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JAMES D. SHELTON, M.D., M.P.H.
Washington, D.C.
ROBERT N. TAYLOR, JR., M.P.H.
Research Triangle Park, North Carolina

From the International Fertility Research Program, Research Triangle Park, and the Agency for International Development, Washington, D.C.

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The Pearl Pregnancy Index reexamined: Still useful for clinical trials of contraceptives

JAMES D. SHELTON, M.D., M.P.H.
Washington, D. C.
ROBERT N. TAYLOR, JR., M.P.H.
Research Triangle Park, North Carolina

Data from 25 studies of intrauterine contraceptive devices show close agreement between the Pearl Pregnancy Index and a cumulative, 12 month, life-table pregnancy rate. Analysis of data from the early stages of these clinical trials shows the Pearl Index to be superior to the short-term life table in predicting the outcome of the study. The error introduced by using the Pearl Index as a single measure of contraceptive efficacy in clinical trials, under conditions in which those trials are often carried out, is probably very minor compared to the effect of situational factors that affect studies and to differences among various life-table methodologies. The real strength of the life-table analysis of contraceptive performance is not the single, summary, 12 month pregnancy rate it provides, but the complete picture of various reasons for termination over time, particularly when a large number of woman-months of experience has accrued. (AM. J. OBSTET. GYNECOL. 139:592, 1981.)

PRIOR TO THE EARLY 1960s, the conventional measure of the incidence of accidental pregnancy in a cohort of women was the Pearl Pregnancy Index,[1] defined as:

$$\text{pregnancies per 100 woman-years of use} = \frac{\text{number of accidental pregnancies}}{\text{number of woman-months of observation}} \times 1{,}200$$

The number of woman-months of observation in the cohort was defined as the sum of the number of months each woman used the contraceptive method until becoming pregnant or until terminating use. The Pearl Index was designed to provide a single measure of the use-effectiveness of a contraceptive method, expressed as the number of pregnancies to be expected in 100 woman-years of method use.

After the Pearl Index had been used in studies of conventional contraceptives, investigators became aware of serious deficiencies. It was found that the risk of pregnancy declined with duration of use of the method, with early pregnancies occurring "among the less motivated or less skillful couples, and perhaps among the more fecund couples."[2] Thus, since the risk of pregnancy declined with experience in using a method, studies of short duration generally produced less favorable results than long studies. Pearl's basic assumption that all woman-months of use could be treated equally was found to be theoretically incorrect; 10 years of use by 10 women were quite different from 1 year of use by 100 women.

In the early 1960s, Potter and Tietze were instrumental in alerting investigators to the problems with the Pearl Index and in promoting the substitute use of actuarial techniques based on life-table methods. The major advantage was that the technique controlled for the decreasing risk of pregnancy over time by treating each month of use individually.[1-8] The pregnancy rate was computed for each specific month of use as well as cumulatively up to a certain point, such as 12 months, by the calculation of conditional probabilities of becoming pregnant or continuing use.[3] Life-table rates have typically been expressed in terms of pregnancies per 100 women in the first 12 months of use.

Since life-table techniques were introduced, they

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Reprint requests: Dr. James D. Shelton, Office of Population, Agency for International Development, United States International Development Cooperation Agency, Washington, D. C. 20523.

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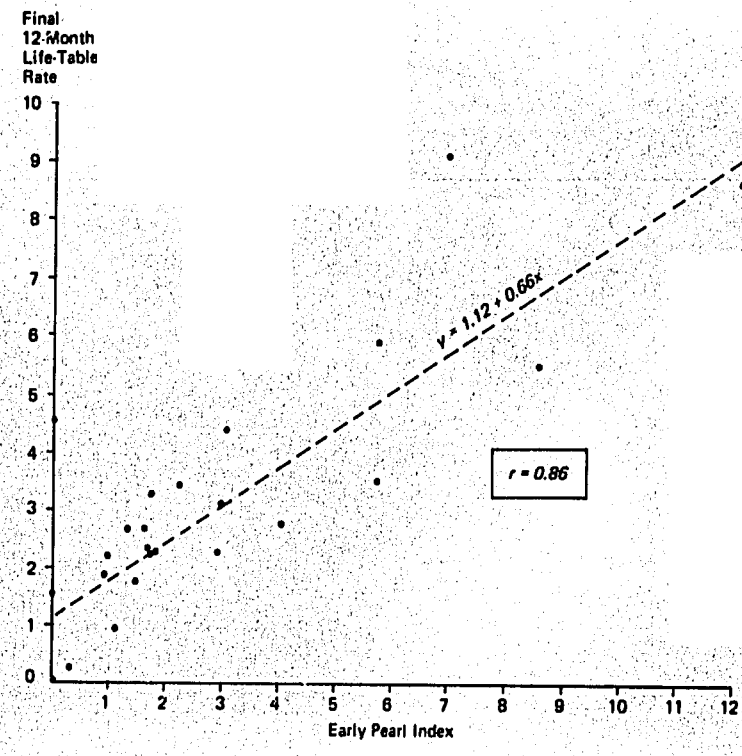

