Methodological Issues in Analyzing Time Trends in Biologic Fertility: Protection Bias

Jane Key, Nicky Best, Michael Joffe, Tina Kold Jensen, and Niels Keiding

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One method of assessing biologic fertility is to measure time to pregnancy (TTP). Accidental pregnancies do not generate a valid TTP value and lead to nonrandom missing data if couples experiencing accidental pregnancies are more fertile than the general population. If factors affecting the rate of accidental pregnancies, such as availability of effective contraception and induced abortion, vary over time, then the result may be protection bias in the estimates of fertility time trends. Six European data sets were analyzed to investigate whether evidence of protection bias exists in TTP studies of fertility trends in Europe over the past 50 years. Couples experiencing accidental pregnancies tended to be more fertile than the general population. However, trends in accidental pregnancy rates were inconsistent across countries and were insufficient to produce substantial bias in fertility trends in simulated data. Where protection bias is suspected, the authors demonstrate use of 2 multiple imputation methods to generate realizations for the missing TTP values for accidental pregnancies. Simulation studies show that both methods successfully reduce or eliminate protection bias. The authors also demonstrate that standard sensitivity analyses for dealing with accidental pregnancies provide an upper bound on the extent of any bias.

Abbreviation: TTP, time to pregnancy.

The study of trends in biologic fertility is important. The significance of the reported deterioration in semen quality (1–4) needs to be assessed by using a functional measure of fertility, and, for women, no equivalent biomarkers are available.

One method that has been used to assess biologic fertility is to measure time to pregnancy (TTP), the number of months or cycles of unprotected intercourse that a couple takes to conceive, based on retrospective reports (5, 6). In these studies, subjects are interviewed about duration of time from initiation of unprotected intercourse to conception (and, in some studies, also of “unsuccessful attempts” in which conception has not, or not yet, occurred). This method is highly acceptable in practice, and its validity has been demonstrated (7–10). However, TTP studies are prone to several biases and require care in their design and analysis (11, 12).

There is now consensus that a TTP study of this kind should include, in addition to TTP itself, the proportion of accidental pregnancies (12, 13). The term accidental pregnancy here indicates a conception that was not terminated and was reported as resulting from a contraceptive failure. The distinguishing feature of an accidental pregnancy is that information is available on only the single act of intercourse that led to conception and not on the weeks or months during which unprotected intercourse did not lead to conception. TTP and accidental pregnancy relate to behavioral assessment and are distinct from “trying” or “planning” (intentional overlay on behavioral assessment) and from whether a pregnancy is “wanted” (affective desire) (14–20). Information on accidental pregnancies leading to a birth is readily obtainable in retrospective studies; some prospective studies also include such pregnancies (21), in which case similar considerations apply in the study of trends, but most are based on pregnancy planners only, thus excluding accidental pregnancies, and are unable to address the issues discussed here.
Information on accidental pregnancies is important in addressing biases such as that arising when the degree of risk taking differs in exposure groups (generally called "planning bias," despite the psychological oversimplification). Couples who experience an accidental pregnancy may be more fertile than the rest of the population, and accidental pregnancies are not eligible for a TTP value, so removing them from a TTP distribution may decrease apparent biologic fertility. If a particular group, for example, smokers compared with nonsmokers, has a higher propensity to take risks, a higher proportion of accidental pregnancies could remove some of the most fertile couples who smoke from the TTP-eligible population, which would bias the study of the effect of smoking on TTP (11, 12).

The situation is further complicated because variations in TTP can be influenced by knowledge and behavior as well as by biologic factors (12), for example, knowledge of the days of fertility in a woman's menstrual cycle. Such behavioral factors tend to change over time, which could affect the study of trends in TTP. In particular, when studying trends (or comparing radically different societies), bias could occur as a result of increasing availability of effective contraception and legal abortion.

