Design 1: Study **KNOWN** amounts of experience, PT_1 & PT_0

Observe c cases; classify into $_1$ & $_0$ categories $\rightarrow c_1$ & c_0
[the *case-series*, i.e., the *numerator-series*]

$\widehat{ID}_1 = c_1/PT_1$ & $\widehat{ID}_0 = c_0/PT_0 \rightarrow \widehat{IDR} = \widehat{ID}_1 \div \widehat{ID}_0$

Model: $c_i \sim Poisson(\mu_i = ID_i \times PT_i), i = 0, 1$; c_1 indep't of c_0.

CI for $\log IDR$: $\log \widehat{IDR} \pm z_{a/2}(1/c_1 + 1/c_0)^{1/2}$ SE a fn. of numbers of cases

Design 2: Study the same base (source).

Observe c cases; classify into $_1$ & $_0$ categories $\rightarrow c_1$ & c_0
[the *case-series*, i.e., the *numerator-series*]

ESTIMATE the *relative* magnitudes of PT_1 & PT_0 via a *base-series* (a *denominator-series)*, i.e., a representative sample of d person-moments from the base:
... classify these into $_1$ & $_0$ categories $\rightarrow d_1$ & d_0

$\rightarrow \widehat{PT_1} = (d_1/d) \times PT \quad \& \quad \widehat{PT_0} = (d_0/d) \times PT$

$\rightarrow \widehat{\widehat{ID}_1} = c_1/\{(d_1/d) \times PT\} \quad \& \quad \widehat{\widehat{ID}_0} = c_0/\{(d_0/d) \times PT\}$

$\rightarrow \widehat{\widehat{IDR}} = \widehat{\widehat{ID}_1} \div \widehat{\widehat{ID}_0} = (c_1/d_1) \div (c_0/d_0)$ ..... classical $\frac{ad}{bc}$

Model: $c_i \sim Poisson(\mu_i = ID_i \times PT_i), i = 0, 1$; c_1 indep't of c_0.

$d_1 \mid d \sim Binomial('n' = d,\ p_1 = PT_1/PT)$.

CI for $\log IDR$: $\log \widehat{\widehat{IDR}} \pm z_{a/2}(1/c_1 + 1/c_0 + 1/d_1 + 1/d_0)^{1/2}$ ...$v = \frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}$

$1/d_1 + 1/d_0$: price for *estimating* $PT_1 : PT_0$ ratio from a *sample*.

SE: fn. of numbers c_1, c_0 in case, and d_1, d_0 in denominator, series.

Design 2: **modern** way to view "case-control" variant of *the* etiologic study.

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ESTIMABILITY AND ESTIMATION IN CASE-REFERENT STUDIES

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The concepts that case-referent studies provide for the estimation of "relative risk" only if the illness is "rare," and that the rates and risks themselves are inestimable, are overly superficial and restrictive. The ratio of incidence densities (forces of morbidity)—and thereby the instantaneous risk-ratio—is estimable without any rarity-assumption. Long-term risk-ratio can be computed through the coupling of case-referent data on exposure rates for various age-categories with estimates, possibly from the study itself, of the corresponding age-specific incidence-densities for the exposed and nonexposed combined —but again, no rarity-assumption is involved. Such data also provide for the assessment of exposure-specific absolute incidence-rates and risks. Point estimation of the various parameters can be based on simple relationships among them, and in interval estimation it is sufficient simply to couple the point estimate with the value of the chi square statistic used in significance testing.

biometry; statistics

The principles that currently govern epidemiologic thinking as to the fundamentals of case-referent (case-"control") studies do not apply to the most common type of such study in chronic-disease epidemiology. Here the principles are extended to encompass this kind of study. A simple, general-purpose statistical approach is also proposed. The results presented are generally self-evident, but some explanations are offered in appendix 1.

1. The classical principles

1.1. Essence. The prevailing principles concerning the estimability of parameters in case-referent studies derive from a classical paper by Cornfield (1). The principles might be expressed as follows (1, 2): First, the ratio of the odds of developing the illness for the exposed as compared to the non-exposed equals the ratio of the odds of having been exposed, contrasting cases of the illness to a reference series, and therefore the illness-odds ratio contrasting the exposed to the non-exposed is estimable from case-referent studies; and second, this parameter is approximately equal to the risk ratio when the illness is rare. The rationale is as follows (1, 2): Given risks of illness $R_1 = A/(A + C)$ and $R_0 = B/(B + D)$ for exposed and non-exposed people, respectively, the odds ratio for the illness is $[R_1/(1 - R_1)]/[R_0/(1 - R_0)] = AD/BC = (A/B)/(C/D)$. The last formulation for the odds ratio for illness between the exposed and the non-exposed reveals the identity of this parameter with the odds ratio for past exposure between cases and non-cases. Obviously, the ratio A/B is estimable from a series of cases, and C/D can be estimated from a reference (comparison, "control") series. Finally, the odds ratio parameter can be seen to equal the risk ratio (R_1/R_0) itself on the condition that $(1 - R_0)/(1 - R_1) = 1$, and this condition obtains with

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e.g.	Index cat.$(_1)$	Ref. cat. $(_0)$	Subjects	Event	c_1	c_0	PT_1 (D_1)	PT_0 (D_0)	d_1	d_0
4	Women	Men	Pilots	Crash	2	136	0.06PT	0.94PT		
10	Essex	non-Essex	Women 16-24y	Visit GU Clinic	13	1449	$0.0203 \times W \times$ 1yr	$0.9797 \times W \times$ 1yr		
26	Southwark & Vauxhall	Lambeth	Water Co. Clients	Cholera death	286	14	40,046 homes $\times$ 4 weeks	26,107 homes $\times$ 4 weeks		
13	Bas du filet	Milieu/haut du filet	Tirs	Buts	36	15				
9	Adult-size soccer ball	Junior-size soccer size ball	Children $\leq 11y$	Wrist fracture	12	3				
11	Received MMR vaccine	Did not	Children	Dx. of autism	263	53	1.65×10^6c-y	0.48×10^6c-y		
11	Received HPV vaccine	Received Placebo	HPV – Women	Persistent HPV	0	41	1048 w-y	1076.9 w-y		
	Received Salk vaccine	Received Placebo	Children 1954	Paralytic polio	33	115	200,745 children $\times$ 8 months	201,229 children $\times$ 8 months		
31	Hx + Smoking	Hx- Smoking	Men 50-54	Bladder cancer	24	1			22	4
	Heat/cook $\bar{c}$ woodstove	Do Not	residents of Gaspé	Nasal polyposis	45	10			14	41
	On cell phone	Not on phone	automobile drivers	Traffic accident	c_1	c_0				
	Wear helmet	Do not	cyclists	Serious head injury	c_1	c_0				
	Blood Group O	Blood Group A	UK adults	Peptic ulcer						
			London		911	590			4578	4219
			Manchester		361	246			4532	3775
			Newcastle		396	219			6598	5261