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Statistical Inference in Contraception

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Abstract

A comprehensive statistical model is developed for the correct evaluation of contraception effectiveness. From the probability of a woman, using some contraceptive procedure, conceiving in a single cycle, the pregnant woman rate and the pregnancy rate are defined and calculated. This is used to infer the values of these rates from experimental trials, accounting for the number of followed women and for the period they are followed for, whatever kind of events may be counted up in the trials, either pregnant women or pregnancies. However, computing pregnancies can bias the results of a trial, since the conceiving women, supposedly with a greater risk of pregnancy, should be replaced in the sample by new ones, whereas computing pregnant women allows more objectivity, since those pregnant women can stay in the sample up to the end of the trial. Thus, a more realistic effectiveness rate can be deduced from the investigation.

Mathematics Subject Classification: 62P10

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1 Introduction

Human contraception is a highly important current issue and this is particularly true of the statistical aspects of clinical investigation referred to the effectiveness of different contraceptive procedures. This is why there has always been abundant literature devoted to this subject, of which we only quote some examples [1]-[5].

Actually, the competitivity, both scientific and commercial, in this field is very high and demands much accuracy when performing the investigation and much reliability when applying the results to potential users of contraception.

The evaluation of contraception effectiveness starts from experimental data obtained from clinical trials and needs go through statistical processing, which sometimes is not performed with the required mathematical rigour, but runs up against some difficulty as noticed by Trussell (1991), [6].

In fact selecting the sample for a trial may have the first difficulty, for, whereas the contraception is of universal utility and will be used by very different populations, it may be very difficult to get a sample really representative of such variable populations.

Then, once the trial has been performed, to take the clinical results from it could be an easy task, but to draw some significant general conclusion with respect to the tested contraceptive method may involve some difficulty. Effectively, nowadays the contraception effectiveness being very high, the failure rates are extremely small and consequently its evaluation requires much accuracy.

This paper seeks to give contraceptive statistics a solid base, via four main objectives:

1.- to accurately define different failure rates,

2.- to show how contraceptive trials should be conducted to ensure statistical rigour,

3.- to describe a method for deriving from trial results reliable failure rates, with a well defined statistical confidence, and

4.- to recognize and to establish some limitations to the validity of the conclusions from contraceptive clinical trials.

While this paper does not deal with any clinical feature of contraception, these notes may be very valuable referring in general to methodological aspects of statistics and in particular to clinical research into contraceptive effectiveness.

Moreover, the present model is self-contained and easy to carry on, since it deals in a comprehensive way, including extensive tables, with a practical subject such as the statistical inference in contraception.

2 Contraception Failure Rates

There are two main failure rates in use. In this section they are precisely defined and related to each other.

Actually, the failure of any contraceptive method may be evaluated through the rate *R/100* women-years, which admits at least two versions:

A) the pregnant woman rate, if *R* is the average number of pregnant women in a group of *W* women, in *t* years, being $Wt = 100$, and

B) the pregnancy rate, if *R* is the average number of pregnancies of *W* women during *t* years, also being $Wt = 100$. The pregnancy rate so defined is commonly named as the Pearl rate or Pearl index.

To avoid confussion, the percentages of these two versions of the failure rate will be named *RA* and *RB*, respectively. In fact, they correspond to different statistical parameters. Therefore, equating them, when possible, requires an analytical justification, and, in any case, it seems appropriate to relate one to the other. The statistical inference process to determine the actual values of the failure rates with a certain confidence will be explained later.

2.1 Pregnant Woman Rate

If q is the probability of pregnancy of a woman, using some contraceptive procedure, in a menstrual cycle, then the probability of this woman having no pregnancies in t years, each assumed to comprise 13 menstrual cycles, is given by

$$P(0,t) = (1-q)^{13t} \tag{1}$$

whereas the probability of one woman having $x \neq 0$ pregnancies, within the same time interval, is

$$P(x,t) = 1-(1-q)^{13t} \tag{2}$$

Hence the pregnant woman rate, that is the average number of pregnant women, out of a total of W women, in t years, can be written as $WP(x,t)$, giving

$$RA = W\left[1-(1-q)^{13t}\right] \tag{3}$$

This expression proves that RA depends on W, which means that the condition $Wt = 100$ is insufficient. For example, when q = 0.003, if W = 100 and t =1, RA = 3.831, whereas, if W = 20 and t = 5, RA = 3.548. Thus, if the pregnant woman rate is to be meaningful, it needs to be precisely defined for specific W and t, and we recommend that the convention W = 100 and t = 1 should be adopted, such that RA be the average percentage of pregnant women in one year. It is this definition of RA that will be utilized for the remainder of this paper, such that