**PROTECTION BIAS**

An increased ability to prevent unintended births can introduce bias because fewer fertile couples are then excluded from TTP distributions in later years. This possibility is described by Sallmén et al. (22) as "attrition bias," but we think that protection bias is more appropriate because it does not involve attrition in the usual sense; rather, it concerns the effect of the ability to protect against giving birth to an unintended child. Similar to planning bias, protection bias involves the effect of a changing proportion of non-TTP-eligible accidental pregnancies on the remaining TTP-eligible pregnancy distribution, and thus the apparent degree of population fertility, but it differs in being situational rather than due to risk-taking behavior (refer to Table 1 for a comparison of definitions). Protection bias may itself be accompanied by compensating behavior change, similar to planning bias, but this topic is beyond the scope of the present paper (discussed below).

Logically, protection bias operates the same way whether unintended births are prevented by increased use of contraception, by induced abortion, or both—only the presence or absence of the accidental pregnancy matters. The purpose of this paper is to explore this bias by using a sensitivity analysis approach and to evaluate how important it may be in estimating the fecundity (biologic fertility) of a population, especially trends in fecundity.

Another way of describing protection bias is that accidental pregnancies create nonrandom missing values in the observed TTP distribution. A TTP value, when available, is a realization of the underlying fecundity of the couple at that time. An accidental pregnancy reflects a different realization, which gives rise to a pregnancy for which a TTP value is missing. We know that this situation has occurred if information on accidental pregnancies is collected, so one can impute a TTP value for this couple. When the TTP distributions in population subgroups are compared, provided that a similar proportion of each group experiences accidental pregnancies, the missing data will not lead to protection bias. However, if some groups are more successful at preventing or terminating accidental pregnancies by effective contraception or abortion, respectively, comparisons between groups may be biased. Specifically, bias will occur if couples who have prevented or aborted an accidental pregnancy are more fertile than the population as a whole and they subsequently experience a planned pregnancy with an eligible TTP value; this situation will increase the proportion of observed TTP values from more fertile couples in that group. (The nonreplacement case is discussed below.)

It should be clear from this description in terms of missing values that the extent of reported accidental pregnancies generates the bias because it creates the missing TTP values; the validity of a subject's judgment as a reflection of actual biologic events is not the point. A corollary, explored in the Discussion section below, is that a change in reporting behavior, without a change in underlying objective reality, could affect the bias—specifically that, over time, pregnancies become reclassified from accidental to (rapid) TTP eligible, a form of "wantedness bias" (11).

To be concrete, suppose we investigate time trends in fecundity by comparing the TTP distribution for couples conceiving in 1950 and in 1980. The 1950 couple experiencing an accidental pregnancy would be more likely to give birth and would be included in the data set with a missing TTP value because it was more difficult at that time to prevent or terminate accidental pregnancies. The equivalent

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**Table 1. Definitions of Bias**

<table>
<thead>
<tr>
<th>Name of Bias</th>
<th>Process</th>
<th>Impact on Accidental Pregnancies</th>
<th>Impact on TTP Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protection bias</td>
<td>Couples in different time periods or groups have differential access to methods (effective contraception, legal abortion) for preventing unintended births</td>
<td>A higher proportion of accidental pregnancies in time periods/groups with less access to prevention methods</td>
<td>Lower representation of time periods/groups with less access to prevention methods</td>
</tr>
<tr>
<td>Planning bias</td>
<td>Couples in different time periods or groups exhibit different degrees of risk-taking behavior</td>
<td>A higher proportion of accidental pregnancies in time periods/groups with riskier behavior</td>
<td>Lower representation of time periods/groups with riskier behavior</td>
</tr>
</tbody>
</table>

*a For bias to arise in a study of time trends, the following assumptions are also needed: 1) the distribution of fertility among couples experiencing accidental pregnancies is different from that in the general population; 2) accidental pregnancies that are prevented (through effective contraception, legal abortion, or a lower propensity for risk taking) are subsequently replaced by a time-to-pregnancy (TTP)–eligible pregnancy; and 3) there is a time trend in method(s) of prevented unintended births or in risk-taking behavior, as appropriate.
couple in 1980 would be likely to avoid or terminate the accidental pregnancy because of improved contraception and availability of induced abortion; assuming they then “replace” this pregnancy with a nonaccidental one, their reported pregnancy would be eligible for a TTP value. Hence, the more fertile of the 1980 couples are more likely to experience a pregnancy eligible for a TTP value than they would have been in 1950. If the missing TTP values for accidental pregnancies are excluded from analysis, it would appear that fecundity increased between 1950 and 1980 despite no change in underlying population fecundity.

