newspaper reporting, should answer five basic “W” questions—who, what, why, when, and where—and an implicit sixth question, so what?

Who has the disease in question? Age and sex are universally described, but other characteristics might be important too, including race, occupation, or recreational activities. The risk of venous thromboembolism, for example, increases exponentially with age.⁶ Only 1% of breast cancers arise in men, but Klinefelter’s syndrome or a family history of breast cancer increase their risk.^{7,8} Race affects the risk of leiomyomas of the uterus.⁹ Commercial fishing remains a risky business,¹⁰ and having fun with an

all-terrain vehicle¹¹ or snowmobile,¹² especially when drunk, can be lethal.

What is the condition or disease being studied? Development of a clear, specific, and measurable case definition is an essential step in descriptive epidemiology. Without such a description, the reader cannot interpret the report. Some conditions, such as fractures, can be overt. Other diagnoses might be challenging: multiple sclerosis, systemic lupus erythematosus, and pelvic inflammatory disease (salpingitis), for example. By use of the consensus or Delphi panel¹³ approach rather than evidence, some organisations have promulgated case definitions that have subsequently been shown to be invalid.¹⁴ For instance, evidence indicates that vaginal discharge and a raised erythrocyte sedimentation rate predict salpingitis,¹⁵ yet these predictors are not included in widely-used diagnostic criteria.¹⁴

Generally, stringent criteria for case definitions are desirable. Admittedly, if only the more severe cases of disease are targeted, milder or earlier cases will be missed. Although this approach inevitably leads to some loss of information, the trade-off is better specificity; severe cases of a disease are less likely to be confused with other conditions than are mild cases. An example would be the stringent case definition used for toxic shock syndrome, which requires involvement of multiple organ systems.¹⁶ More recently, expanding the case definition of AIDS has yielded a sudden surge in “new” cases.¹⁷

Why did the condition or disease arise? Descriptive studies often provide clues about cause that can be pursued with more sophisticated research designs (panel).

When is the condition common or rare? Time provides important clues about health events. The prototype might be the outbreak of gastroenteritis soon after ingestion of staphylococcal toxin. Some temporal relations can be long—eg, vaginal adenosis and clear cell carcinoma of the vagina appeared years after intrauterine exposure to diethylstilboestrol.¹⁸ Furthermore, cervical and other epithelial cancers develop decades after infection with human papillomavirus, and births and deaths from pneumonia and influenza have regular seasonal patterns, as might sperm counts.¹⁹

Lancet 2002; 359: 145–49

Family Health International, PO Box 13950, Research Triangle Park, NC 27709, USA (D A Grimes MD, K F Schulz PhD)

Correspondence to: Dr David A Grimes
(e-mail: dgrimes@fhi.org)

2

Examples of early leads from descriptive studies

Clinical observation	Underlying association
Hepatocellular adenoma in young women	Exposure to high-dose oral contraceptives
Blindness in newborn infants	High ambient oxygen concentrations in incubators
Kaposi's sarcoma in young men	Infection with HIV-1
Angiosarcoma of the liver in employees	Industrial exposure to vinyl chloride
Cataracts, heart defects, and deafness in newborns	Maternal infection with rubella during pregnancy

Where does or does not the disease or condition arise? Geography has had a huge effect on health. Living close to rodents and insects (and thus their parasites) has shaped both medical and political history.²⁰ Living where drinking water has high fluoride protects against dental caries,²¹ whereas residing downwind from a lead smelter is less salutary.²² Latitude plays a part in both multiple sclerosis²³ and vitamin D deficiency;²⁴ sunlight might decrease²⁵ or increase²⁶ cancer risk.

So What? The implicit "W" relates to the public health effect. In view of the proliferation of descriptive reports,² what is their import? Is the condition a current and timely one? Is it serious? Are large numbers involved? Are its societal implications broad? Has it been studied before?²⁷ Although many descriptive reports herald new illnesses or monitor health, the net effect of others might be only thicker curricula vitae at the expense of thinner forests.

