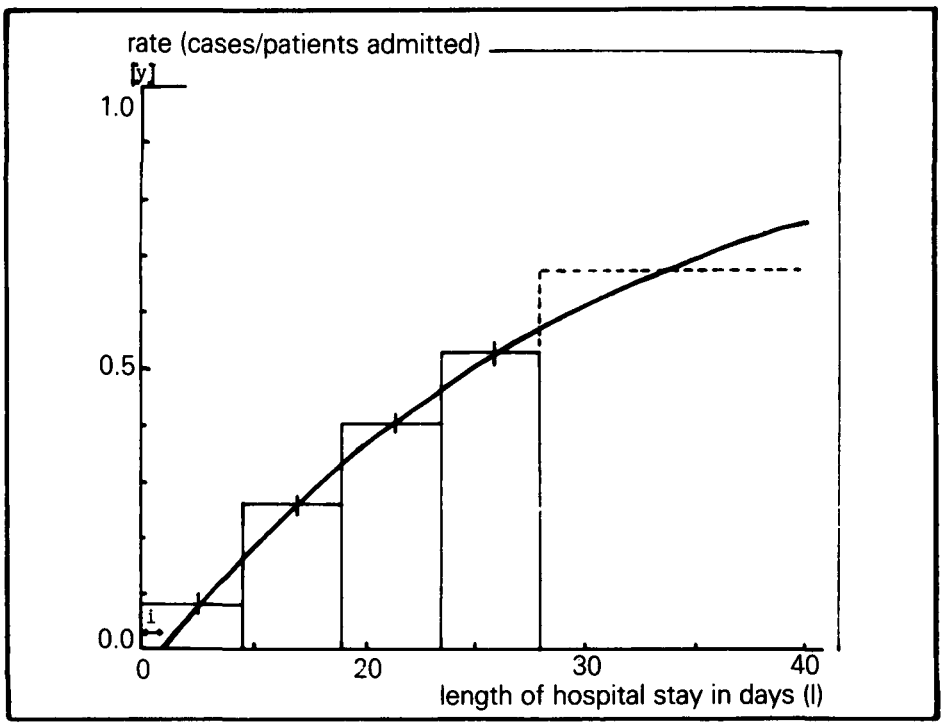


Figure. *Relation between the rate of cases of hospital infection (y) and length of hospital stay (l).* The curve $y=1-e^{-0.0246(l-i)}$ is drawn. i is the incubation period according to linear regression analysis (1.61 days).

that it allows for an incubation period. An advantage is that the force of infection may be calculated both in incidence and in prevalence surveys. The results may be different, depending on how well reality corresponds with the underlying assumptions of the model.

The contribution to the total force of infection of different kinds of nosocomial infections may be analyzed using the same model. One would expect that the catalytic model is not applicable in all instances (for example, postoperative wound infections).

We conclude that in the hospitals of Chavigny and Fischer's study the catalytic model may be used to describe the epidemiology of hospital infections.[1] Once the length of the incubation period is established, it seems possible to get a fair estimate of the "force of infection" by determining the number of infected persons in relatively small samples of patients (see the calculation of a'). Further evaluation in these and other hospitals is needed to evaluate the possible use of this parameter.

REFERENCES

1. Chavigny KH, Fischer J: Nosocomial infection in a high risk cohort: An illustration of a sampling method. *Infect Control* 1983; 4:19-24.
2. Muench H: *Catalytic Models in Epidemiology.* Cambridge, Massachusetts, Harvard University Press, 1959.
3. Pinner RW, Haley RW, Blumenstein BA, et al: High cost nosocomial infections. *Infect Control* 1982; 3:143-149.
4. Madison R, Afifi AA: Definition and comparability of nosocomial infection rates. *Am J Infect Control* 1982; 10:49-52.

A.J.A. van Griethuysen
Streeklaboratorium voor de Volksgezondheid, CW2
Nijmegen, The Netherlands

Dr. Chavigny was invited to respond to A.J.A. van Griethuysen's comments.