Protection bias was considered in a study of fecundity trends in Britain, in which the absence of an observed downward trend in accidental pregnancies was taken as evidence that the bias was not operating in this population (23). More recently, Sallmén et al. alleged that “changes in social factors that affect the rate and fate of unintended pregnancies could substantially bias time trends in fertility” (22, p. 494) to the extent that “we may never know” whether a trend exists. However, they overlook that it is standard practice to collect information on accidental pregnancies, with the same covariate data as for TTP itself, and to use it to investigate whether potential bias may affect the study results (11, 12). They also overlook the logical point that the operation of protection bias requires a change in the proportion of reported accidental pregnancies. That is, pregnancies would have to shift from the accidental (1950) to the eligible (1980) category, and therefore the proportion of reported accidental pregnancies would have to decrease. Without such a difference in the proportion of accidental pregnancies, this bias cannot arise—a logical point that can be empirically investigated (24).

In this paper, we examine the empirical trend in accidental pregnancies and the assumption that accidental pregnancies are associated with greater fecundity. We then simulate data sets and analyze them to evaluate methods of imputing missing TTP values. Finally, we examine the possible quantitative effects of this bias on estimation of trends in fecundity.

**EMPIRICAL ANALYSES**

Here, we reproduce and extend the simulation method developed by Sallmén et al. (22). We also incorporate empirical evidence, for which we draw on several data sets (refer to Table 2), each of which received ethical clearance. Information on accidental pregnancies was obtained by questioning, for each birth, whether this pregnancy resulted from a contraceptive failure.

<table>
<thead>
<tr>
<th>Table 2. Data Sets Used in the Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EMs</strong></td>
</tr>
<tr>
<td>Study design</td>
</tr>
<tr>
<td>Sample size</td>
</tr>
<tr>
<td>Eligibility</td>
</tr>
<tr>
<td>Country or countries</td>
</tr>
<tr>
<td>Duration of recall</td>
</tr>
<tr>
<td>First author</td>
</tr>
</tbody>
</table>

**Abbreviations:** AS, Asclepios Study; DTS, Danish Twin Study; EMS, European Multicentre Study; NCDS, National Child Development Survey; OPS, Odense Prenatal Study; OS, Omnibus Survey.

a The AS included men exposed to lead or styrene, but these exposures were not associated with time to pregnancy, so exposed men were included.

There were sufficient data covering a long-enough period (1950s–1990s) from studies in Denmark (European Multicentre Study, Odense Prenatal Study, Asclepios Study, Danish Twin Study; Figure 1A) and Britain (Asclepios Study, Omnibus Survey; Figure 1B) to assess country-specific trends in accidental pregnancies. We also assessed the pooled trend for the remaining countries (Germany, Poland, Italy, Spain) included in the European Multicentre...
confidence intervals for the proportions. Study (Figure 1C). In Denmark, there was no clear trend, the proportion being approximately 7%, possibly with a slightly higher proportion in the 1950s (but based on small numbers) and a transient rise in the early 1980s. In Britain, the proportion was approximately 12% until 1980, and it increased after that. In the other European Multicentre Study countries, reported accidental pregnancies fell slightly from 14% to 11% in the late 1970s and have remained stable since then.

Assumption that accidental pregnancies are associated with greater fecundity

As a preliminary step, using the 3 data sets that included multiple pregnancies per couple, we conducted Cox regression of the first TTP on the second TTP (where available) and confirmed that reported TTP is a stable marker of underlying couple fecundity (Table 3). The proportions of variation explained, using Schemper’s method (25, 26) adjusted for maternal age, were 11%, 2%, and 14% for the European Multicentre Study, Odense Prenatal Study, and the National Child Development Survey, respectively.