Types of descriptive studies

Descriptive studies consist of two major groups: those that deal with individuals and those that relate to populations. Studies that involve individuals are the case report, the case-series report, cross-sectional studies, and surveillance, whereas ecological correlational studies examine populations.⁴

Case report

The case report is the least publishable unit in the medical literature. Often, an observant clinician reports an unusual disease or association, which prompts further investigations with more rigorous study designs (panel). For example, a clinician, among others, reported benign hepatocellular adenomas, a rare tumour, in women who had taken oral contraceptives.²⁸ A large case-control study pursued this lead and confirmed a strong association between long-term use of high-dose pills and this rare, but sometimes deadly, tumour.²⁹ Not all case reports deal with serious health threats, however; some simply enliven the generally drab medical literature.³⁰⁻³²

Case-series report

A case-series aggregates individual cases in one report. Sometimes, the appearance of several similar cases in a short period heralds an epidemic. For example, a cluster of homosexual men in Los Angeles with a similar clinical syndrome alerted the medical community to the AIDS epidemic in North America.³³ Whereas a report of a single unusual case might not trigger further investigation, a case-series of several unusual cases (in excess of what might be expected) adds to the concern. A convenient feature of case-series reports is that they can constitute the case group for a case-control study, which can then explore hunches about causes of disease.

Cross-sectional (prevalence) studies

Prevalence studies describe the health of populations. For example, in the USA, periodic surveys of the health status of the population are done by the federal government—eg, the Health Interview Survey and the Health and Nutrition Examination Survey. Analogous to the decennial census, these studies provide a snapshot of the population at a particular time.

Prevalence studies can be done in smaller populations as well. For example, the results of a survey done in a Puerto Rican pharmaceutical factory indicated an exceptionally high prevalence of gynaecomastia among employees (figure). This finding led to the hypothesis that exposure to ambient oestrogen dust in the plant might be the cause; serum concentrations of oestrogen lent support to the hypothesis. After improvements in dust control in the factory, the epidemic disappeared.³⁴ Similar prevalence studies have linked gynaecomastia with feeding of refugees³⁵ and tainted food.³⁶

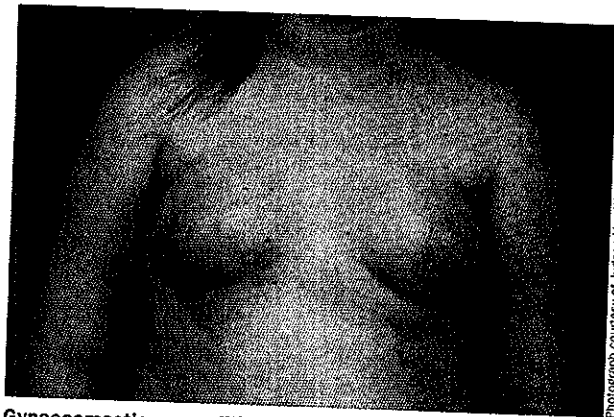
Although generally distinguished from cohort and case-control studies, the cross-sectional study can be thought of as the case-control analogue of a population cohort study.³⁷ Since both exposure and outcome are ascertained at the same time (the defining feature of a cross-sectional study), costs are small and loss to follow-up is not a problem. However, because exposure and outcome are identified at one time point, the temporal sequence is often impossible to work out. An exception would be long-standing exposures, such as sex or blood type, which unquestionably preceded the outcome. For exposures that vary, information of aetiological relevance from the past might be more useful than current information.³⁷

Surveillance

Surveillance is another important type of descriptive study. Surveillance can be thought of as watchfulness over a community. A more formal definition is "the ongoing systematic collection, analysis, and interpretation of health data essential to the planning, implementation, and evaluation of public health practice, closely integrated with the timely dissemination of these data to those who need to know."³⁸ The key feature here is feedback, as in a servomechanism. Prevention and control of the problem are fundamental parts of the feedback loop.