$$RA = 100\left[1-(1-q)^{13}\right] \tag{4}$$

2.2 Pregnancy Rate

Now, the probability of one woman having n pregnancies in t years of exposure is

$$P(n,t) = q^n(1-q)^{13t-n}C_n^{13t} \tag{5}$$

and the pregnancy rate, as previously defined, is

$$RB = W\sum_{n=0}^{13t} nP(n,t) = 13Wtq \tag{6}$$

The definition of the pregnancy rate in this way does not account for the fact that a woman is not exposed to pregnancy uninterruptedly, but a pregnancy makes impossible another one for some time. Nevertheless, the question would be how long a pregnancy takes before a new pregnancy is possible. Since it can vary from nearly nothing, in case of abortion, up to about eighteen months, in case of normal delivery and lactancy, the correct approach is to define the pregnancy rate and calculate it under the most unfavourable hypothesis, when the rate can reach the highest value. The same applies to other causes that prevent from pregnancy.

According to this, *RB* is defined and calculated as the average number of pregnancies of *W* women during *t* years (*Wt* = 100), as if they could conceive in all their possible cycles of the *t* years.

Then, *RB* does not depend on *W* and *t*, but on the product *Wt* and is given by

$$RB = 1{,}300q \tag{7}$$

whatever *W* may be, provided that *Wt* = 100.

Now we can talk of the pregnancy rate as *RB*/100 women-years. In this case, referring the pregnancy rate to one woman during a hypothetical period of 100 years, although unrealistic, may be useful to evaluate easily the expected number of pregnancies of a woman in a real period of exposure of 100/*x* fertile years, for it would be worth *RB*/*x*.

2.3 Comparison of Failure Rates

Beyond the above considerations, Eqs. (4) and (7) show that $RA \neq RB$. For instance, when *q* = 0.003, *RA* = 3.831 (pregnant women) whereas *RB* = 3.900 (pregnancies). Nevertheless, within certain conditions, both failure rates become virtually numerically equal.

Effectively, if the right hand side of Eq. (4) is developed in series, it remains

$$RA = \frac{100x13}{1!}q - \frac{100x13x12}{2!}q^2 + \frac{100x13x12x11}{3!}q^3 - .....$$

Then, equating

$$RA = 1{,}300q = RB \tag{8}$$

and leaving out all the remaining terms results in a relative error of *RA*

$$\frac{\varepsilon}{RA} < 6q \tag{9}$$

This error depends only on *q* and when *q* is very small the error is negligible, so equating the two failure rates is justified. This means that the average number of pregnant women in a group of 100 women, during one year, if it is samll enough, yields as well the average number of pregnancies of *W* women during 100/*W* years.

In any case, the relation between the pregnant woman rate and the pregnancy rate is proportioned by Eqs. (4) and (7). Therefore, determining *RA* allows in all cases the calculation of *RB*, and vice versa. In this way, once one of them has been determined, inequality (9) bounds the error from equating *RA* = *RB* and indicates whether this is acceptable or the calculation of the other rate must be performed more accurately through Eqs. (4) and (7).

3 Design and Conduct of Contraception Trials

Contraception trials need to be carried out with statistical rigour in order to infer any statistical parameter with a well determined confidence, so that the investigation into this subject can be reliable to potential users.

In this section two important features of any contraception statistical research are analysed, the outcome event of the trial and the characteristics of the samples.

3.1 Choice of Outcome Event

In a contraception trial a number *W* of women, who are using certain contraceptive procedure, are exposed to pregnancy during a time period of *t* years. In the course of the trial there are two events that may be accounted for, either pregnant women or pregnancies. According to this, it is quite true that the trial must be performed in a different way in each case, and also the result takes different forms and has to be dealt with differently.

If pregnant women are counted up, once a woman becomes pregnant, she may be removed from the trial, and there is no need neither to replace her nor to wait until the resolution of her pregnancy. Paradoxically, she remains in the sample, but no further information is required from her, since she is accounted for as having an undetermined number of pregnancies (one or more). In this case, the result of the trial will be that, among *W* women, *N* of them have conceived within a period of *t* years.

Otherwise, if pregnancies are counted up, each woman getting pregnant has to be replaced, so that the sample always contains a constant number of women at risk of pregnancy and it can be said properly that the result of the trial has been of *S* pregnancies among *W* women, during *t* years.

Evidently, from a statistical point of view, the two ways of performing a trial are correct, provided that the result is treated in the appropriate way, in order to determine, by statistical inference, the failure rates of the tested method.

It is noted that, if pregnant women are computed, a sample of *W* women followed for *t* years is not equivalent to other sample of *W´* women followed for *t´* years, even when $Wt = W´t´$, since the number *N* of pregnant women will depend obviously on the total number of women of the sample. This is in agreement with Eq. (3).

On the contrary, if pregnancies are computed, instead of pregnant women, the two above mentioned samples of women are equivalent, as long as the number of followed cycles is the same in both cases. This is in accordance with Eq. (6).

