M. M. M. Farahani

A Model for Estimating Delay to Return to Fertility Following Discontinuation of Different Contraceptives

Introduction

AN important approach in evaluating the effectiveness of contraceptive programmes is through the estimation of the delay to return to fertility, following discontinuation of different contraceptions or the delay to conception, following discontinuation of different contraceptions. In order to estimate the latter we need, firstly to calculate fecundability : the monthly probability of conceiving.

In the past at least four diiferent methods for estimation of fecundability in population have been explored [Bongaarts (1975)].

Bongaarts classified these four different methods which are as follows :

1. Estimating fecundability using data on coital frequency and duration of the viability of sperm and ovum.
2. The proportion of women conceiving during one-month period (cycle) of exposure to risk of conception.
3. Mathematical models for fitting to the distribution of waiting times to conception.
4. Fitting models to distribution of parities attained within a certain period of time with a group of women.

There are some other works on this subject by different authors : Pathak (1978), Das Gupta and Hickman (1974) and Farahani (1980). Each of these methods has its particular strength and weaknesses. Women who have discontinued contraception are exposed to the risk of conception after discontinuing contraceptive. In such cases there is a delay to return to fertility (because of the effect of the contraceptive) and in all previous studies this has not been considered.

The present model is an attempt to deal with this delay before exposure to risk (delay to return to fertility) and this mode! is applied to prospective data for the number of months required to conceive after discontinuing different contraceptives collected in Chiang Mai in the north of Thailand.

Our present study is based on the number of menstrual intervals between the onset of discontinuing a contraceptive and first conception after that time. In this study the data contains three cohorts of women : the first group contains 794 women who were followed up after discontinuing Depo-provera for 37 months; the second group contains 121 women followed up after discontinuing I.U.D. (Intra-Uterine Device Contraceptive) for 27 months; the third group contains 432 women followed up after discontinuing pill for 25 months.

For computing the distribution of conception time from observation data, the life table method (Cutter and Ederer, 1953) is used. In this work we shall assume that there may be a residual effect of contraceptive use for some time after its discontinuation. The assumptions are as follows :

Assumption I: Delay of conception following discontinuation of contraceptive has a negative binomial delay distribution with parameters *'g'* and *'h'* where *g* is normal level of fecundability.

Assumption II: All women have identical constant monthly fecundability *'g'*.

Assumption III: 'g' is constant over time for a woman but it varies among women with a Beta density function.

The assumption I is based mainly on works of Barratt (1977, 1978) using a Pascal distribution for the insusceptible period following a live birth. The advantages of a Pascal distribution in this connection have been discussed by Potter *et al.* (1973). To obtain a tractable function we made use of the fact that a negative binomial delay followed by a geometric (with the same ratio parameters) gives another negative binomial.

Assumptions II and III are the same as used by Potter and Parker (1964) and also by Majumdar and Sheps (1970), and Sheps and Menken (1972, 1973).

The Model

Let there be a delay until fecundability resumes its normal level (effect of contraceptive); assume that *G(XI)* is the probability that the woman who is in this delay and her fecundability resumes its normal level at *xth* month and also that this probability follows a negative binomial delay (Assumption I). The probability generating function and the probability of $G(x)$ are given by :

$$\Pr\{X_1 = x_1/g\} = G(x_1, g) = g^h \frac{(h + x_1 - 1)!}{(h - 1)!\, x_1!} (1 - g)^{x_1} \qquad \text{(B.1)}$$

$$x_1 = 0, 1, 2, \ldots$$
$$h > 0, \quad 1 > g > 0$$

and

$$B(s) = \sum_{y=0}^{\infty} G(y/g) s^y = \left(\frac{g}{1 - \bar{g}s}\right)^h \qquad \text{(B'.1)}$$

where $\bar{g} = 1 - g$ (g is the normal level of fecundability and h can be interpreted as characteristic of the delay).