Van Griethuysen's suggestion to calculate the "force of infection" from data collected from a fixed cohort with varying lengths of stay as described in the original article "Nosocomial infection in a high risk cohort: An illustration of a sampling method," presents interesting challenges.[1] In response, three issues will be raised: first, the effects of definitions and calculations in applying a catalytic formula; second, the appropriateness of using the type of analysis on data collected by this particular sampling method; and third, the implications of the suggested method of analysis for infection control practice.

A catalytic model originally applied by Muench is suggested as a method of estimating the force of infection, defined as effective contacts per patient per time unit. By changing the original formula to a simple linear regression equation, a good approximation of the infection force, "a," and the incubation period, "i," are determined. The formula for the catalytic model has been restated by Kleinbaum and Kupper[2] as follows:

$$CI \approx I - e^{-(ID)\ (t''-t')}$$

where

CI = Cumulative Incidence (number of cases of nosocomial infection divided by the population at risk); and

ID = Incidence Density rate (the number of nosocomial infection case "inceptions" over a time period (t, $t+\Delta t$) divided by the integral of the specified period during which the population at risk was followed; $(t''-t')$ is the time period over which it is reasonable to suppose a constant value for $ID_{(t,t+\Delta t)}$.

The formula can be adjusted to nearly coincide with van Griethuysen's nomenclature as follows:

$$\text{Equation (1): } y = 1 - e^{-(ID)\cdot\Delta t}$$

In other words, the catalytic model is a statement of the relationship between cumulative incidence ("CI" or "y") rates used in the original article and incidence density ("ID" or "a"[3]) rates of cases of infection per time in days. Van Griethuysen suggests the use of this method to produce "more quantitative conclusions" for the study; however, the use of ID rates for infection control practice is important and van Griethuysen raises a question of general interest to practice.

The original data has, in fact, been quantified through a (modified) life table analysis (Figure 1).

Figure 1 shows an (extrapolated) average population infected at 30 days of not more than 40%. The author of the letter computes > 50% infected population at 29.8 days. In addition, incidence density rates for each hospital are equal to 2.1 (Hospital A) and 1.52 (Hospital B) per 100 days, for a total rate in both hospitals of 1.76 per