The pregnant woman rate and the pregnancy rate of the tested contraceptive method can be determined with the desired statistical confidence in the two cases, either having computed the pregnant women or the pregnancies.

This is sound from a statistical point of view, and would be correct in real practice, if all women could be considered equivalent with respect to the risk of pregnancy. But it is not so, and the matter needs some important clarification.

Effectively, if pregnancies are being computed in a trial and each pregnant woman needs to be substituted by a new one, so that the number of women at risk of pregnancy remains constant in the sample, there is a trend to eliminate from the sample those women with a greater risk of pregnancy, leaving a more homogeneous population, with lower pregnancy risk. Thus, the longer this population is followed, the lower the observed rate of pregnancies will be, with which the evaluation of contraception could be severely biassed.

To avoid this effect, the use of a life table analysis was suggested by Potter [7] (1986). However, the life table analysis, besides complicating the interpretation of the trial results, also tends to make the experience of the participants seem homogeneous and to lack precision to identify patterns of use, as Keller et al.[8] (1981) had already indicated.

For this reason, we suggest simply to carry out the contraception trials by computing the pregnant women, instead of the pregnancies. This makes much easier to perform a trial and to evaluate its results.

In fact, if one computes the pregnant women, each pregnant woman is acccounted for as having an undetermined number of pregnancies (one or more). In this case, the pregnant women have not to be replaced, but they remain in the sample, with the only difference that they enter the group af pregnant women, from which the investigator does not inquire further information. They are counted up as pregnant women, irrespectively of how many pregnancies they could have during the whole time the trial may last. Thus, the population of the sample does not degenerate into a group of low pregnancy risk, but the sample remains the

same from the beginning of the trial up to the end.

Of course, the result of a clinical trial consisting of N pregnant women, among W women in t years, has to be dealt with accordingly, in order to infer the limits of the failure rates of contraception with a well defined confidence. This is shown in the following section.

3.2 Standardization of Samples

The aim of finding statistically the failure rates of contraceptive procedures is double. First, it makes possible to compare the effectiveness of different methods; second, it provides potential users with useful information about unwanted pregnancies.

Referring to the latter objective, it is clear that each couple is a particular one, in the sense that the correctness and consistency with which they are to use the contraception, in some cases, depends mainly on them. For this reason, the application of statistical data to a couple may need to consider their particular circumstances.

It is also well known that different couples have different grades of fertility and that the fertility of a couple varies with time. This means certainly that the risk of pregnancy per cycle and so the probability q of Eq. (1) is not the same for all couples and does not remain constant for every couple.

This being absolutely true, as noted by Trussell[9] (2014), and precisely for it, it is clear that contraception samples cannot adapt to every population, but need to be standardized and so the failure rates will correspond to an ideal population. Therefore, the application of statistical results has to be carried out in every case after considering all general, particular and even private circumstances.

As for the former objective, the comparison of results drawn from different contraception trials also implies some standardization of the samples. To achieve this, there are several points, which may be accomplished in the selection of the

sample. These are:

1.- all the women of the sample have given at least one birth,

2.- none of them has a known cause that makes impossible a new pregnancy,

3.- all the women keep a regular sexual partner, and

4.- the age of the women is uniformly distributed within a determined interval, say from 25 to 35 years.

4 Confidence Limits of Failure Rates

Although we discard conducting contraception trials by measuring the number of pregnancies for the above mentioned reasons, for the sake of clarity, we present the statistical inference process to calculate the confidence limitis of a contraceptive method in the two cases, after measuring the number of pregnant women and after measuring the number of pregnancies. In all cases the limits of contraception failure rates must be defined with precise confidence.

4.1 Confidence Limits after computing the Number of Pregnant Women

If pregnant women have been counted up in a trial, one can consider that the probability of N women conceiving, within a sample of W women in t years, is

$$P(N/W,t) = P(x,t)^N \left[1 - P(x,t)\right]^{W-N} C_N^W \tag{10}$$

which is ploted in Figure. 1 in the three assumptions: $N = 0$, $N = 1$ and $N > 1$.