Surveillance can be either active or passive. Passive surveillance relies on data generally gathered through traditional channels, such as death certificates. By contrast, active surveillance searches for cases. The reporting of abortion-related deaths provides an example. Since 1972, the US Centers for Disease Control and Prevention has been doing active surveillance of these deaths in the USA, using multiple overlapping sources—ie, state maternal mortality study committees, professional organisations, newspapers, and colleagues in the specialty. By comparison with official statistics, active surveillance identifies about twice as many deaths.³⁹ Similarly, underreporting of maternal deaths remains an international problem.⁴⁰⁻⁴³

Epidemiological surveillance has made important contributions to health, but none more impressive than smallpox eradication. Surveillance and containment were responsible for the elimination of smallpox from the world, an extraordinary public-health achievement.⁴⁴ Whereas mass immunisation of the world's population had failed, the approach of identification of cases through surveillance and then immunisation of susceptible persons in the surrounding communities stopped transmission. Without a non-human vector, the virus died out.



Photograph courtesy of Judson Van Wyk, M.D., University of North Carolina School of Medicine, NC, USA.

Gynaecomastia, a condition associated with occupational exposure to oestrogen dust, feeding of refugees, and ingestion of tainted food

Ecological correlational studies

Correlational studies look for associations between exposures and outcomes in populations rather than in individuals.⁴ Because much data might already have been collected, correlational studies can be a convenient initial search for hypotheses. The measure of association between exposure and outcome is the correlation coefficient r , which indicates how linear is the relation between exposure and outcome. For example, death rates from coronary artery disease correlate with per capita sales of cigarettes.⁴⁵ By contrast, access to safe legal abortion is inversely correlated with maternal mortality.⁴⁶⁻⁴⁹ The range of potential associations to be explored is nearly limitless.⁵⁰

Correlational studies have important limitations—ie, the inability to link exposure to outcome in individuals and to control for confounding (a mixing or blurring of effects). An example of the latter is the observation that death rates from coronary artery disease also correlate with the number of colour television sets per capita.⁴ Even television's harshest critics are unlikely to argue that it clogs coronary vessels, an example of "ecological fallacy".³⁷ Although a link between television violence and violence in schools seems more plausible, whether this association is indeed causal is difficult to establish.⁵¹

Uses of descriptive studies

Trend analysis

Descriptive studies have several useful roles. Being able to monitor the health of populations is important to health-care administrators. Trend analysis is often provided by ongoing surveillance. Examples include the emerging epidemic of syphilis in the Russian Federation,^{52,53} and the international epidemic of multiple births, prematurity, and low birthweight caused by assisted reproductive technologies.⁵⁴⁻⁵⁸ Both epidemics raise troubling societal issues.

Planning

A second use is health-care planning. For example, the introduction of laparoscopy, coupled with bad press about oral contraceptives and intrauterine devices, tripled US rates of tubal sterilisation in the 1970s.⁵⁹ Hospitals and ambulatory surgery centres had a surge in demand for operations, yet less need for hospital beds. Similarly, the introduction of highly active antiretroviral therapy for patients with AIDS decreased bed occupancy.⁶⁰

Clues about cause

A third use of descriptive studies is to develop hypotheses about cause (panel). Observant clinicians noted an association between high concentrations of oxygen in incubators and blindness in babies; this finding led to analytical studies, then a randomised controlled trial, confirming the association.⁶¹ Unexpectedly high rates of cancer among women who had painted radium dials in watches alerted investigators to the danger of this occupational exposure.⁶²

Advantages and disadvantages

Descriptive studies have both strengths and weaknesses. Often, the data are already available and thus inexpensive and efficient to use. Furthermore, few ethical difficulties exist. However, descriptive studies have important limitations. Temporal associations between putative causes and effects might be unclear. A dangerous pitfall is that the investigators might draw causal inferences when none is possible.³⁷

Overstepping the data

A common mistake in inference is post hoc ergo propter hoc reasoning (after the thing, therefore on account of the thing), an example of a false cause.⁶³ In other words, a temporal association is incorrectly inferred to be a causal one. In one egregious example, seven women in Pasadena, California, created controversy around the world in the late 1980s. Seen in one physician's office, the women had developed functional ovarian cysts while taking the new multiphasic oral contraceptive pills.⁶⁴ Based on this uncontrolled observation, a case-series report warned that phasic pills might pose a threat to patient health and safety. The media printed the story, and unknown numbers of women around the world stopped taking their pills,⁶⁵ because they did not understand the difference between functional cysts and ovarian cancer. Since the report had no comparison group—eg, women using monophasic pills or those using none—the authors could not draw any conclusions about cause of disease.