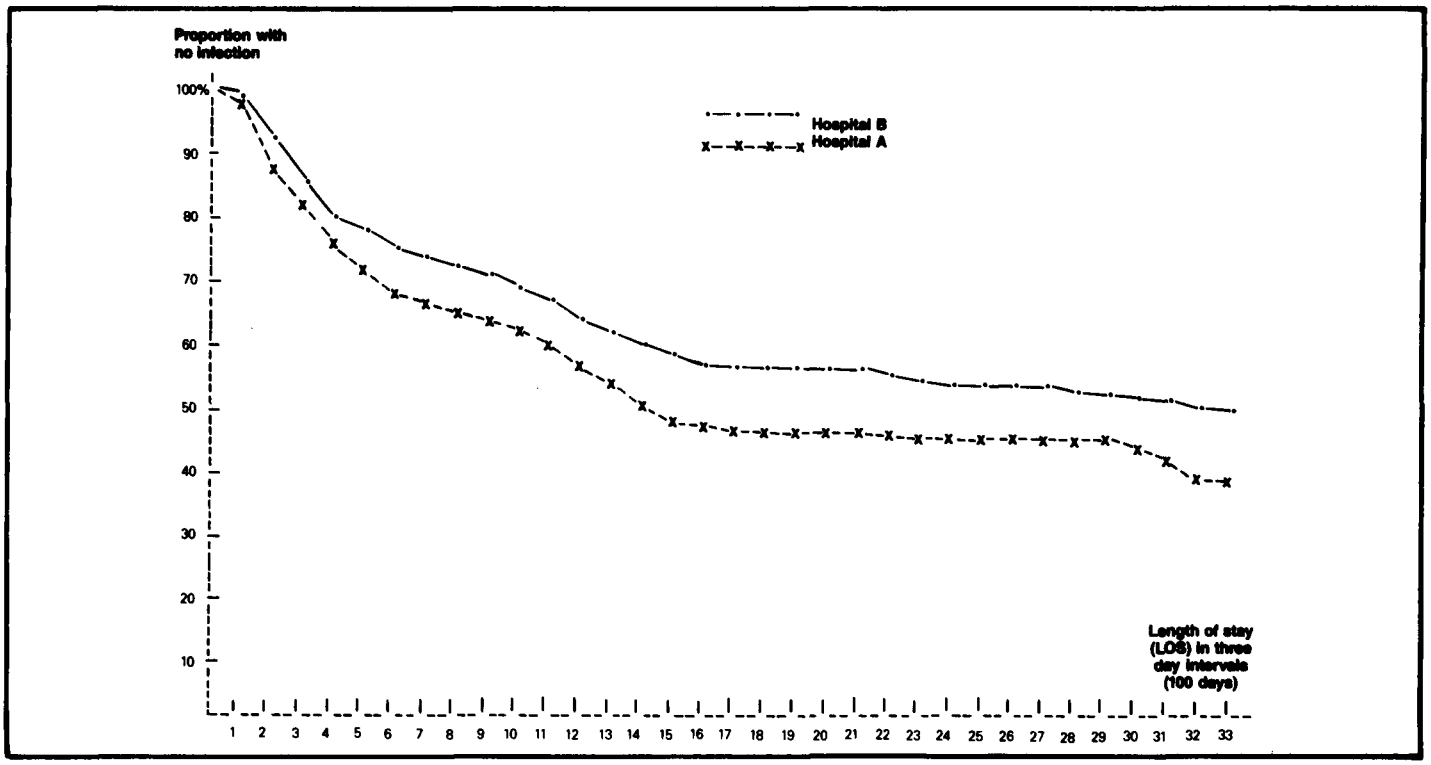


Figure 1. A comparison of proportions of patients surviving without infection in two university hospitals.

100 days. Another discrepancy arises concerning the incubation period of 1.61 computed from the linear regression analysis, for which we have no figures for comparison and must resort to observed facts.

A three-day incubation period was applied for defining a case of nosocomial infection using the Centers for Disease Control[4] definitions for the 272 cases of disease. Eight cases of the 272 were "non-typical": for instance, two cases suffered B-streptococcal infection after 24 hours in the hospital, and four other cases were readmissions after a three-day discharge period for a nosocomial infection. A level of 2.5 days is suggested as a lower limit for an estimate of "i," the incubation period, to allow an acceptable approximation.

The discrepancies between van Griethuysen's results and the quantifications from the original data require further exploration. Let us begin with the calculation of the incubation period "i=1.61." The estimate "i" is less than 2.5 days, perhaps because these data have borderline amenability to estimate such a delicate parameter, especially using the overall equation $y=1-e^{-0.0246(1.16)}$ for each length of stay (LOS) stratum or group. Additionally, the incidence density rate, "a," is calculated for each LOS interval; however, "i" applies to all strata (perhaps as a weighted average?). It is likely that the incubation period will vary in each group, particularly if cases occur at the beginning of each LOS time period, necessitating the inclusion of incubation days from the previous LOS stratum.

The difference between the incidence density rate "a" of 0.0176 calculated from the original data, and 0.0246, calculated by van Griethuysen, is more complex to explain and the following discussion may also apply to the differences in survival rates, as well as the difference in ID rates.

The method of calculation can alter the magnitude of the ID rate. Consider the following: from Equation (1) above, we get:

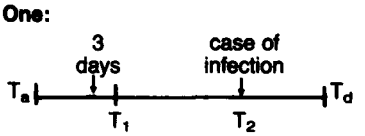
Equation (2):

$$ID = \frac{\ln(1 - y)}{\Delta t}$$

From the percentage rates from Figure 4 of the original paper, for values of "y" we compute the results listed in Table 1, which yields a population weighted average, ID=0.0221 (Table 1). This ID of 0.0221 is larger than the value of 0.0175 obtained from the raw data, and slightly less than the estimate of 0.0246, but very close given that the methods of calculation differ.