A crucial assumption necessary for protection bias to exist is that the fertility distribution of couples who experience an accidental pregnancy is different from that of the general population. We examined the empirical evidence by fitting a beta-geometric distribution (27) to the TTP values of first pregnancies within a study and adjusting for whether or not the pregnancy was accidental. For an accidental pregnancy, the TTP was taken as the value given for the next pregnancy if it was TTP eligible. However, the fertility estimate based on this analysis excludes couples with 2 accidental pregnancies, so we also calculated an upper bound by assigning a TTP of 0 to such couples (similar to the “superfertile” assumption corresponding to standard practice in TTP analysis (11, 12)). The mean fecundity is given by \( \frac{\mu}{\text{intercept} + 0} \), and the ratio of the fecundity of couples who experienced an accidental pregnancy to that of the population as a whole is given by \( s = \frac{\text{intercept}}{\text{intercept} + 0} \), where \( \theta \) is the coefficient for the accidental pregnancy group. Table 4 shows values for \( \mu \) and \( s \) for our data sets. The values of \( s \) are consistently greater than 1.0, confirming the higher fecundity of couples who experience an accidental pregnancy. The true value of \( s \) is probably closer to that estimated from just those couples with one accidental and one TTP-eligible pregnancy because couples experiencing two accidental pregnancies are far less common, as shown in Table 4. The corresponding TTP distributions are shown in Figure 2.

Analysis of simulated data sets to evaluate methods of imputing missing TTP values

We first simulated TTP data sets to use to develop and test suitable methods for imputing missing TTP values for accidental pregnancies. We used the approach of Sallmén et al. (22) to simulate TTP distributions, in which a proportion of couples experience accidental pregnancies that are either retained or terminated (Web Appendix 1). (This information is described in the first of 3 supplementary appendixes; each is referred to as “Web Appendix” in the text and is posted on the Journal’s website (http://aje.oupjournals.org/)). Three data sets were simulated to match as closely as possible the empirical TTP distributions in the European Multicentre Study, Odense Prenatal Study, and National Child Development Survey, including their proportion of accidental pregnancies. For couples simulated to experience an accidental pregnancy that was not terminated, the TTP value was treated as unknown. The simulated data sets, denoted EMS*, OPS*, and NCDS*, respectively, were then analyzed as if the data were real, using each of the following methods to handle the missing TTP values for accidental pregnancies:

1. Omit accidental pregnancies from the analysis (case considered by Sallmén et al.).
2. Omit accidental pregnancies and all pregnancies with a TTP value of \( \leq 1 \) (standard sensitivity analysis; refer to Joffe et al. (12)).
3. Represent accidental pregnancies by TTP values of 0 (superfertile assumption, equivalent to the sensitivity analysis recommended by Joffe et al. (12)).
4. Use the TTP value from another pregnancy for the same couple, if available; otherwise, exclude (empirical replacement).

5. Generate TTP values from an appropriate beta-geometric distribution with parameters estimated as follows:
   a. If multiple pregnancies are available in the data set, fit a beta-geometric to the observed TTP distribution of couples experiencing an accidental pregnancy and at least one further pregnancy with a valid TTP value (beta-geometric imputation 1).
   b. If only one pregnancy is available, fit a beta-geometric to the observed TTP distribution of non-accidental pregnancies and then carry out a sensitivity analysis, adjusting the mean of this beta-geometric distribution to be $\mu = \mu \times s$, taking a range of values of $s$ (beta-geometric imputation 2). Here, we consider values of $s$ from 1.25 to 2.0.

Web Appendix 2 gives technical details for implementing the 2 beta-geometric methods, including how to adjust for covariates. Results reported below are based on multiple imputation averaged over 10 replicates (28).

