Alex Richman, Beth Israel Medical Center Helen Abbey, Johns Hopkins School of Hygiene

"But, of course, having regard to the data it would have been more than genius, it would have been magic."

Greenwood, M. 1948

INTRODUCTION

Smooth, unimodal, skewed distributions of year of onset of heroin use, derived from groups of treated heroin addicts, are called "epidemiclike" curves and are generally alleged to reflect incidence.

This paper shows how "epidemic-like" curves can be produced from treatment data without associated changes in incidence, ascertainment or duration of disorder. These findings are relevant to other types of non-infectious disorders where the number of patients ascertained is a non-linear function of time since onset.

BACKGROUND

Identification of "new cases" of heroin addiction in the community is difficult since voluntary reporting is unlikely and other forms of ascertainment are unreliable. Community surveys have difficulties in constructing suitable frames for probability sampling; establishing reliable and valid instrumentation; inferring the characteristics of those non-interviewed; relating the quantity, frequency, duration and recency of heroin use to the "need for treatment" and assessing the characteristics of the relatively small proportion of the population who admit heroin use. O'Donnell et al's probability survey of Selective Service registrants elicited 148 heroin users out of the 2,510 men interviewed (471 were not interviewed). Half of those who admitted heroin use had "used" heroin less than 10 times.

In contrast to the relatively low yield of heroin users in community surveys is the large amount of data available for heroin addicts entering treatment programs. These treatment data have been considered to be "valid" indicators of the year of onset of heroin use or heroin addiction in the community.

Graphs of these data show a rise and fall in the year of onset of heroin use among admissions; the rise and fall is considered to reflect experience in the community. Although this interpretation seems rational, it is the purpose of this paper to show how such "epidemiclike" curves can occur independently of changes in onset in the community. "Epidemic-like" curves of heroin use do not necessarily indicate a common time for exposure; the results of person-to-person spread; the removal of susceptibles; or changes in virulence. "Epidemic-like" curves of year of onset of heroin use in treated populations do not prove that there were corresponding peaks of heroin use in the community. Factors other than changes in incidence can produce "epidemic-like" distributions of the year of onset of heroin use.

PEAK YEAR OF ONSET - Assumptions

Much attention has been directed to the year of onset of heroin use (or addiction) among patients entering treatment programs. This distribution has been used to infer changes in morbidity in the community, to predict future needs for treatment, to assess the effectiveness of intervention programs, and for surveillance and monitoring of national trends. (Hunt and Chambers; Greene)

Various assumptions are implied when changes in morbidity in the community are inferred from persons entering treatment. These <u>assumptions</u> include:

i. The ratio of admissions to onsets is assumed to be constant. Changes in the number and type of admissions are assumed to represent proportionate changes in the number and types of persons in the community in need of treatment for the first time.

We can only use treatment data to reflect changes in morbidity if we know that the ratio of admissions to onsets has not changed over time. Since the probability of admission may vary over time, among different demographic subgroups and between places, assessments of community morbidity from admissions to treatment must be based on knowledge of the proportion of onsets who are admitted. If that proportion were known, treatment data would not be needed to infer changes in morbidity. A doubling in the number of new patients admitted to treatment doesn't demonstrate a doubling in the number of persons in the community in need of treatment for the first time.

ii. Smooth frequency distributions are assumed to represent homogeneous sub-populations. The greater the number of random and independent variables which are combined, the more likely the output will result in a normal distribution function with a "peak". (King)

function with a "peak". (King) The sum $x_1 + \ldots + x_n$ of independent random variables, regardless of their individual distributions, has approximately the normal distribution under very general conditions (Ljapunov Theorem). Addition of data from populations with diverse distributions of year of onset will result in a smooth distribution with a peak. (Richman and Richman, 1975) iii. Changes in percentage distributions are assumed to be equivalent to changes in population based rates.

The number of admissions of long-term addicts varies from time to time, and fluctuations in the number of long-term addicts will affect the percentage of short-term addicts among the total number admitted even without any changes in the absolute number of shortterm addicts. Changes in onset must be inferred from population based rates.

iv. The probability distribution of admission for addicts in the community (specific for time since onset) is assumed to be stable over calendar time.