In the wake of this report, damage-control efforts started quickly. Within 2 years, a publication showed no temporal association between the marketing of multiphasic pills and the number of women admitted to hospital for treatment of benign ovarian cysts.⁶⁶ However, 5 years elapsed before cohort⁶⁷ and case-control studies⁶⁸ confirmed no association between multiphasic pills and ovarian cysts. By this time, the public-health damage had been done.⁶⁹

Another sad example in which misinterpretation of descriptive studies hurt public health is routine electronic fetal monitoring in labour. A quarter of a century ago, temporal associations between the introduction of electronic fetal monitoring and falling perinatal mortality rates led to the conclusion that continuous fetal heart rate monitoring was a good thing.⁷⁰ Moreover, authorities of the day predicted a 50% reduction in perinatal morbidity and mortality from its use.⁷⁰

Based on this rosy assessment from prominent obstetricians, this expensive and intrusive technology took obstetrics by storm. However, the initial upbeat assessment did not survive scientific scrutiny. Years later, a meta-analysis of the randomised controlled trials showed that, by comparison with routine intermittent auscultation, routine electronic fetal monitoring confers no lasting benefit to infants, whereas it significantly increases operative deliveries; thus harming women.⁷¹ Based on objective reviews, both the Canadian Task Force on the Periodic Health Examination⁷² and the US

Preventive Services Task Force⁷³ have given routine electronic fetal monitoring a D recommendation (fair evidence against its routine use). Despite this advice, about three-fourths of all births in the USA include electronic fetal monitoring.⁷³ Failure to appreciate the limitations of descriptive studies has caused lasting harm and squandered billions of dollars.

Conclusion

Descriptive studies are often the first, tentative approach to a new event or condition. These studies generally emphasise features of a new disease or assess the health status of communities. Health administrators use descriptive studies to monitor trends and plan for resources. By contrast, epidemiologists and clinicians generally use descriptive reports to search for clues of cause of disease—ie, generation of hypotheses. In this role, descriptive studies are often a springboard into more rigorous studies with comparison groups. Common pitfalls of descriptive reports include an absence of a clear, specific, and reproducible case definition, and interpretations that overstep the data. Studies without a comparison group do not allow conclusions about cause of disease.

We thank Willard Cates and David L Sackett for their helpful comments on an earlier version of this report. Much of this material stems from our 15 years of teaching the Berlex Foundation Faculty Development Course.