Of more critical importance than methods of calculation is the definition of Δt in Equation (1), the time difference over which the cases occur. Four definitions are illustrated below:

One:

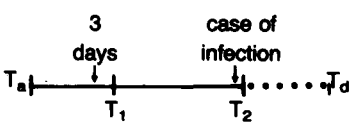


where $\Delta t = T_a - T_d$

Time admission (T_a) and discharge (T_d) = LOS

Δt = LENGTH OF STAY

Two:



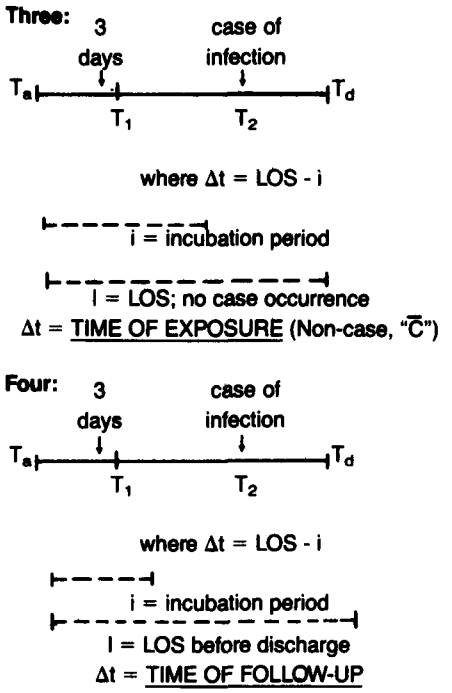
where Δt = LOS - i

i = incubation period

I = LOS before case occurrence

Δt = TIME OF EXPOSURE (Case, "C")

https://doi.org/10.1017/S0195941700058409 Published online by Cambridge University Press



Length of stay, definition one, does not consider the three-day incubation period and reflects the total hospital admission period. Definition two considers the exposure period for a case (C) of nosocomial disease to be up to the time of case diagnoses less the incubation period; however, definition three shows the exposure period to be up to the time of discharge for a non-case ($\bar{C}$). The only difference between definitions three and four is the focus of concern where definition three expresses exposure as risk to the patient and community, and definition four is time of follow-up or the period when the hospital epidemiologist is interested in providing a protected and safe environment.

Van Griethuysen equates time of exposure with length of stay. He then uses an average LOS for each time stratum for his calculations, as we did in Table 1. By redefining Δ/t to mean period of follow-up (definition four) for each stratum, the values of "a," the LOS stratum specific ID rates change as shown in Table 2.

These computations yield a population weighted average ID=.0188, with 0.0188 much closer to 0.0175 calculated from the original data. Now, of course, the ID departs from 0.0246 and this number, 0.0188, is smaller than our first number 0.0221 because we have added more days in the denominator. This should give a slightly low estimate of ID, yet it is still larger than 0.0175. This latter value was computed using the formula for fixed cohorts recommended by Morganstern et al,[5] which utilizes definitions two and three to define exposure period for cases and non-cases. The reason for this difference between the ID rates may be that the formula is an approximation compared to the precise computations from the original figures and applies information not available to the author. What is interesting is that the catalytic model gives a better "fit" using definition four of Δt —the follow-up period, and raises the question: is the better approximation due to these figures reflecting the assumptions required to use the catalytic model? This question is also related to the use and applications of incidence density rates rather than cumulative incidence rates.