HUNT'S ESTIMATION OF "LAG" IN ENTERING TREATMENT

The delay between onset of heroin use and subsequent entry into treatment is referred to as "lag". Recently "lag" data have been used to project future admissions to treatment for a given program. Hunt (1975) asserts that "lag" is stable from time-to-time, consistent from place-to-place and can be estimated from onset cohorts.

Hunt has published data on the distribution of lag intervals to be used in projecting future admissions. He assumes probability of admission is the same for addicts of specific duration of addiction regardless of year of onset, clinical correlates or complications, availability of treatment in previous years, type of current treatment or demographic characteristics. Hunt assumes that the duration of addiction or prospect of remission, or death are fixed, and do not change.

The distribution of year of onset of heroin use (or addiction) resembles graphs of time of exposure or onset of contagious disorders to such an extent that their assumptions and implications for heroin addiction have not been adequately tested. The following model has been developed for testing assumptions, implications and programmatic relevance of statistical approaches to inferring changes in incidence from distributions of year of onset among treated populations.

- <u>input variables</u> various number of years for which data collated.
- time-specific probabilities of admission among new onsets in the community.
- <u>output variables</u> distribution of time since onset among admissions for treatment.
- status variables conditions which are kept constant throughout operation of the model are incidence, duration of disorder, remission, mortality, treatment capacity, and perceptions of treatment needs.

To begin, let's construct a model with stable incidence, ratio of admissions to onsets, and duration - specific probabilities of admission from year to year. (FIGURE 1)

Later, we plan to extend this model to include other cells of Figure 1 and to consider the effect of changes on some of the factors previously listed as status variables. We will also defer consideration of the differential effect of readmissions to long standing programs being called first admissions in newly established programs.

What type of distribution of years of onset will result from the steady-state situation in Figure 1? Can we get "epidemic-like" curves without any change in incidence?

TIME SPECIFIC PROBABILITIES OF ADMISSION AMONG NEW ONSETS IN THE COMMUNITY

Let us use Hunt's projection of the time between onset and admission for those addicts entering treatment. (Later, we will use other estimates for this distribution). Hunt projected that 12% of addicts would enter treatment within 1 year, 22% within 1-2 years, 26% within 2-3 years, 26% within 3-4 years, 6% within 4-5 years, 3% within 5-6 years and 3% within 6-7 years. (FIGURE 2)

FIGURE 3 shows Hunt's projection with the number of dots representing the value of the percentage distribution. Each pattern depicts the number of patients entering treatment in a specific year following onset.

DEVELOPMENT OF THE GRAPHIC MODEL

Figure 4 shows the result of using Figure 3 (an onset-year cohort with admissions in successive years) as a module to build up the distribution of patients admitted during 1965-1975 with onset of heroin use in 1965-1975. A stable state is assumed with constant incidence of heroin use, a constant rate of treatment entry and no changes in duration of the disorder, perceptions of treatment, or treatment capacity. The onsetvear cohorts are shown horizontally, the admission groups are represented vertically. The group admitted during 1971 is flagged; it can be seen that 12 of the patients began heroin use in 1971, 22 in 1970,...and 3 began in 1965. With no change in incidence of heroin use in the community, what is the distribution of year of onset of heroin use among the 1971 group of admissions?

Figure 4 was rotated and the 1971 admission group separated in Figure 5. What was the time since onset of heroin use among patients admitted in 1971? Among the 1971 admissions the onset of heroin use had peaked 3-4 years earlier. Figure 6 converts the abscissa from years since onset to calendar year of onset. "Epidemic-like" curves occur with distributions of years between onset and admission other than Hunt's projection. (Fig.7) The model is based on assumptions of a stable state with:

- no changes in onset in the community;
- constant probability of eventual admission for addicts in the community;
- unchanging time-specific probabilities of admission;
- uniform duration of the disorder, or rate of mortality;
- fixed capacity for admitting new patients.

Such a stable state has the properties of a stationary population in a life table. In a stationary population the numbers of births and deaths are constant and the age distribution of deaths in the cohort and the age distribution in the life table population are identical (Lotka). In our demographic model for heroin addiction, the number of onsets (births) and the number of admissions (deaths) are constant over time; the distribution of time since onset of heroin use in onset cohorts is identical with the distribution of time since of heroin use in a group of admissions. Figure 6 is a mirror image of Figure 2.