References

- 1 Hulley SB, Cummings SR, Browner WS, Grady D, Hearst N, Newman RB, eds. *Designing clinical research: an epidemiologic approach*, 2nd edn. Baltimore: Lippincott Williams and Wilkins, 2001.
- 2 Fletcher RH, Fletcher SW. Clinical research in general medical journals: a 30-year perspective. *N Engl J Med* 1979; 301: 180-83.
- 3 Last JM, ed. *A dictionary of epidemiology*, 2nd edn. New York: Oxford University Press, 1988.
- 4 Hennekens CH, Buring JE. *Epidemiology in medicine*. Boston: Little, Brown and Company, 1987.
- 5 Lilienfeld AM, Lilienfeld DE. *Foundations of epidemiology*, 2nd edn. New York: Oxford University Press, 1980.
- 6 Anderson FA Jr, Wheeler HB, Goldberg RJ, et al. A population-based perspective of the hospital incidence and case-fatality rates of deep vein thrombosis and pulmonary embolism. The Worcester DVT Study. *Arch Intern Med* 1991; 151: 933-38.
- 7 Sasco AJ, Lowenfels AB, Pasker-de Jong P. Review article: epidemiology of male breast cancer—a meta-analysis of published case-control studies and discussion of selected aetiological factors. *Int J Cancer* 1993; 53: 538-49.
- 8 Thomas DB. Breast cancer in men. *Epidemiol Rev* 1993; 15: 220-31.
- 9 Marshall LM, Spiegelman D, Barbieri RL, et al. Variation in the incidence of uterine leiomyoma among premenopausal women by age and race. *Obstet Gynecol* 1997; 90: 967-73.
- 10 Jaremin B, Kotulak E, Starnawska M, Mrozinski W, Wojciechowski E. Death at sea: certain factors responsible for occupational hazard in Polish seamen and deep-sea fishermen. *Int J Occup Med Environ Health* 1997; 10: 405-16.
- 11 Krane BD, Ricci MA, Sweeney WB, Deshmukh N. All-terrain vehicle injuries: a review at a rural level II trauma center. *Am Surg* 1988; 54: 471-74.
- 12 Gabert T, Stueland DT. Recreational injuries and deaths in northern Wisconsin: analysis of injuries and fatalities from snowmobiles over 3 years. *Wis Med J* 1993; 92: 671-75.
- 13 Zinn J, Zalokowski A. The use of the Delphi panel for consensus development on indicators of laboratory performance. *Clin Lab Manage Rev* 1999; 13: 386-408.
- 14 Hager WD, Eschenbach DA, Spence MR, Sweet RL. Criteria for diagnosis and grading of salpingitis. *Obstet Gynecol* 1983; 61: 113-14.
- 15 Hadgu A, Westrom L, Brooks CA, Reynolds GH, Thompson SE. Predicting acute pelvic inflammatory disease: a multivariate analysis. *Am J Obstet Gynecol* 1986; 155: 954-60.
- 16 Wiesenthal AM, Ressler M, Caston SA, Todd JK. Toxic shock syndrome, I: clinical exclusion of other syndromes by strict and screening definitions. *Am J Epidemiol* 1985; 122: 847-56.
- 17 Anon. 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. *MMWR Morb Mortal Wkly Rep* 1992; 41: 1-19.
- 18 Yon JL Jr, Lutz MH, Girtanner RE, Averette HE. Adenosis and adenocarcinoma of the vagina in young women: a review. *Gynecol Oncol* 1974; 2: 508-17.
- 19 Levine RJ, Mathew RM, Chenault CB, et al. Differences in the quality of semen in outdoor workers during summer and winter. *N Engl J Med* 1990; 323: 12-16.
- 20 McNeill WH. *Plagues and peoples*. New York: Anchor Books, 1998.
- 21 Parko A. Longitudinal study of dental caries prevalence and incidence in the rapakivi (high fluoride) and olivine diabase (low fluoride) areas of Laitila, Finland. *Proc Finn Dent Soc* 1990; 86: 103-06.
- 22 Diaz-Barriga F, Batres L, Calderon J, et al. The El Paso smelter 20 years later: residual impact on Mexican children. *Environ Res* 1997; 74: 11-16.
- 23 Ebers GC, Sadovnick AD. The geographic distribution of multiple sclerosis: a review. *Neuroepidemiology* 1993; 12: 1-5.