Again, if $p(x_2)$ is the probability that the first conception occurs at month x_2 irrespective of the delay, then we have :

$$\Pr\{X_2 = x_2/g\} = P(x_2/g) = g(1 - g)^{x_2 - 1} \qquad \text{(A.1)}$$
$$x_2 = 1, 2, \ldots.$$

with the probability generating function :

$$B_2(s) = \sum_{x=0}^{\infty} P(x/g) s^x = \frac{gs}{1 - \bar{g}s}. \qquad \text{(A'.1)}$$

Therefore, the probability that the first conception occurs at time x is given by :

$$\Pr\{X = x/g\} = P(x : g) = g^{h+1} \frac{(h + x - 1)!}{h!\, (x - 1)!} (1 - g)^{x-1} \qquad \text{(B.2)}$$

$$x = 1, 2, \ldots.$$

where $X = X_1 + X_2$.

Let us assume that the fecundability of women follows a Beta density (Pearson type I) (Assumption III). This is given by :

$$f(g) = \frac{1}{B(\alpha, \beta)} g^{\alpha-1} (1 - g)^{\beta-1} \qquad \text{(B.3)}$$

where $< g < 1$

$\alpha, \beta > 0.$

The mean and the variance of g are

$$E(g) = \bar{g} = \frac{\alpha}{\alpha + \beta} \tag{B.4}$$

$$V(g) = \frac{\alpha\beta}{(\alpha + \beta)^2 (\alpha + \beta + 1)} \tag{B.5}$$

and then we find that an unconditional distribution of number of menstrual intervals needed for the first conception after discontinuing contraceptive is :

$$\Pr\{X = x\} = P(x) = \int_0^1 P(x; g) f(g)\, dg$$

$$= \frac{1}{\beta(\alpha, \beta)} \int_0^1 g^{h+\alpha} \frac{(h + x - 1)!}{h!\,(x - 1)!} (1 - g)^{\beta+x-2}\, dg$$

$$= \frac{(h + x - 1)!\,(\alpha + \beta - 1)!\,(\alpha + h)!\,(x + \beta - 2)!}{h!\,(x - 1)!\,(\beta - 1)!\,(x + h + \alpha + \beta - 1)!} \tag{B.6}$$

where

$$B(\alpha, \beta) = \frac{\Gamma(\alpha)\,\Gamma(\beta)}{\Gamma(\alpha, \beta)} \tag{B.7}$$

and

$$\Gamma(\alpha) = (\alpha - 1)\,\Gamma(\alpha - 1)\ \alpha > 0 \tag{B.8}$$

$$\Gamma(\alpha) = \int_0^\infty x^{\alpha-1} e^{-x}\, dx \tag{B.9}$$

$$B(\alpha, \beta) = \int_0^1 x^{\alpha-1} (1 - x)^{\beta-1}\, dx. \tag{B.10}$$

From (B.6) we have

$$P(1) = \frac{(\alpha + \beta - 1)!\,(h + \alpha)!}{(\alpha - 1)!\,(h + \alpha + \beta)!} \tag{B.11}$$

and

$$P(x + 1) = \frac{(h + x)(x + \beta - 1)}{x(x + h + \alpha + \beta)} P(x). \tag{B.12}$$

If

$$P(x+1) = P(x). \quad \text{Then } x = \frac{h(\beta - 1)}{\alpha + 1}.$$

Beyond this if m_r is the rth moment of negative binomial distribution (B.2) about zero and $f(g)$ a beta distribution of fecundability then we have

$$\mu_r^0 = \int_0^1 f(g)\, m_r\, dg \tag{B.13}$$

where μ_r^0, the rth moment of distribution (B.6) about zero, but

$$m_1 = 1 + \frac{(h+1)(1-g)}{g} \tag{B.14}$$

$$m_2 = \frac{(h+1)(1-g)}{g^2} + m_1^2 \tag{B.15}$$

$$m_3 = \frac{(h+1)(1-g)}{g^2}\left(1 + \frac{2(1-g)}{g}\right) + 3m_2m_1 - 2m_1^3 \tag{B.16}$$