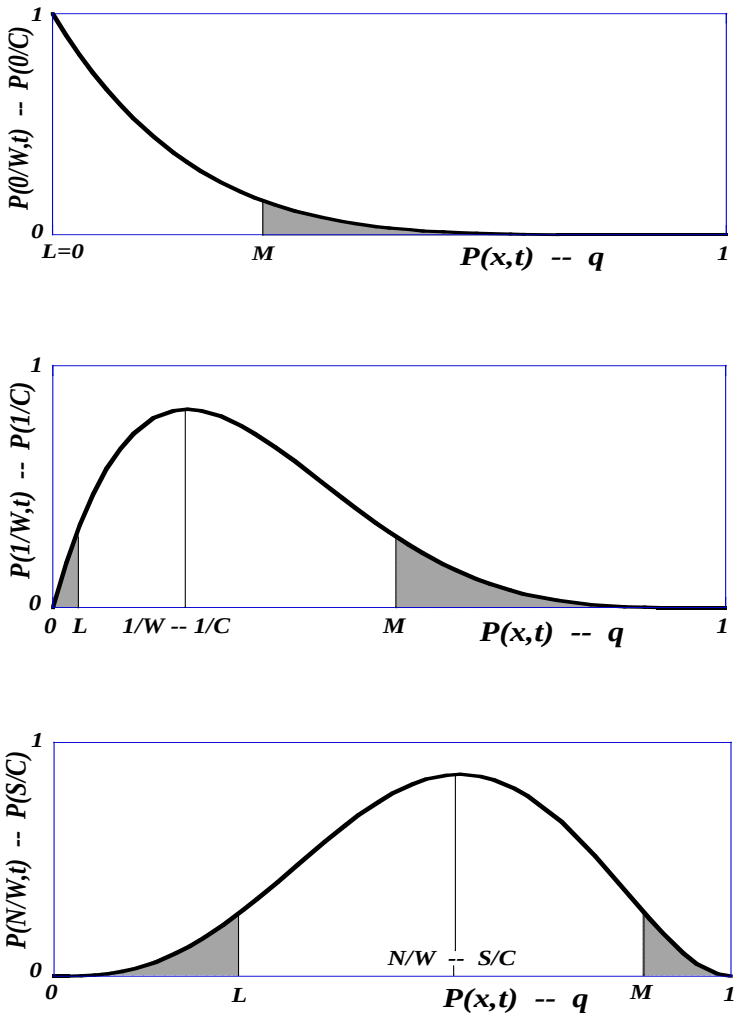

Figure 1: Interval (*L*,*M*): confidence region either of the probability *P*(*x*,*t*) of a woman having one or more pregnancies in *t* years, or of the probability *q* of a woman conceiving in a single cycle.

Then, if a trial yields the result that *N* women, out of a total of *W* women, have become pregnant in *t* years, *P*(*x*,*t*) may have any value between 0 and 1, but it can always be bounded by a pair of values, *L* and *M* (see Figure 1), with a confidence given by the proportion of area left under the corresponding curve

between L and M.

Afterwards, the limits of the pregnant woman rate can be calculated, with the same confidence, by replacing $P(x,t)$ by L and M in the expression

$$RA = 100\left\{1 - \left[1 - P(x,t)\right]^{1/t}\right\} \tag{11}$$

which is derived from Eqs. (2) and (4).

In a similar way, the limits of the pregnancy rate, with equal confidence, can be calculated through the expression

$$RB = 1{,}300\left\{1 - \left[1 - P(x,t)\right]^{1/13t}\right\} \tag{12}$$

which is derived by combining Eqs. (2) and (7).

4.2 Confidence Limits after counting up the Number of Pregnancies

Otherwise, if pregnancies had been computed, it would be advisable to proceed in the following way.

The probability of S pregnancies in a total of C menstrual cycles is given by

$$P(S/C) = q^S (1-q)^{C-S} C_S^C \tag{13}$$

which is also plotted in Figure 1, in the three assumtions: $S = 0$, $S = 1$ and $S > 1$, coinciding with the graphs of Eq. (10).

Then, if a trial yields the result that S pregnancies have been counted up after C cycles of exposure, q may have any value between 0 and 1, but it can always be bounded by a pair of values, L and M (see Figure 1), with a confidence given by the proportion of area left under the corresponding curve between L and M.

Next, the limits of the pregnant woman rate can be calculated, with the same confidence, by replacing q by L and M in Eq. (4), and, similarly, the limits of the pregnancy rate, with equal confidence, can be calculated through Eq. (7).

4.3 Tables to calculate Confidence Limits

The calculation of the confidence limits L and M in this way, in principle, is a very simple task. Nevertheless, the difficulty arises from the fact that, nowadays, scientific and social requirements from contraception are very high, and the resulting failure rates must be very low. Therefore, the sample size W, as well as C, need to be large numbers, while $N<<W$ and $S<<C$, with which the curves of Figure 1 become very sharp. Thus, calculations to obtain L and M require a very accurate mathematical process, which can only be carried out with the help of a computer.

For this reason we offer in the Appendix a set of tables, Tables 1(a), 1(b) and 1(c), representing such limits L and M (see Figure 1) of the 95 per cent confidence region of the probability $P(x,t)$ of a woman having any number pregnancies in t years, as a function of the size of the sample W (controlled women during t years) and the number N of pregnant women.

Since Eqs. (10) and (13) are of the same form, the limits L and M which appear in the tables also apply to the probability q of a woman conceiving in a single cycle, as a function of C (followed cycles) and S (pregnancies).