Fig. 1. Regression of "early study" Pearl rate (with 9 month cutoff) on "complete study" 12 month life-table rate (with 24 month cutoff).

have become generally accepted as the preferred method for assessing contraceptive use-effectiveness. Improvements to the methods have allowed for evaluation of the statistical significance of differences between cohorts of users, and for control for the effects of extraneous variables in these comparisons.[9] The current reliance on life-table techniques is further demonstrated by the strong recommendation by a Food and Drug Administration advisory panel[10] that only life-table methods be used to evaluate the effectiveness of vaginal contraceptives in phase III trials.

Yet, the Pearl Index continues to be viewed as a useful statistical measurement by many investigators, particularly clinicians. It was used recently in the Oxford long-term follow-up study of women in the United Kingdom who used different methods of contraception.[11] It continues to have proponents, including some who have used the life tables extensively. Sivin,[12] for instance, has characterized the Pearl Index as "an excellent summary statistic that mirrors an incidence rate in a population."

Why is the Pearl Index so persistent? Certainly, its conceptual simplicity and its expression as a single summary statistic make it attractive. Perhaps many investigators who conduct clinical trials appreciate that the Pearl Index is a better statistical method under real-world situations than consideration of its theoretic deficiencies might suggest.

The usefulness of the literature on contraception is limited by the presence of two different measures of efficacy, especially with respect to methods that have been studied extensively using the Pearl Index, such as vaginal contraceptives. Use-effectiveness rates estimated by the Pearl Index cannot be translated mathematically into a life-table rate because of the inherent differences in the two methodologies. However, given a sufficient number of studies to which both methods can be applied, it is possible to statistically estimate regression equations that relate the two techniques and to measure the correlation between them. With such information, it is possible to evaluate the differences in results obtained by using the two methods.

The International Fertility Research Program (IFRP) has conducted numerous clinical trials to assess the effectiveness of contraceptive methods, particularly intrauterine contraceptive devices (IUDs). We have reviewed a large number of the IUD studies in order to examine the following specific questions:

1. Under the conditions that the IFRP and others typically conduct clinical trials, how well does the Pearl Index correlate with the life-table, 12 month, cumulative pregnancy rate, the standard summary statistic generally used to report contraceptive efficacy?

2. In assessing contraceptive efficacy early in clinical trials, how well do Pearl rates calculated after 6 or 9 study months predict the ultimate 12 month life-table

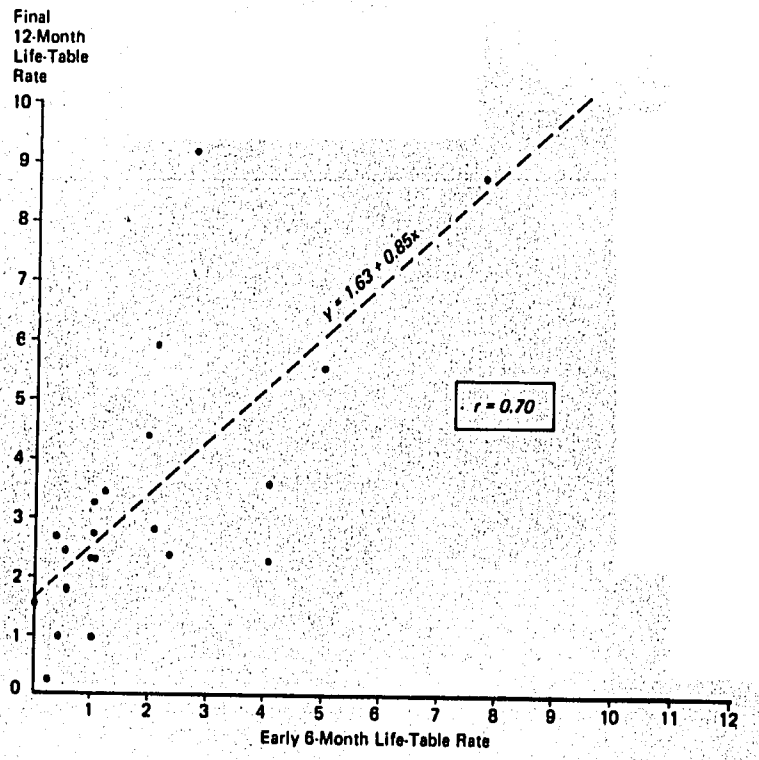

Fig. 2. Regression of "early study" 6 month life-table rate (with 9 month cutoff) on "complete study" 12 month life-table rate (with 24 month cutoff).