if we put these values instead of m_r and $f(g)$ we have

$$\mu_1^0 = 1 + \frac{(h+1)\beta}{\alpha - 1} \tag{B.17}$$

and $\mu_1 = \mu_1^0$ mean time to conception from untruncted data

$$\mu_2^0 = 1 + \frac{2(h+1)\beta}{\alpha - 1} + \frac{\beta(h+1)(\alpha + 2\beta)}{(\alpha - 1)(\alpha - 2)} \tag{B.18}$$

and

$$\mu_2 = \mu_2^0 - \mu_1^2 = \frac{(h+1)\beta(\alpha^2 + \alpha\beta - \alpha - h\alpha\beta + 2h\beta)}{(\alpha - 1)^2(\alpha - 2)} \tag{B.19}$$

$$\mu_3^0 = 1 + 3(h+1)\frac{\beta}{\alpha} + 3(h+1)^2\frac{(\beta+1)\beta}{(\alpha-1)\alpha} + 4(h+1)\frac{(\alpha+\beta-1)\beta}{(\alpha-1)(\alpha-2)}$$
$$+ (h+1)^3\frac{(\beta+2)(\beta+1)\beta}{(\alpha-1)(\alpha-2)(\alpha-3)}$$
$$+ (h+1)(3h+5)\frac{(\alpha+\beta-1)(\beta+1)\beta}{(\alpha-1)(\alpha-2)(\alpha-3)} \tag{B.20}$$

and we can find μ_3 as follows :

$$\mu_3 = 3\mu^0_3 - \mu^0_2 \mu^0_1 + 2\mu^{0^3}_1 \tag{B.21}$$

when data are not truncated we can use (B.17), (B.19) and (B.21) and use moment method to find the α, β and h.

Note

From (B.12) and (B.11) we have : If $h = k$ and $\beta = k'$ are one set of results then $h = k' - 1$ and $\beta = k + 1$ will have the same result with fix α because

$$P(1) = \frac{(\alpha + k' - 1)!\,(k + \alpha)!}{(\alpha - 1)!\,(k + \alpha + k')!} = \frac{(\alpha + k + 1 - 1)!\,(k' - 1 + \alpha)!}{(\alpha - 1)!\,(k' - 1 + \alpha + k + 1)!}$$

and

$$P(x + 1) = \frac{(k + x)(x + k' - 1)}{x(x + \alpha + k + k)} P(x) = \frac{(k' - 1 + x)(x + k + 1 - 1)}{x(x + \alpha + k' - 1 + k + 1)} P(x)$$

If $\beta = 1$, then $h = 0$; means there is no delay.

If $h > 1$ and $\beta > 1$, then usually $h > \beta$ i.e. the effect of delay before exposure to risk during the onset of discontinuation is bigger than later on.

Application and Result

For estimation of α, β and h we used maximum likelihood estimators with two assumptions : first we assume that we have no withdrawal and loss to follow-up, but we have truncated at t; in other words we ignore all withdrawal and drop-out until t. In this case (case 1) we denote by n_x those who conceive in month x ($x = 1, 2, \ldots t$) and by c_x those for whom observations are truncated at t.

The logarithm of the likelihood function (B.6) in this case is

$$\log L = \text{const} + \sum_{x=1}^{t} n_x \log P(x) + C_t \log Q(t) \tag{B.29}$$

where

$$Q(x) = \Pr\{x > x\} = 1 - \sum_{x=1}^{x=x} P(x) \tag{B.30}$$

in discrete case, and in the continuous case it is :

$$Q(x) = \Pr\{x > x) = 1 - \int_0^x P(x)\, dx. \tag{B.31}$$

Here we are not going to make any use of theoretical solutions. We seek the best value for α, β and h in a space of four dimensions.

We changed β from 1 to 10 and α from 1 to 15 and h from 1 to 20, and between these 3,000 numbers we found the maximum likelihood, using data from Chiang Mai in the north of Thailand as described.

In this case we found for each type of contraceptive α, β and h.

In Table 1 a comparison is made between the observed and estimated distributions of conception time following the discontinuation of three different contraceptives.