The use of Tables 1 is shown in the following examples, in which our statistical model is applied to hypothetic contraception trials, to infer the failure rates with a well defined 95 per cent confidence.

Example 1

A trial has been conducted by observing 500 women during 2 years, in which time 11 women have become pregnant.

In the corresponding table (W = 500 and N = 11) the following limits of the probability $P(x,t)$ of a woman having one or more pregnancies in t years are seen:

$$L = 11.437800 \times 10^{-3} \qquad \text{and} \qquad M = 37.483515 \times 10^{-3}$$

If these values replace $P(x,t)$ and t = 2 in Eq. (11) the limits $RA1$ and $RA2$ of the 95 per cent confidence region of the pregnant woman rate are obtained:

$$RA1 = 100\left[1-(1-L)^{1/2}\right] = 0.574$$

and $RA2 = 100\left[1-(1-M)^{1/2}\right] = 1.892$

Otherwise, if L and M substitute $P(x,t)$ in Eq. (12) the limits $RB1$ and $RB2$ of the pregnancy rate are obatined with the same confidence:

$$RB1 = 1{,}300\left[1-(1-L)^{1/26}\right] = 0.575$$

and $RB2 = 1{,}300\left[1-(1-M)^{1/26}\right] = 1.909$

In this case the trial has been conducted by counting up the number of pregnant women irrespective of the number of pregnancies they could have in the end.

Table 2 of the Appendix was completed in this way.

Example 2

Now we consider a trial with 500 women, each during 20 cycles, in which 9 pregnancies have taken place. In this case, every time a woman became pregnant she was substituted by a new one, so that the sample always contained the same number of women at exposure.

The appropriate table (C = 10,000 and S = 9) gives the following limits for the probability q of a woman conceiving in a single cycle

$L = 0.429300 \times 10^{-3}$ and $M = 1.629778 \times 10^{-3}$

Now, if these values replace q in Eq. (4) the limits $RA1$ and $RA2$ of the 95 per cent confidence region of the pregnant woman rate are obtained:

$$RA1 = 100\left[1-(1-L)^{13}\right] = 0.557$$

and $RA2 = 100\left[1-(1-M)^{13}\right] = 2.098$

whereas, if L and M substitute q in Eq. (7), the limits $RB1$ and $RB2$ of the pregnancy rate are obtained with the same confidence:

$$RB1 = 1{,}300L = 0.558$$

and $RB2 = 1300M = 2.119$

Table 3 of the Appendix was built in this manner.

5 Advising on Trials

Tables 2 and 3 are not exhaustive, but allow to draw some consequences as for the possibilities of contraception trials. The size of the sample and the number of failures have been combined in each case to have the upper limit of the failure rates successively under 5 per cent, 2 per cent, 1 per cent, 0.5 per cent, 0.2 per cent and 0.1 percent.

It is evident from these tables that the upper and lower limits of the failure rates get closer when the number of controlled cycles, or of the women in the sample, is increased, as it had to be. Accordingly, the larger the sample the better, since the confidence region of the failure rate narrows and this means a higher precision.

Tables 2 and 3 also show the relation between the expected upper limit of the failure rate and both the required size of the sample and the length of the trial. It may be seen that to prove the failure rate of a contraceptive procedure to be very samll, with 95 per cent confidence, demands a determined sample, which may be very large. Therefore, the choice of the sample size depends basically on the order of the result expected from the trial. Thus, one has to assess in advance the possibilities of different samples before planning any research in this field.

Nevertheless, it should be pointed out that samples may be accumulative, which means that the whole sample of women does not have to be necessarily one closed and compact group, but it may be dispersed in location and time. This could lead to unsolvable problems in other fields of statistical research, but it does not seem so concerning clinical research of contraception, in which the standardization conditions of the sample may be easily achieved.

Also it is noted that, if the failure rate is not small, as it was not for the first occlusive methods, one has to distinguish between the pregnant woman rate and the Pearl index or pregnancy rate. For instance, a pregnant woman rate of 28/100 women-year, as reported by Beebe and Overton (1942) for the use of an occlusive device combined with a spermicide, represents a pregnancy rate of 32/100

women-years, as deduced from Eqs. (4) and (7). But now, when failure rates of modern contraceptive methods are not higher than 2 per cent, the pregnant woman rate and the pregnancy rate become nearly numerically equal.

Traditionally it has been controversial the combination of the size of the sample and the duration of the trial. In this point the Pearl index has been criticized because it does not distinguish between a small number of women being followed for a long period of time and a large number of women being followed for a short period of time.

In our model we have made clear several points:

A) Performing the trial.

One has to choose which events are going to be counted up in the trial, either pregnant women or pregnancies.

If pregnant women are accounted for, both the number W of women of the sample and the duration t (years) of the trial are relevant and need to be specified.