Table I. Pearl and life-table pregnancy rates obtained at 9 and 24 months after study initiation for 25 IUD studies

	9 mo cutoff		*24 mo cutoff*	
Study	*6 mo life table*	*Pearl rate*	*12 mo life table*	*Pearl rate*
1	0.38	1.32	2.64	2.99
2	2.07	5.68	5.88	4.01
3	7.71	12.00	8.64	8.07
4	2.31	1.64	2.35	1.73
5	0.44	0.84	0.97	1.20
6	1.94	3.00	4.36	3.87
7	4.97	8.54	5.52	5.94
8	1.23	2.20	3.41	2.12
9	0.23	0.34	0.23	0.25
10	0.97	1.14	0.97	0.66
11	1.68	2.94	3.12	2.98
12	2.72	6.92	9.12	7.62
13	1.00	1.66	3.22	3.63
14	0.94	1.76	2.26	2.33
15	4.07	5.68	3.48	4.28
16	0.00	0.00	1.51	1.76
17	4.08	2.94	2.24	2.24
18	0.00	0.00	0.00	0.39
19	0.54	0.98	2.20	1.22
20	*	*	4.54	4.32
21	0.54	1.46	1.77	1.65
22	1.03	1.82	2.24	1.63
23	2.06	4.04	2.79	2.63
24	1.03	1.58	2.68	1.97
25	0.00	0.00	0.00	0.21

*Fewer than 20 cases followed for 6 months.

rate? Are they more or less accurate than the corresponding early life-table rates?

Method

Twenty-five IUD studies were analyzed. Each study included at least 50 patients who were followed up for 12 or more months and in whom at least one pregnancy was reported during that period. The average study size was 382 subjects.

Life-table and Pearl pregnancy rates were calculated for each study at two points in time using cutoff dates. The first cutoff date simulates the earliest point in the study when reliable preliminary results could be expected and we refer to it as an "early study." The second cutoff date simulates a "complete study."

The early cutoff date was chosen to allow computation of 6 month life-table rates. Because of the time involved in case recruitment in contraceptive trials, typically, 9 months elapse after the admission of the first patient before 20 or more cases have been followed for 6 months. And similarly, 24 study months usually elapse before 12 month follow-up is complete in large studies. Thus, the early cutoff date was chosen to be 9 months and the final cutoff date was set at 24 months after the first IUD insertion.

Pearl and life-table pregnancy rates were calculated at the two cutoff dates using ordinal months and first

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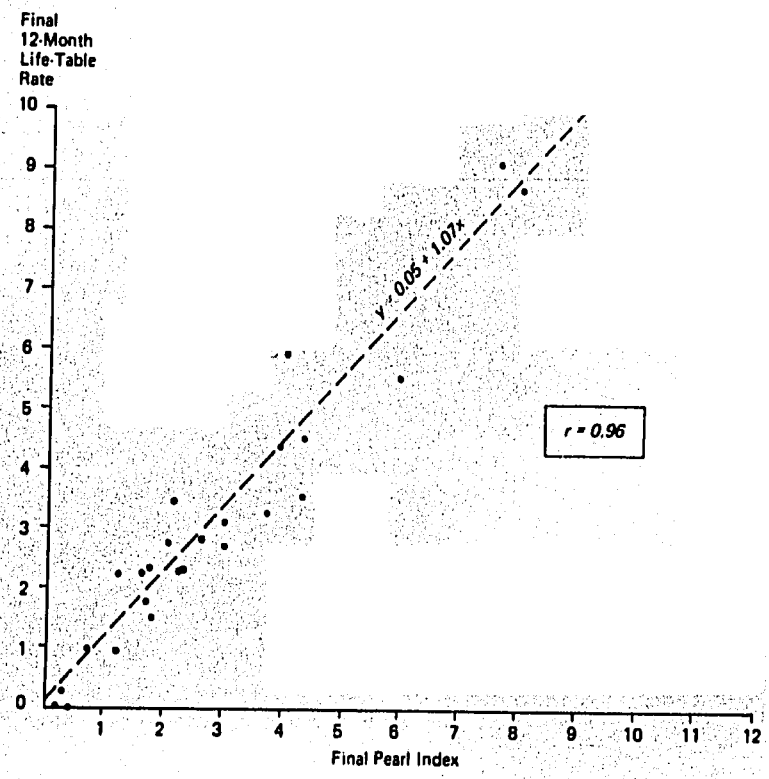

Fig. 3. Regression of "complete study" Pearl rate (with 24 month cutoff) on 12 month "complete study" life-table rate (with 24 month cutoff).

segment of use. Pearl rates were computed by use of the formula presented earlier, and life-table gross cumulative pregnancy rates were computed using the methodology of Potter.[4] Regression analysis (linear and nonlinear) was used to address the question of the predictive ability of early Pearl rates vs. early life-table rates as well as the question of correlation between the Pearl Index and the life-table rates calculated at the end of the study.

