**eAppendix A: Proof that the FR and the FOR cannot both be constant across attempt time**No**.** The proof proceeds by assuming both constancy assumptions hold true and then algebraically showing that that would imply something that is impossible. Suppose that both the FR and the FOR are constant over time. For any two cycles j and k, let poj and p1j be the conception rates at cycle j for the unexposed and the exposed, respectively. We presume that both must decline over cycle time, due to attrition. By our assumptions:

Together, those equations imply:

which implies that

which implies that

which implies that

which can only be true if either p0j=p0k or p1j=p0j

**eAppendix B: Estimating the standard error for ln(RMF):**

Suppose the inverse of the probability of conception is linear in cycle number and covariates. The generalized linear model for a dichotomous exposure E (coded 0, 1) is as follows:

(1-E) + (j-1)(1-E) + E + (j-1)E +

Let the maximum likelihood estimates for the model parameters be denoted by ,, . . . . Suppose each of the variables other than the exposure has been centered at its mean (or median) value so that the value estimates the mean of the fecundability distribution for someone at the mean (or median) for all covariates, and 0 for . The value (i.e., the estimated conception probability for cycle 1) will estimate the mean of the fecundability beta distribution for the exposed who are also at the mean (or median) for all covariates, but exposed. We would like to estimate the variance for the log of the ratio of the two means, namely ln[] = ln(). The partial derivatives for that statistic are as follows:

and

So if we denote the corresponding 1-by-2 vector of those two partial derivatives as V, and the estimated 2x2 submatrix involving and of the variance-covariance matrix as , then the estimated variance for ln[would be V VT.

Suppose the estimated var-covar matrix for and is

. Then the estimated variance for ln[is
a ) + b(

Suppose instead one wishes to estimate the ln(FOR) at cycle 1 (presuming it stays constant across j), which is ln[]. Then the above approach leads to the following approximation for the sample variance:

a )+b(

**eAppendix C**: **The parameter being estimated in the ongoing attempt design.**
Under a beta distribution for fecundability, the expected time to pregnancy is (1- q)/(m - q).

Accounting for length-biased sampling, the proportion sampled at cycle 1 is (m - q)/(1- q), which is the “c” parameter for the beta model for ongoing attempt data (3). Thus, the ratio of those two is the ratio of mean times to pregnancy for the exposed versus the unexposed.

**eAppendix D: Methods used to generate simulations**

We first empirically assigned cycle-specific fecundabilities for the unexposed by fitting a spline to observed cycle-specific conception rates taken from a large prospective study (23) and used the assumed model (constant FR or constant FOR) to calculate fecundabilities for the exposed. The “no constancy” scenarios used a FR that started at 0.5 (or 0.75 for the power simulations) at cycle 1 and declined by 0.01 at each cycle until it reached 0.33, after which it stayed level.

1. **Incident cohort study**. Simulate conception events cycle by cycle, beginning at cycle 1 until either conception occurs or they reach cycle 100.

2. **Retrospective study**. We complete step 1 and keep if TTP<100.

3. **Ongoing attempt study**. Generate each couple as in step 1 and apply a sampling probability of TTP/100.  For those who are sampled, assign a random ongoing attempt time by sampling digits randomly from 1 to TTP or from 1 to 100 if they did not conceive.  These range from 1 to 100, but we will censor all four of the analyses at the end of cycle 12, so many of the couples will have outcomes that are all 0’s up through cycle 12.

4. **Prevalent cohort study**. Generate each couple as in steps 1-3. If the random ongoing attempt time is <7, keep as the recruitment time, which is treated in the analysis as the left-censoring time and the first cycle of followup.