The mean delay before return to fertility, following discontinuation of contraceptive use can be found from (B.1) and it is :

$$m = \text{mean delay} = \frac{h(1-g)}{g}$$

and if we assume g as the mean fecundability then : $m = h\beta/\alpha$. (In fact, without the above assumption, the mean delay before return to fertility, following discontinuation of contraceptive use, varying with a Beta function is $h\beta/\alpha - 1$.)

The value of the delay before return to fertility following discontinuation of contraceptive use, in this case for Depo-provera is : $h = 6$, $\beta = 3$ and $\alpha = 4$ and the mean delay $\mu_0 = h\beta/\alpha = 4.5$ months.

For I.U.D. :

$$h = 0, \beta = 12 \text{ and } \alpha = 2 \text{ and the mean delay } \mu_I = 0.$$

For the Pill :

$$h = 3, \beta = 2 \text{ and } \alpha = 3 \text{ and the mean delay } \mu_P = 2 \text{ months.}$$

If we assume that when women become at risk the waiting time for conception is equal to 5.5 months (Potter and Parker, 1964), we have for Depo-provera 10 months; I.U.D. 5.5 months and the Pill 7.5 months to become pregnant after discontinuing contraceptive use respectively.

Effect of Dropout in Calculating α, β and h

In maximum likelihood estimates of α, β and h previously we ignored all dropout during the observation and we find some values for α, β and h as described.

TABLE 1— OBSERVED AND ESTIMATED DISTRIBUTION OF CONCEPTION TIMES FOR DEPO-PROVERA, I.U.D. AND PILL (Chiang Mai Thailand)

Months after observation	Depo-provera		I.U.D.		Pill	
	Observed	Estimated	Observed	Estimated	Observed	Estimated
1	.C693	.06993	.1240	.14286	.1806	.17847
2	.9781	.10490	.C996	.11429	.1527	.17857
3	.1121	.11189	.1335	.09286	.1802	.14216
4	.0995	.10490	.0511	.07647	.1111	.10823
5	.0907	.09355	.0701	.06373	.0741	.08117
6	.0768	.07919	.0501	.05366	.0694	.06119
7	.0491	.06668	.0446	.C4561	.0278	.04662
8	.0567	.05573	.0361	.03910	.0233	.03596
9	.0429	.04644	.0360	.03377	.0094	.02810
10	.0405	.03870	.0183	.02936	.0143	.02222
11	.0217	.03231	.0000	.02509	.0146	.01778
12	.0128	.02704	.0092	.02261	.0098	.01437
13	.0232	.02272	.0555	.02000	.0173	.01174
14	.0182	.01915	.0092	.01778	.0152	.00967
15	.C275	.01622	.0278	.01587	.0128	.00804
16	.0/73	.01378	.0185	.01423	.0026	.00674
17	.0135	.01176	,0284	.01281	.0079	.00568
18	.0168	.01008	.0097	.01157	.0053	.00483
19	.C072	.00867	.0194	.01048	.0000	.00413
20	.0103	.00749	,0193	X0953	.0139	.00355
21	.C092	.00649	.0000	.00869	.0000	.00307
22	.0114	.00564	.0194	.00794	.0032	.00266
23	.0017	.00493	.0194	.00728	.0068	.00232
24	.0055	.00431	.0000	.00669	.0038	.00204
25	.0059	.00379	.0000	.00616	.0000	.00179
26	.0C00	.00334	.0000	.00569		
27	.0000	.00295	.0107	.(0526		
28	.0000	.00261				
29	.0000	.00232				
30	.0035	.00207				
31	.0000	.00185				
32	.0043	.00165				
33	.0000	.00148				
34	.0000	.00133				
35	.0000	.00120				
36	.0048	.00109				
37	.0000	.00098				

(Case 1. Ignore all dropout between period of observation)

Now, including dropouts and using the maximum likelihood method, as follows :

$$L = \prod_{x=1}^{t} [P(x)]^{n_x} [Q(x)]^{C_x} \qquad \text{(B.32)}$$

or taking the logarithm of

$$\log L = \text{const} + \sum_{x=1}^{t} n_x \log P(x) + \sum_{x=1}^{t} C_x \log Q(x). \qquad \text{(B.33)}$$

In this case (case 2), again we seek for α, β and h in space with four dimensions, with the same range for α, β and h in the first case, and applying the same data.