Otherwise, if pregnancies are considered, only the product $W\,t$ matters.

In any case the result of the trial needs to be dealt with accordingly and the two defined failure rates can be appropriately calculated from the trial results in the two cases, as shown in Tables 2 and 3.

Nevertheless, as it was said, it is more convenient to count up the pregnant women, instead of the pregnancies, when carrying out the trial, for it keeps the sample unchanged and prevents it from degenerating into a group of low pregnancy risk.

Finally, it is necessary to choose a sufficient and suitable size of the sample of women so that it may meet all the standardization requirements.

B) Failure rates.

Similarly, the pregnant woman rate, in principle, would depend on both the number W of women and the time t (years) it refers to, even when the product $W\,t = 100$ were determined. However, we have chosen $W = 100$ (women) and $t = 1$

(year), for which reason the pregnant woman rate is given as *RA* (pregnant women)/100 women-year.

Otherwise, as for the pregnancy rate, or Pearl index, effectively W and t are irrelevant, provided the product $W\,t = 100$ is determined, for which reason it is given as *RB* (pregnancies)/100 women-years.

The two defined failure rates are different statistical parameters, although they are related to each other. Nevertheless, when they are small enough, as they are nowadays, they are nearly numerically equal.

6 Conclusions

A comprehensive statistical model has been developed for the evaluation of contraception effectiveness. The precise definition of the failure rates of contraception and the accurate way to calculate them, as well as to relate one to the other, will help assess the available contraceptive possibilities realistically.

We reject performing a contraception trial by computing the pregnancies and replacing the pregnant women, for this can bias the result of the investigation by artificially lowering the failure cases in the sample. Instead, we propose to count up the number of pregnant women, who have not to be substituted. Then the sample may remain unchanged and does not degenerate into a group of low pregnancy risk. Thus the trial is more accurate and allows one to infer the pregnant woman rate as well as the pregnancy rate without bias and with the desired confidence.

The model is as general as contraception may be. It is applicable to any contraceptive procedure (IUDs, pills, injectables, implants, rithm methods, etcetera). Therefore, it can be useful to standardize the results of investigations on different contraceptive methods, so that those results are comparable.

Finally, this statistical model is very easy to follow in research practice, for it needs only some very simple tables like those provided in the Appendix. So it can

help investigators in planning their contraception research and in evaluating the results they get.

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Appendix

Tables 1(a), 1(b) and 1(c) show the limits L and M (see Figure 1) of the 95 per cent confidence region of both,

1) the probability $P(x,t)$ of a woman having some pregnancies, one or more, in t years, as a function of the size of the sample W (exposed woman during t years) and of the number N of pregnant woman, and
1) the probability q of a woman conceiving in a single cycle, as a function of C (followed cycles) and of the number of pregnancies S counted up in the clinical trial.

The use of these tables to determine, from the results of a contraception trial, the confidence regions of the failure rates is explained in the text.

Tables 1(a)

W = 50 // C = 50		
N // S	*L x 10^3*	*M x 10^3*
0	*0.00000*	*57.04795*
1	*0.92000*	*90.15862*
2	*6.44400*	*120.59988*
3	*15.06000*	*149.15620*
4	*25.49600*	*176.32644*
5	*37.18000*	*202.41517*
6	*49.80000*	*227.65734*
7	*63.14000*	*252.25762*
8	*77.10400*	*276.25589*
9	*91.58400*	*299.75967*
10	*106.52000*	*322.82031*
11	*121.83600*	*345.52860*
12	*137.54400*	*367.83897*

W = 100 // C = 100		
N // S	*L x 10^3*	*M x 10^3*
0	*0.00000*	*29.22515*
1	*0.44100*	*46.35017*
2	*3.12800*	*62.10790*
3	*7.32300*	*76.98377*
4	*12.40400*	*91.16352*
5	*18.07500*	*104.84927*
6	*24.18600*	*118.13853*
7	*30.63200*	*131.12840*
8	*37.36000*	*143.84667*
9	*44.31600*	*156.34826*
10	*51.46000*	*168.68136*
11	*58.78400*	*180.83024*
12	*66.26400*	*192.82773*

W = 500 // C = 500		
N // S	*L x 10^3*	*M x 10^3*
0	*0.000000*	*5.961664*
1	*0.085400*	*9.477569*
2	*0.610400*	*12.726901*
3	*1.432800*	*15.794590*
4	*2.426400*	*18.735216*
5	*3.535000*	*21.576418*
6	*4.726800*	*24.344163*
7	*5.982200*	*27.054117*
8	*7.289600*	*29.714089*
9	*8.638200*	*32.336724*
10	*10.022000*	*34.927082*
11	*11.437800*	*37.483515*
12	*12.878400*	*40.020460*