Because the true fecundity of every couple in EMS*, OPS*, and NCDS* is known, we can use Cox regression to estimate a fecundability ratio (ratio of the estimated to the true odds of conception) representing the degree of bias in the estimate of population fecundity for different analytic strategies (refer to Figure 3). When all accidental pregnancies were omitted, fecundability ratios were underestimated as predicted (22). The bias was almost unaltered when we used the standard alternate analysis also excluding TTP values below 2, whereas the “superfertile” imputation method overcompensated for the bias, as we predicted (24). The empirical replacement method scarcely affected the bias because it omits the couples with 2 accidental pregnancies. The beta-geometric imputation strategy using method 1 only slightly reduced the bias because the mean fecundity of such couples is underestimated. Method 2 was highly sensitive to the value of $s$ and corrected for the bias with a value close to 1.75.

**Impact of protection bias on estimation of trends in fecundity**

Our main motivation was to investigate the impact of protection bias on estimation of fecundity time trends.

<table>
<thead>
<tr>
<th>Study</th>
<th>EMS</th>
<th>Data Set</th>
<th>OPS</th>
<th>NCDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>First pregnancy was TTP eligible</td>
<td>4,379</td>
<td>0.19</td>
<td>1</td>
<td>12,358</td>
</tr>
<tr>
<td>First pregnancy was not TTP eligible, second pregnancy was TTP eligible</td>
<td>109</td>
<td>0.25</td>
<td>1.30</td>
<td>345</td>
</tr>
<tr>
<td>Same group as above, plus couples with first and second pregnancies that were both not TTP eligible and assigned a TTP = 0 value</td>
<td>165</td>
<td>0.40</td>
<td>2.09</td>
<td>405</td>
</tr>
</tbody>
</table>

Abbreviations: EMS, European Multicentre Study; NCDS, National Child Development Survey; OPS, Odense Prenatal Study; TTP, time to pregnancy.

* For a description of the meaning and method of calculation of $\mu$ and $s$, refer to the Empirical Analyses section of the text.

Table 3. Association of Reported Time to Pregnancy for the First Pregnancy With That for the Second Pregnancy

<table>
<thead>
<tr>
<th>TTP for Second Recorded Pregnancy (Months)</th>
<th>EMS</th>
<th>Data Set</th>
<th>OPS</th>
<th>NCDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>Fecundability Ratio</td>
<td>95% CI</td>
<td>No.</td>
<td>Fecundability Ratio</td>
</tr>
<tr>
<td>-----</td>
<td>---------------------</td>
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<td>-----</td>
<td>---------------------</td>
</tr>
<tr>
<td>0–3</td>
<td>1,343</td>
<td>1</td>
<td>2,799</td>
<td>1</td>
</tr>
<tr>
<td>4–8</td>
<td>421</td>
<td>0.61</td>
<td>0.54, 0.68</td>
<td>655</td>
</tr>
<tr>
<td>9–14</td>
<td>189</td>
<td>0.45</td>
<td>0.38, 0.54</td>
<td>276</td>
</tr>
<tr>
<td>&gt;14</td>
<td>379</td>
<td>0.36</td>
<td>0.32, 0.42</td>
<td>262</td>
</tr>
</tbody>
</table>

Abbreviations: EMS, European Multicentre Study; NCDS, National Child Development Survey; OPS, Odense Prenatal Study.

* The fecundability ratios and 95% confidence intervals (CIs) were obtained from Cox regression of the first recorded time to pregnancy (TTP) on the second recorded TTP. All estimates were adjusted for maternal age at the start of the first attempt (quadratic effect) and the difference between maternal age at the start of the second attempt and at the birth/miscarriage of the first baby. Fecundability ratios are interpreted as the relative odds of conception per month during the first pregnancy attempt for couples with a second TTP value in the specified category relative to couples with a second TTP in the shortest category (0–3 months). Values below 1 indicate lower fecundity.