Van Griethuysen expresses concern about the constancy of the force of infection in the sample, sometimes referred to as the stability of the population. This assumption seems robust if the time period Δt is short enough to make it reasonable, particularly when the disease is rare. In the case of the cohort selected by the sampling method, the disease cannot be regarded as rare, as the stated objective of designing the method was to increase case yield. The result was a cumulative incidence rate of over 29%. Clearly the problem of constancy over the nine-day strata becomes a serious issue. It seems unlikely in this cohort that the nine-day period is short enough to ensure stability. The use of the total follow-up period to compute an estimate which is close to the original ID rate seems to support this postulate. If fewer and fewer cases occur unevenly in each time stratum the use of the follow-up period, by increasing the denominator, may also increase precision. Alternatively, the sampling method can be adjusted to decrease case yield, where the model should achieve a better approximation in a lower risk, fixed cohort.

TABLE 1

NINE-DAY STRATUM SPECIFIC INCIDENCE DENSITY RATES CALCULATED WITH EQUATION (1)*

Δ t	y	ID or "a"	Number of Individuals
5	.0847	.0177	189
14	.2606	.0216	188
23	.4052	.0226	116
32	.5302	.0236	149
41	.6750	.0274	120

*Data from reference 1.

TABLE 2

NINE-DAY STRATUM SPECIFIC INCIDENCE DENSITY RATES*

Δt	y	ID or "a"	Number of Individuals
9	.0847	.0098	189
18	.2606	.0168	188
27	.4052	.0193	116
36	.5302	.0210	140
45	.6750	.0250	120

*Δt = Follow-up period.

https://doi.org/10.1017/S0195941700058409 Published online by Cambridge University Press

In order to apply the catalytic model, the CI rate must already be known. In infection control, rates are usually computed using the number of discharges as an estimate of the p.a.r., the denominator, because this information is not easily available. When the CI rates are known, then the decision to calculate ID rates must be made. In the original article, the sampling method was designed in order to define groups of patients representing the populations at risk. It was thought to be an advantage of the method of sampling to identify a fixed cohort with different periods of exposure from dynamic cohorts admitted to two university hospitals. The objectives of the research were to calculate measures of effect ($\widehat{RR}$) and to rank and compare hospital risk factors. The choice to use CI rates was made based on these goals and illustrates that the choice of generating ID rates is a function of the research questions. What is important is that van Griethuysen most aptly points out the use of the sampling method to study the relationship and effects between incidence density and cumulative incidence—an important consideration to the field.

These arguments apply to a fixed cohort where the denominator is available. In a dynamic cohort, admission and discharges are constantly occurring, particularly in acute care hospitals where the lower the average length of stay in the hospital, the greater the velocity of change and the more unlikely it is to compute an accurate cumulative incidence rate. The force of morbidity, "a," in these circumstances may be a descriptive statistic of value and should be considered as a rate of choice for practice in acute care settings. Van Griethuysen's letter draws attention to the potential of this measure of the frequency of hazard in the practice of infection control.

REFERENCES

1. Chavigny K, Fischer J: Nosocomial infection in a high risk cohort: An illustration of a sampling method. *Infect Control* 1983; 4(1):19-25.
2. Kleinbaum DG, Kupper LL, Morgenstern H: *EpidemiologicResearch*. California, Lifetime Learning Publications, 1983.
3. Miettinen OS: Proportion of disease caused or prevented by a given exposure trait or intervention. *Am J Epidemiol* 1975; 99(5):325-332.
4. *Guidelines for Determining Presence and Classification of Infection*, Appendix II. US Dept of Health, Education and Welfare, Public Health Service, CDC, Bureau of Epidemiology, 1970, pp 17-19.
5. Morgenstern H, Kleinbaum DG, Kupper LL: Measures of disease incidence used in epidemiologic research. *Int J Epidemiol* 1980; 9(1):97-104.

K.H. Chavigny, PhD, FACE
Director and Associate Professor of Public Health
Center for Public Health Studies
Portland State University
Portland, Oregon

R. Grimson, PhD
Associate Professor of Biostatistics
Dept. of Community & Preventative Medicine
Medical School and Health Science Center
SUNY
Stony Brook, New York

https://doi.org/10.1017/S0195941700058409 Published online by Cambridge University Press