We follow these steps separately to develop completely independent data sets for each of the four designs.

eTable 1. Residual mean square errors for different models.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|   |   | Constant FR |   | Constant FOR |   | No constancy |
| Study design | Link | N=300 | N=600 | N=1000 | N=2000 |   | N=300 | N=600 | N=1000 | N=2000 |   | N=300 | N=600 | N=1000 | N=2000 |
| Incident cohort | inverse | 0.31 | 0.21 | 0.17 | 0.12 |  | 0.31 | 0.21 | 0.18 | 0.12 |  | 0.31 | 0.22 | 0.18 | 0.12 |
| ln | 0.20 | 0.14 | 0.11 | 0.08 |  | 0.22 | 0.15 | 0.13 | 0.10 |  | 0.22 | 0.15 | 0.13 | 0.10 |
| logit | 0.23 | 0.17 | 0.14 | 0.11 |  | 0.23 | 0.16 | 0.12 | 0.09 |  | 0.23 | 0.16 | 0.12 | 0.09 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Retrospective | inverse | 0.31 | 0.25 | 0.21 | 0.17 |  | 0.33 | 0.27 | 0.24 | 0.21 |  | 0.37 | 0.30 | 0.28 | 0.26 |
|  | ln | 0.25 | 0.22 | 0.20 | 0.18 |  | 0.26 | 0.22 | 0.20 | 0.19 |  | 0.32 | 0.27 | 0.27 | 0.26 |
|  | logit | 0.33 | 0.29 | 0.28 | 0.26 |  | 0.34 | 0.30 | 0.28 | 0.27 |  | 0.41 | 0.36 | 0.36 | 0.35 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Ongoing | inverse | 0.40 | 0.29 | 0.21 | 0.15 |  | 0.42 | 0.29 | 0.24 | 0.16 |  | 0.41 | 0.30 | 0.23 | 0.17 |
|  | ln |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | logit |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Prevalent | inverse | 0.38 | 0.26 | 0.20 | 0.15 |  | 0.38 | 0.26 | 0.21 | 0.14 |  | 0.38 | 0.27 | 0.21 | 0.16 |
|  | ln | 0.19 | 0.14 | 0.10 | 0.08 |  | 0.21 | 0.15 | 0.12 | 0.09 |  | 0.21 | 0.16 | 0.12 | 0.10 |
|   | logit | 0.23 | 0.18 | 0.14 | 0.13 |   | 0.22 | 0.16 | 0.12 | 0.08 |   | 0.23 | 0.17 | 0.12 | 0.09 |

Abbreviations: FR fecundability ratio; FOR Fecundability Odds Ratio

eTable 2. Constancy test for ln- and logit-link models.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|   |   | Constant FR |   | Constant FOR |   | No constancy |
| Study design | Link | N=300 | N=600 | N=1000 | N=2000 |   | N=300 | N=600 | N=1000 | N=2000 |   | N=300 | N=600 | N=1000 | N=2000 |
| Incident cohort | ln | 0.047 | 0.053 | 0.048 | 0.048 |  | 0.052 | 0.051 | 0.081 | 0.09 |  | 0.077 | 0.068 | 0.088 | 0.124 |
| logit | 0.054 | 0.065 | 0.065 | 0.089 |  | 0.055 | 0.045 | 0.067 | 0.046 |  | 0.05 | 0.053 | 0.064 | 0.051 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Retrospective | ln | 0.053 | 0.065 | 0.062 | 0.092 |  | 0.064 | 0.054 | 0.053 | 0.06 |  | 0.062 | 0.06 | 0.058 | 0.07 |
|  | logit | 0.065 | 0.089 | 0.11 | 0.18 |  | 0.076 | 0.065 | 0.073 | 0.094 |  | 0.066 | 0.076 | 0.078 | 0.111 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Prevalent | ln | 0.058 | 0.043 | 0.052 | 0.059 |  | 0.051 | 0.053 | 0.059 | 0.058 |  | 0.047 | 0.056 | 0.077 | 0.117 |
|   | logit | 0.069 | 0.051 | 0.069 | 0.082 |   | 0.045 | 0.039 | 0.05 | 0.045 |   | 0.05 | 0.047 | 0.055 | 0.068 |

Abbreviations: FR fecundability ratio; FOR Fecundability Odds Ratio