W = 1,000 // C = 1,000		
N // S	*L x 10^3*	*M x 10^3*
0	*0.000000*	*2.988266*
1	*0.042500*	*4.752534*
2	*0.304400*	*6.381849*
3	*0.714300*	*7.923369*
4	*1.210000*	*9.399099*
5	*1.762500*	*10.827092*
6	*2.356800*	*12.216845*
7	*2.982000*	*13.580477*
8	*3.633600*	*14.916881*
9	*4.304700*	*16.237583*
10	*4.995000*	*17.537620*
11	*5.699100*	*18.828183*
12	*6.417600*	*20.099642*

Tables 1(b)

W = 2,000 // C = 2,000

N // S	*L x 10^3*	*M x 10^3*
0	*0.000000*	*1.495997*
1	*0.021200*	*2.379898*
2	*0.151900*	*3.196343*
3	*0.356700*	*3.967969*
4	*0.604200*	*4.707409*
5	*0.880000*	*5.423344*
6	*1.176600*	*6.120287*
7	*1.488900*	*6.803087*
8	*1.814000*	*7.473516*
9	*2.149200*	*8.135055*
10	*2.493500*	*8.787682*
11	*2.844600*	*9.434517*
12	*3.202800*	*10.073484*

W = 5,000 // C = 5,000

N // S	*L x 10^3*	*M x 10^3*
0	*0.000000*	*0.598847*
1	*0.008460*	*0.953001*
2	*0.060720*	*1.279568*
3	*0.142560*	*1.588713*
4	*0.241440*	*1.885039*
5	*0.351700*	*2.171627*
6	*0.470280*	*2.450669*
7	*0.595000*	*2.724470*
8	*0.724960*	*2.993046*
9	*0.858780*	*3.258339*
10	*0.996400*	*3.519690*
11	*1.136740*	*3.778619*
12	*1.279920*	*4.034711*

W = 10,000 // C = 10,000

N // S	*L x 10^3*	*M x 10^3*
0	*0.000000*	*0.299498*
1	*0.004230*	*0.476602*
2	*0.030340*	*0.640067*
3	*0.071250*	*0.794637*
4	*0.120720*	*0.942698*
5	*0.175850*	*1.086067*
6	*0.235080*	*1.225803*
7	*0.297430*	*1.362687*
8	*0.362320*	*1.497224*
9	*0.429300*	*1.629778*
10	*0.498000*	*1.760658*
11	*0.568150*	*1.890249*
12	*0.639720*	*2.018333*

W = 20,000 // C = 20,000

N // S	*L x 10^3*	*M x 10^3*
0	*0.000000*	*0.149768*
1	*0.002115*	*0.238311*
2	*0.015170*	*0.320071*
3	*0.035625*	*0.397353*
4	*0.060340*	*0.471469*
5	*0.087900*	*0.543169*
6	*0.117510*	*0.613048*
7	*0.148680*	*0.681522*
8	*0.181120*	*0.748796*
9	*0.214605*	*0.815070*
10	*0.248950*	*0.880532*
11	*0.284075*	*0.945237*
12	*0.319800*	*1.009391*

Tables 1(c)

W = 40,000 // C = 40,000

N // S	*L* x 10^3	*M* x 10^3
0	*0.000000*	*0.074889*
1	*0.001068*	*0.118881*
2	*0.007585*	*0.160041*
3	*0.017813*	*0.198693*
4	*0.030170*	*0.235758*
5	*0.043950*	*0.271591*
6	*0.058755*	*0.306530*
7	*0.074340*	*0.340779*
8	*0.090560*	*0.374423*
9	*0.107303*	*0.407566*
10	*0.124475*	*0.440297*
11	*0.142010*	*0.472706*
12	*0.159870*	*0.504791*

W = 60,000 // C = 60,000

N // S	*L* x 10^3	*M* x 10^3
0	*0.000000*	*0.049927*
1	*0.000768*	*0.077704*
2	*0.005057*	*0.106696*
3	*0.011870*	*0.132492*
4	*0.020113*	*0.157171*
5	*0.029300*	*0.181063*
6	*0.039170*	*0.204359*
7	*0.049560*	*0.227193*
8	*0.060373*	*0.249613*
9	*0.071535*	*0.271706*
10	*0.082983*	*0.293535*
11	*0.094673*	*0.315143*
12	*0.106580*	*0.336530*

W = 80,000 // C = 80,000

N // S	*L* x 10^3	*M* x 10^3
0	*0.000000*	*0.037445*
1	*0.000539*	*0.059300*
2	*0.003793*	*0.080020*
3	*0.008903*	*0.099367*
4	*0.015085*	*0.117882*
5	*0.021975*	*0.135799*
6	*0.029378*	*0.153276*
7	*0.037170*	*0.170398*
8	*0.045280*	*0.187218*
9	*0.053640*	*0.203817*
10	*0.062225*	*0.220181*
11	*0.071005*	*0.236357*
12	*0.079935*	*0.252400*