Table 4. Fecundity of Couples Who Experienced One or More Accidental Pregnancies Compared With Those Who Did Not

<table>
<thead>
<tr>
<th>Study</th>
<th>EMS</th>
<th>Data Set</th>
<th>OPS</th>
<th>NCDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>$\mu$</td>
<td>$s$</td>
<td>No.</td>
<td>$\mu$</td>
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</tr>
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</table>

Abbreviations: EMS, European Multicentre Study; NCDS, National Child Development Survey; OPS, Odense Prenatal Study; TTP, time to pregnancy.
We simulated another data set with TTP values covering five 5-year time periods, such that the underlying fecundity remained constant over time but trends in accidental pregnancy rates were present (Web Appendix 3). These trends in accidental pregnancy rates are rather extreme because it proved difficult to introduce a fecundity trend by using plausible values, and it also proved necessary to use a large generated data set of 100,000 to obtain statistically significant bias. We then fitted Cox regression models to the simulated data and estimated the fecundability ratio for each period relative to the earliest. Figure 4 shows the estimates when each of the methods described in the previous section was used to handle accidental pregnancies. As predicted by Sallmén et al. (22), when accidental pregnancies were excluded, an artificial time trend in fecundity was induced.
However, it was small compared with the magnitude of the substantive increase in fecundity observed in a study in Britain, which found that the TTP distribution had shifted to the left (higher fertility) in the period 1961–1993 (23). The bias remains if all pregnancies with TTP values below 2 months are excluded and also if the empirical replacement method is used. As before, replacing accidental pregnancies with a TTP value of zero overcompensates, inducing a time trend in the opposite direction. Beta-geometric imputation method 1 substantially reduces the bias, whereas beta-geometric imputation method 2 is again sensitive to $s$, with a value of 1.5–1.75 providing accurate correction.

**DISCUSSION**

Protection bias results from a systematic change over time in missing TTP values due to pregnancies being accidental. For it to arise, the following 3 conditions must be met:

1. The fertility distribution of couples experiencing accidental pregnancies must be different from that of the remaining TTP-eligible couples.
2. Rates of accidental pregnancy must differ across population subgroups or time periods of interest.
3. Pregnancies that would otherwise have been accidental but are prevented by effective contraception or termination must be “replaced” by a subsequent nonaccidental pregnancy with a valid TTP during the time period studied.

Our investigation of condition 1 focused on couples in 3 data sets with at least 2 pregnancies. We estimated the underlying fecundity of couples experiencing accidental pregnancies by using TTP values from another TTP-eligible pregnancy, where available. We found that couples who experience accidental pregnancies tend to be more fertile than the general population, indicating that the first condition for protection bias is likely to hold in practice.

Empirical evidence for condition 2 is less clear. We found that the proportion of pregnancies that were accidental had fallen historically in some populations but not others. In particular, it had not fallen in Britain, which accords with other information, for example, that teenage birth rates show a similar differential trend between Britain and other western European countries during this period (29). When standard checks on the proportion of accidental pregnancies show negligible trends, protection bias is logically precluded. (Sallmén et al. (22) ignored this when citing the paper by Joffe (23) and wrongly stated that self-reported abortion data were used (30).)

We also found that the change in the proportion of accidental pregnancies over time necessary to produce protection bias in simulated data was much greater than the changes seen in the real data because we had to introduce extreme and implausible trends in accidental pregnancy rates into our simulations and consider unrealistically large sample sizes before a trend in fecundity became apparent (Web Appendix 3). Therefore, protection bias, although potentially present, may not be quantitatively important in practice.

We have assumed until now that condition 3 holds—that prevented pregnancies are later replaced—because it is necessary for protection bias (Sallmén et al. (22) also made this assumption but did not make it explicit). With nonreplacement, the 1950 couple experiences an accidental pregnancy and the 1980 couple no pregnancy, so that both are absent from the TTP distribution and no bias occurs. Replacement may not occur in all cases, and, to that extent, the bias may be even less quantitatively important than our estimates suggest. In addition, if the proportion of replacements is low, the standard TTP analysis ignoring accidental

![Figure 4. Impact of protection bias on estimated time trends in fecundity ratios (odds of conception per month relative to the first period) and 95% confidence intervals (CIs) for different methods of handling accidental pregnancies. True fecundability ratios are estimated by replacing the missing time-to-pregnancy (TTP) value for couples experiencing accidental pregnancies in the simulated data set with a TTP value generated from their (known) underlying fecundity distribution. For a description of the meaning and method of calculation of $s$, refer to the Empirical Analyses section of the text. BG, beta-geometric.](image-url)
pregnancies will be unbiased (the equivalent pregnancies are excluded in both periods), whereas the sensitivity analysis we propose may introduce some bias. It may be possible to investigate the question of replacement empirically. We believe that the nonreplacement case is likely to affect quite small numbers, primarily of later children.