- 24 Chapuy MC, Preziosi P, Maamer M, et al. Prevalence of vitamin D insufficiency in an adult normal population. *Osteoporos Int* 1997; 7: 439-43.
- 25 Ainsleigh HG. Beneficial effects of sun exposure on cancer mortality. *Prev Med* 1993; 22: 132-40.
- 26 Fears TR, Scotto J, Schneiderman MA. Skin cancer, melanoma, and sunlight. *Am J Public Health* 1976; 66: 461-64.
- 27 Wingo PA, Higgins JE, Rubin GL, Zahner SC, eds. *An epidemiologic approach to reproductive health*. Geneva: WHO, 1994.
- 28 Schenken JR. Hepatocellular adenoma: relationship to oral contraceptives? *JAMA* 1976; 236: 559.
- 29 Rooks JB, Ory HW, Ishak KG, et al. Epidemiology of hepatocellular adenoma: the role of oral contraceptive use. *JAMA* 1979; 242: 644-48.
- 30 Waugh RJ. Penile frostbite, an unforeseen hazard of jogging. *N Engl J Med* 1977; 296: 178.
- 31 Levit F. Jogger's nipples. *N Engl J Med* 1977; 297: 1127.
- 32 McBride DQ, Lehman LP, Mangiardi JR. Break-dancing neck. *N Engl J Med* 1985; 312: 186.
- 33 Anon. Pneumocystis pneumonia: Los Angeles. *MMWR Morb Mortal Wkly Rep* 1981; 30: 250-52.
- 34 Harrington JM, Stein GF, Rivera RO, de Morales AV. The occupational hazards of formulating oral contraceptives: a survey of plant employees. *Arch Environ Health* 1978; 33: 12-15.
- 35 Sattin RW, Roisin A, Kafriksen ME, Dugan JB, Farer LS. Epidemic of gynecomastia among illegal Haitian entrants. *Public Health Rep* 1984; 99: 504-10.
- 36 Fara GM, Del Corvo G, Bernuzzi S, et al. Epidemic of breast enlargement in an Italian school. *Lancet* 1979; 2: 295-97.
- 37 Rothman KJ. *Modern epidemiology*. Boston: Little, Brown and Company, 1986.
- 38 Centers for Disease Control. *Comprehensive plan for epidemiologic surveillance*. Atlanta, GA: Centers for Disease Control, 1986.
- 39 Cates W Jr, Smith JC, Rochat RW, Patterson JE, Dolman A. Assessment of surveillance and vital statistics data for monitoring abortion mortality, United States, 1972-1975. *Am J Epidemiol* 1978; 108: 200-06.
- 40 Kao S, Chen LM, Shi L, Weinrich MC. Underreporting and misclassification of maternal mortality in Taiwan. *Acta Obstet Gynecol Scand* 1997; 76: 629-36.
- 41 Schuitemaker N, Van Roosmalen J, Dekker G, Van Dongen P, Van Geijn H, Gravenhorst JB. Underreporting of maternal mortality in The Netherlands. *Obstet Gynecol* 1997; 90: 78-82.
- 42 Bouvier-Colle MH, Varnoux N, Costes P, Hatton F. Reasons for the underreporting of maternal mortality in France, as indicated by a survey of all deaths among women of childbearing age. *Int J Epidemiol* 1991; 20: 717-21.
- 43 Comas A, Navarro A, Conde J, Blasini I, Adamsons K. Misreporting of maternal mortality in Puerto Rico. *Bol Asoc Med P R* 1990; 82: 343-46.
- 44 Foege WH. Smallpox eradication in west and central Africa revisited. *Bull World Health Organ* 1998; 76: 233-35.
- 45 Friedman GD. Cigarette smoking and geographic variation in coronary heart disease mortality in the United States. *J Chronic Dis* 1967; 20: 769-79.
- 46 Anon. Abortion: one Romania is enough. *Lancet* 1995; 345: 137-38.
- 47 Stephenson P, Wagner M, Badea M, Serbanescu F. The public health consequences of restricted induced abortion: lessons from Romania. *Am J Public Health* 1992; 82: 1328-31.
- 48 Seward PN, Ballard CA, Ulene AL. The effect of legal abortion on the rate of septic abortion at a large county hospital. *Am J Obstet Gynecol* 1973; 115: 335-38.
- 49 Stewart GK, Goldstein PJ. Therapeutic abortion in California: effects of septic abortion and maternal mortality. *Obstet Gynecol* 1971; 37: 510-14.