W = 100,000 // C = 100,000

N // S	*L* x 10^3	*M* x 10^3
0	*0.000000*	*0.029957*
1	*0.000425*	*0.047611*
2	*0.003034*	*0.064018*
3	*0.007122*	*0.079496*
4	*0.012068*	*0.094306*
5	*0.017580*	*0.108642*
6	*0.023496*	*0.122636*
7	*0.029736*	*0.136319*
8	*0.036224*	*0.149775*
9	*0.042921*	*0.163028*
10	*0.049790*	*0.176126*
11	*0.056804*	*0.189089*
12	*0.063948*	*0.201922*

Table 2 shows the confidence regions of the failure rates, according to hypothetical trials, in which pregnant women have been counted up.

W (women) = size of the sample,

t (years) = length of the trial,

N = number of pregnant women,

RA1 and *RA2* (per cent women-year)

= lower and upper limits of the pregnant woman rate,

RB1 and *RB2* (per cent women-years)

= lower and upper limits of the pregnancy rate or Pearl Index.

Table 2

W	*t*	*N*	*RA1*	*RA2*	*RB1*	*RB2*
50	*2*	*1*	*0.046*	*4.614*	*0.046*	*4.716*
100	*1*	*1*	*0.044*	*4.635*	*0.044*	*4.737*
100	*2*	*4*	*0.622*	*4.667*	*0.624*	*4.771*
500	*1*	*4*	*0.243*	*1.874*	*0.243*	*1.890*
500	*2*	*11*	*0.574*	*1.892*	*0.575*	*1.909*
1,000	*1*	*11*	*0.570*	*1.883*	*0.571*	*1.899*
1,000	*1*	*4*	*0.121*	*0.940*	*.0.121*	*0.944*
1,000	*2*	*11*	*0.285*	*0.946*	*0.286*	*0.950*
2,000	*1*	*11*	*0.284*	*0.943*	*0.285*	*0.948*
1,000	*4*	*11*	*0.143*	*0.474*	*0.143*	*0.475*
2,000	*1*	*4*	*0.060*	*0.471*	*0.060*	*0.472*
2,000	*2*	*11*	*0.142*	*0.473*	*0.142*	*0.474*
5,000	*1*	*4*	*0.024*	*0.189*	*0.024*	*0.189*
5,000	*2*	*11*	*0.057*	*0.189*	*0.057*	*0.189*
10,000	*1*	*4*	*0.057*	*0.189*	*0.057*	*0.189*
10,000	*1*	*4*	*0.012*	*0.094*	*0.012*	*0.094*
10,000	*2*	*11*	*0.028*	*0.095*	*0.028*	*0.095*
20,000	*1*	*11*	*0.028*	*0.095*	*0.028*	*0.095*

Table 3 shows the confidence regions of the failure rates, according to hypothetical trials, in which pregnancies have been counted up.

W (women) = size of the sample,

t (years) = length of the trial,

N = number of pregnant women,

RA1 and *RA2* (per cent women-year)
= lower and upper limits of the pregnant woman rate,

RB1 and *RB2* (per cent women-years)
= lower and upper limits of the pregnancy rate or Pearl Index.

Table 3

C = 13 W t	*S*	*RA1*	*RA2*	*RB1*	*RB2*
1,000	*1*	*0.055*	*6.005*	*0.055*	*6.178*
2,000	*3*	*0.463*	*5.037*	*0.464*	*5.158*
5,000	*12*	*1.651*	*5.120*	*1.664*	*5.245*
2,000	*0*	*0.000*	*1.927*	*0.000*	*1.945*
5,000	*3*	*0.185*	*2.046*	*0.185*	*2.065*
10,000	*8*	*0.470*	*1.929*	*0.471*	*1.946*
5,000	*0*	*0.000*	*0.776*	*0.000*	*0.779*
10,000	*3*	*0.093*	*1.028*	*0.093*	*1.033*
20,000	*9*	*0.279*	*1.054*	*0.279*	*1.060*
10,000	*0*	*0.000*	*0.389*	*0.000*	*0.389*
20,000	*3*	*0.046*	*0.515*	*0.046*	*0.517*
40,000	*9*	*0.139*	*0.529*	*0.139*	*0.530*
40,000	*2*	*0.010*	*0.208*	*0.010*	*0.209*
60,000	*4*	*0.026*	*0.204*	*0.026*	*0.204*
80,000	*6*	*0.038*	*0.199*	*0.038*	*0.199*
60,000	*1*	*0.001*	*0.101*	*0.001*	*0.101*
80,000	*2*	*0.005*	*0.104*	*0.005*	*0.104*
100,000	*3*	*0.009*	*0.103*	*0.009*	*0.103*