Results

Table I presents the Pearl Index and life-table rates obtained for each of the 25 studies at each of the two cutoff dates.

Scattergrams with least-squares regression lines were used to evaluate the correlations of interest. Scattergrams provide a plot of two variables with each variable forming an axis and each point representing the values of the two variables for a single study. The least-squares regression line drawn in the plot represents the best equation with which the two variables can be related. The related correlation coefficient (r), ranging between 0 and 1, provides a measure of the extent of association between the two variables. Variables with little association demonstrate a random scatter in the plot and a correlation coefficient close to zero. If the two variables have a high level of association, the points will fall closely along the regression line and the correlation coefficient will approach 1.

Scattergrams depicting the ability of "early" life-table and Pearl rates to predict the "final" life-table rate are shown in Figs. 1 and 2. Regression equations fitted to these data demonstrate that the Pearl rate calculated after 9 study months better predicts the life-table rate calculated at the end of the study (r = 0.86) than does a 6 month life-table rate calculated at the same early point in the study (r = 0.70). The use of nonlinear regression lines did not alter this relationship, but tended to reduce the correlation coefficient of both regression equations. Similarly, the use of alternative cutoff dates (such as comparison of the Pearl rate with the 6 month life-table rate at 6 study months) also demonstrated the superiority of the early Pearl rate.

Fig. 3 depicts the relationship between the *final* Pearl Index and life-table rates after completion of the studies. It shows a remarkably close correlation between the two methods (r = 0.96). Again, the use of alternative earlier cutoff dates did not alter this relationship.

Comment

Considering the conditions under which these IUD studies were conducted, the Pearl Index performs markedly better than conventional wisdom would have us believe.

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The conditions include: (1) a relatively low pregnancy rate, (2) use of first-segment rates and a cutoff date, (3) study duration of about 2 years, and (4) a contraceptive method with a relatively smooth curve of failures over time.

These conditions frequently do exist for clinical trials as they are conducted in the real world. Furthermore, the relationship found between the Pearl Index and life-table rate is so close that it may accommodate to other situations as well. Female sterilization is an example of a contraceptive method that probably falls outside of condition 4 listed previously. Failures do not occur smoothly over time. Nevertheless, examination of a comparison of failure rates among four sterilization techniques made by Cheng and associates[13] reveals a fairly close correspondence of the Pearl Index and the 24 month life-table rate, which these authors felt provided the best estimate of the failure rate of the two techniques. A recent study of the ovulation method that was clearly at variance with conditions 1, 2, and 4 also showed reasonably good agreement between the Pearl Index and 12 month life-table rates (17 and 21, respectively).[14]

When one considers the very sizable variation introduced by other factors in clinical trials, the effect of using a Pearl Index rather than a life-table pregnancy rate as a single summary statistic pales in comparison. Factors such as the population studied, subjects' level of motivation and education, the level of loss to follow-up, and the characteristics of the investigator are well known as powerful determinants of contraceptive performance in a clinical trial.[15] Furthermore, not all "life tables" are the same. As Jain and Sivin[16] have shown, different life-table methodologies can produce considerably different results, particularly when observations are incomplete.

The reason for the superiority of the Pearl Index in the early phases of a clinical trial probably derives from the stability inherent in its calculation; all pregnancies are in the numerator and all months of exposure are in the denominator. In contrast, the life-table technique fragments observations into several monthly rate calculations, which are then combined. In the early months of a study when numbers are small, the monthly rates are susceptible to wide fluctuations when small changes occur in the raw numbers, thereby providing early results that have little bearing for the final outcome of the study. Conversely, the effects of these fluctuations are minimized in the Pearl Index as data from all months are aggregated to form a single ratio.

The real virtue of the life-table methodology is not the single, summary, 12 month cumulative pregnancy statistic it provides, but the complete picture of various reasons for termination it provides over a large number of points in time. Although the Pearl methodology cannot model the "competing risk" nature of contraceptive discontinuation, it can provide a stable and reasonably accurate measure of the incidence of accidental pregnancy in many circumstances. For completed clinical trials, the Pearl rate appears to be reasonably accurate. For early results, it may well be even more accurate.

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