In a non-truncated version of Figure 4 any column and any row would be identical, e.g., the distribution of time since onset of heroin use is identical for the cohort with onset of heroin use in 1970 and the group admitted in 1970.

Therefore, a log-normal distribution of time since onset of heroin use will appear in a group of admissions if that is the distribution among the onset cohort. This log-normal distribution is an "epidemic-like" curve.

This phenomenon of apparent clustering in time is not restricted to log-normal distributions, but also applies to normal distributions and other non-linear functions.

Pseudo-epidemics (or clustering in time without change in incidence) can occur in other conditions where there is a log-normal distribution of time between exposure and diagnosis. These conditions include, in addition to bacterial and viral diseases (Sartwell), postradiation leukemia, iatrogenic blood dyscrasias and bladder tumors in dye stuff workers (Armenian and Lilienfeld). If data on the year of exposure were graphed for groups of patients diagnosed with chronic conditions, we would get a clustering in year of exposure, a rise and fall in the distribution of patients with the condition even if there had been no change in the extent of environmental exposure. It is essential to be able to differentiate this pseudoepidemic from situations where there have been true changes in exposure and incidence in the community.

Further work is necessary to assess the effect on the model of other factors. What is the effect on the nature and characteristics of the "epidemic'like" curve when there are varia-

tions in the following individual factors:

- <u>ascertainment</u> probability of eventual admission; time specific rates of admission for those who are admitted; availability, accessibility of different types of treatment.
- <u>natural history</u> probability of becoming addicted after initial trial of heroin; interval between initial use of heroin to onset of addiction among those addicted; demographic characteristics of addicts (ethnic, sex, age); remission of addiction, or mortality.
- social or community factors short term changes in law enforcement, availability of heroin, methadone on the street, social sanctions.

An epidemiologist has been defined as an expert from out of town who slides to glory on the descending limb of the epidemic curve. (Fox, Holland, Elveback) Let us strive to differentiate the descending limbs of onsets in the community from the descending limb of pseudo-epidemics.

* * * *

REFERENCES

- Armenian HK and Lilienfeld AM: The distribution of incubation periods of neoplastic diseases, Am. J. Epidemiol. 99: 92-100, 1974.
- Greene MH, Kozel NJ, Hunt LG and Appletree RL: <u>An assessment of the diffusion of heroin abuse</u> <u>to medium sized American Cities</u>, Washington: USGPO, 1974.
- Greenwood M: <u>Medical statistics from Graunt to</u> Farr, Cambridge University Press, 1948.
- Hajek J: Probability theory (Ljapunov theorem) in <u>Survey of Applicable Mathematics</u> (K. Rektorys ed.) Cambridge, Mass: The M.I.T. Press, 1969.
- Hunt LG: <u>Admission Records. A tool for treat</u>-<u>ment program planning</u>, Washington: Drug Abuse Council, 1975.
- Hunt LG and Chambers CD: <u>The Heroin Epidemics</u>, New York: Spectrum Publications, 1968.
- King JR: <u>Probability Charts for Decision Making</u> New York: Industrial Press, 1971.
- Lotka AJ: Elements of Mathematical Biology, New York: Dover, 1956.
- O'Donnell JA, Voss HL, Clayton RC, Slatin GT and Room RGW: Young Men and Drugs-A nationwide survey, Washington: USGPO, 1976.
- Richman A and Richman VV: Heroin addict forecasting-statistical fallacies and disputed facts, <u>Proceedings of the American Statistical</u> <u>Association, Social Statistics Section,</u> <u>Annual Meeting, 1975.</u>
- Sartwell PE: The distribution of incubation periods of infectious disease. <u>Amer. J.Hyg</u>. 51:310-318, 1950.



(NOTE: THESE ARE THE SAME DATA AS IN FIG. 2)

714







The assistance of Ms. T. Dubrow and Ms. P. Zappel, and the comments of: Drs. P. Kohn, P.V. Lemkau, B. Locke, F. Lundin, R.W. Morgan, J.A. Newmeyer, J.O'Donnell, P. Person, S.B. Sells, D.T. Wigle and K.W. Deuschle are acknowledged. This research is supported by Grant Number 00666-03 from the National Institute on Drug Abuse.

307 Second Avenue New York, N.Y. 10003