This time we find α, β and h for Depo-provera 2, 3, 3 respectively and 2, 1, 12 for I.U.D. and 2, 2, 2 for the pill and time delay to return to fertility 4.5 months, 0 month, 2 months for Depo-provera, I.U.D. and pill respectively. If we compare these delays with those obtained in the first case we see we have no change in delay (because numbers of withdrawal were so small). Again, if we assume that women with natural fecundability (after women become at risk) the waiting time for conception is equal to 5.5 months. We have for Depo-provera 10 months, I.U.D. 5.5 months and pill 7.5 months to become pregnant after discontinuation of contraceptive.

Table 2 shows the probability of conception in month x and comparison of these probabilities with observed probabilities.

Conclusion

The model used for estimation of the delay of conception following discontinuation of different methods of contraception has given a good fit. This will be a valuable instrument in the analysis of fecundability and waiting time to conception after discontinuation of contraception and in evaluating the effectiveness of family planning programmes.

Acknowledgements

I wish to express may deep gratitude to Professor William Brass, who first directed my interest towards this subject, and I am also indebted to Dr. John Barrett for valuable suggestions during this work. I would like also to express my deep gratitude to Dr. Jane Menken for guidance and encouragement in the preparation of this paper.

TABLE 2—OBSERVED AND ESTIMATED DISTRIBUTION OF CONCEPTION TIMES FOR DEPO-PROVERA, I.U.D. AND PILL IN CHAING MAI
(in the north of Thailand)

Months after observation	Depo-provera		I.U.D.		Pill	
	Observed	Estimated	Observed	Estimated	Observed	Estimated
1	.0693	.07143	.1240	.1333	.1806	.20000
2	.0781	.09524	.0996	.10833	.1524	.17143
3	.1121	.09524	.1.135	.08921	.1802	.12857
4	.0995	.08658	.0511	.07435	.1111	.09524
5	.0907	.07576	.0701	.0626!	.0741	.07143
6	.0768	.06527	.0501	.05322	.0694	.05455
7	.0491	.05594	.0446	.04560	.0278	.04242
8	.0567	.04795	.0361	.03999	.0233	.03357
9	.0429	.04121	.0360	.03426	.0094	.02697
10	.0405	.03555	.0183	.02997	.0143	.02198
11	.0217	.03081	.0000	.02638	.0146	.01813
12	.0128	.02683	.0092	.02333	.0098	.01513
13	.0232	.02348	.0555	.02074	.0173	.01275
14	.0182	.02064	.0092	.01852	.0152	.01084
15	.0275	.01823	.('278	.01660	.0128	.00929
16	.0173	.01617	.0185	.01494	.0026	.00802
17	.0135	.01440	.0284	.01350	.0079	.00697
18	.0168	.01287	.0097	.01223	.0053	.00610
19	.0072	.01155	.0194	.01112	.0000	.00536
20	.0103	.01041	.0193	.01014	.0139	.00474
21	.0092	.00940	.0000	.00427	.0000	.00021
22	.0114	.00852	.0194	.00850	.0032	.00376
23	.0017	.00775	.0194	.00781	.0068	.00337
24	.0055	.00706	.0000	.00719	.0038	.00303
25	.0059	.00646	.0000	.00664	.0000	.00274
26	.0000	.00592	.0000	.00614		
27	.0000	.00543	.0107	.00569		
28	.0000	.00500				
29	.0000	.00462				
30	.0035	.00427				
31	.0000	.00395				
32	.0043	.00367				
33	.0000	.00341				
34	.0000	.00318				
35	.0000	.00296				
36	.0048	.00277				
37	.0000	.00259				

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