Although TTP applies to couples, data are usually collected from one or the other partner (typically the woman). Protection bias involves considering more than 1 pregnancy per respondent, and the partner may change for different pregnancies. Thus, although we discuss the bias in terms of “couples,” in some cases the partner may have changed, which would dilute the empirical estimates shown here, in much the same way as with measurement error.

Our results show that one of the standard sensitivity analyses (12, 24), the “superfertile assumption” with missing values set to TTP = 0, provides upper bounds on the true fecundability ratio. In some situations, this may be sufficient to show that there is no problem with protection bias (23) or, if not the case, to estimate the upper bound of the bias.

When protection bias is suspected, it is possible to use the multiple imputation methods proposed in this paper to provide an additional technique for sensitivity analysis. There is an advantage in collecting information on all pregnancies to enable the difference in fecundity between those with and without accidental pregnancies to be estimated empirically. If only one pregnancy per couple is available, however, a fallback position is to examine sensitivity by using the range of values of x that we estimated here, under the assumption that the same associations between couples with and without accidental pregnancies apply in the population under study.

Protection bias is not the only potential problem in assessing fecundity trends using TTP. We need to consider the possible effect of reporting bias because accurate reporting of accidental pregnancies is not guaranteed. In particular, there is concern that, over time, subjects reclassify less recent pregnancies from accidental to rapid TTP-eligible conceptions (“wantedness bias” (11)). Our data support a tendency in this direction because the proportion of accidental pregnancies reported in the Odense Prenatal Study, in which women were interviewed during pregnancy, is slightly higher than that reported in other Danish data sets with pregnancies occurring in the same historical period but with longer recall (details available from the authors on request). By replacing some accidental pregnancies with short TTP values, response bias mimics a partial form of the sensitivity analysis that puts TTP = 0 for accidental pregnancies. It thus reduces the effect of protection bias.

Another issue, well recognized in the literature, is truncation bias (12). For example, if data collection takes place in June 2009, couples who started unprotected intercourse in June 2008 are included in the sample only if they conceived within 3 months (assuming a gestational length of 9 months), and less fertile couples are systematically excluded. We carried out simulation analyses to compare the distorting effects of truncation bias and protection bias, and we found the latter to be small compared with the former (results available on request).

When protection bias is present, compensatory behavior change is also likely, a form of risk compensation in an apparently safer environment (31) that reduces the extent of protection bias. Risk behavior has apparently altered with the availability of effective contraception and induced abortion, and as social norms on single parenthood have changed; thus, the proportion of pregnancies reported as accidental has not fallen by as much as the increased ease of preventing them would predict and, in some cases (e.g., in Britain in 1961–1993), not at all (23). This topic is important for future research, but detailed exploration of this bias requires a richer TTP data set with more behavioral information than is currently available.

It has previously been recommended that more attention be paid to the effect on TTP of behavior and knowledge (12). There is evidence that persistence (32) and knowledge about the fertile days of a woman’s menstrual cycle (33) can influence fecundity. More research on reporting bias in this context is required, and more general exploration is needed of the relation between behavior such as use of contraception and abortion, which is what is biologically important, and attitudinal constructs such as trying, wanting, or planning to conceive (14–20).

In conclusion, our investigations confirm empirically that the protection bias suggested by Sallmén et al. (22) probably does exist but is quantitatively not very important. In any study of fecundity trends or cross-cultural differences, the proportion of accidental pregnancies can be used to screen for it. The traditional alternate analysis setting TTP = 0 for accidental pregnancies is not in itself a satisfactory estimate, but, together with the naı̈ve analysis, it indicates the bounds within which the true answer lies. If present, the bias can be addressed by the imputation methods proposed here. Future TTP research should focus on not only biologic but also behavioral factors affecting biological fertility.

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