- 50 Noller KL, Resseguie LJ, Voss V. The effect of changes in atmospheric pressure on the occurrence of the spontaneous onset of labor in term pregnancies. *Am J Obstet Gynecol* 1996; 174: 1192-99.
- 51 Centervall BS. Television and violence: the scale of the problem and where to go from here. *JAMA* 1992; 267: 3059-63.
- 52 Borisenko KK, Tichonova LI, Renton AM. Syphilis and other sexually transmitted infections in the Russian Federation. *Int J STD AIDS* 1999; 10: 665-68.
- 53 Tichonova L, Borisenko K, Ward H, Meheus A, Gromyko A, Renton A. Epidemics of syphilis in the Russian Federation: trends, origins, and priorities for control. *Lancet* 1997; 350: 210-13.
- 54 Tough SC, Greene CA, Svenson LW, Belik J. Effects of in vitro fertilization on low birth weight, preterm delivery, and multiple birth. *J Pediatr* 2000; 136: 618-22.
- 55 Bider D, Livshitz A, Tur Kaspa I, Shulman A, Levron J, Dor J. Incidence and perinatal outcome of multiple pregnancies after intracytoplasmic sperm injection compared to standard in vitro fertilization. *J Assist Reprod Genet* 1999; 16: 221-26.
- 56 Steegers-Theunissen RP, Zwertbroek WM, Huisjes AJ, Kanhai HH, Bruinse HW, Merkus HM. Multiple birth prevalence in The Netherlands: impact of maternal age and assisted reproductive techniques. *J Reprod Med* 1998; 43: 173-79.
- 57 Dunn A, Macfarlane A. Recent trends in the incidence of multiple births and associated mortality in England and Wales. *Arch Dis Child Fetal Neonatal Ed* 1996; 75: F10-19.
- 58 Anon. Pregnancies and births resulting from in vitro fertilization: French national registry, analysis of data 1986 to 1990. FIVNAT (French In Vitro National). *Fertil Steril* 1995; 64: 746-56.
- 59 Peterson HB, Greenspan JR, DeStefano F, Ory HW, Layde PM. The impact of laparoscopy on tubal sterilization in United States hospitals, 1970 and 1975 to 1978. *Am J Obstet Gynecol* 1981; 140: 811-14.
- 60 Anon. Update: trends in AIDS incidence, deaths, and prevalence—United States, 1996. *MMWR Morb Mortal Wkly Rep* 1997; 46: 165-73.
- 61 Silverman WA. Memories of the 1953-54 Oxygen Trial and its aftermath: the failure of success. *Control Clin Trials* 1991; 12: 355-58.
- 62 Stebbings JH, Lucas HF, Stehney AF. Mortality from cancers of major sites in female radium dial workers. *Am J Ind Med* 1984; 5: 435-59.
- 63 Copi IM, Cohen C. Introduction to logic, 10th edn. Upper Saddle River, NJ: Prentice Hall, 1998.
- 64 Caillouette JC, Kochler AL. Phasic contraceptive pills and functional ovarian cysts. *Am J Obstet Gynecol* 1987; 156: 1538-42.
- 65 Martinez F. Responsibility of health providers and the media in response to scientific information. *Eur J Contracept Reprod Health Care* 1997; 2: 25-30.
- 66 Grimes DA, Hughes JM. Use of multiphasic oral contraceptives and hospitalizations of women with functional ovarian cysts in the United States. *Obstet Gynecol* 1989; 73: 1037-39.
- 67 Lanes SF, Birmann B, Walker AM, Singer S. Oral contraceptive type and functional ovarian cysts. *Am J Obstet Gynecol* 1992; 166: 956-61.
- 68 Holt VL, Daling JR, McKnight B, Moore D, Stergachis A, Weiss NS. Functional ovarian cysts in relation to the use of monophasic and triphasic oral contraceptives. *Obstet Gynecol* 1992; 79: 529-33.
- 69 Jones EF, Beniger JR, Westoff CF. Pill and IUD discontinuation in the United States, 1970-1975: the influence of the media. *Fam Plann Perspect* 1980; 12: 293-300.
- 70 Quilligan EJ, Paul RH. Fetal monitoring: is it worth it? *Obstet Gynecol* 1975; 45: 96-100.
- 71 Thacker SB, Stroup DF, Peterson HB. Efficacy and safety of intrapartum electronic fetal monitoring: an update. *Obstet Gynecol* 1995; 86: 613-20.
- 72 Canadian Task Force on the Periodic Health Examination. The Canadian guide to clinical preventive care. Ottawa: Minister of Supply and Services Canada, 1994.
- 73 US Preventive Services Task Force. Guide to clinical preventive services, 2nd edn. Baltimore, MD: Williams and Wilkins, 1996.