Online Supplementary Material

"Reducing the prevalence of alcohol-exposed pregnancies in the U.S.: A simulation modeling study"

S1. Analyzing the 2013-2015 National Survey on Family Growth (NSFG)

The 2013-2015 National Survey on Family Growth (NSFG) provides a nationally representative sample of the U.S. household population of males and females, ages 15–44 years.[1] The survey includes a total of 5,699 female participants, but we excluded observations with inconsistent responses:

1. Four individuals indicated that they were seeking pregnancy but were not sexually active
2. Twenty-four individuals reported being sexually inactive (i.e. didn't have a male sexual partner in the last year) but reported having had sex with a man in the last month.

Table S1 displays the age-distribution of female participants in this survey. Table S2 lists the proportion of women in each sexual-behavior group by age category. Additional details of how the parameters of our simulation models are informed by 2013-2015 NSFG data are provided in the following subsections.

Table S1: Age-distribution female participants of the 2013-2015 National Survey on Family Growth

Age Group	Percentage
[15, 19]	17.81%
[20, 24]	16.72%
[25, 29]	18.29%
[30, 34]	18.13%
[35, 39]	15.32%
[40, 44]	13.74%
Sum	100.00%

Table S2: Age-specific proportion of female participants of the 2013-2015 National Survey on Family Growth that belong to each sexual-behavior category

Sexual Behavior Group	[15-19]	[20-24]	[25-29]	[30-34]	[35-39]	[40-44]
Sterile	1.2%	3.3%	11.2%	23.6%	36.1%	51.9%
Inactive	61.4%	18.9%	12.7%	7.8%	9.9%	10.1%
Protected sex	23.7%	54.3%	50.5%	42.1%	34.3%	22.6%
Unprotected Sex	10.9%	14.2%	12.9%	14.2%	12.0%	9.1%
Seeking Pregnancy	0.1%	2.6%	5.3%	6.7%	5.4%	5.7%
Pregnant	2.8%	6.7%	7.3%	5.6%	2.3%	0.7%
Sum	100%	100%	100%	100%	100%	100%

Determining Level of Sexual Activity

An interviewee must have had at least 1 sexual partner in the last year (variable PARTS1YR from the NSFG data) to be considered sexually active. Participants who were considered sexually active were asked for the number of times they had sex in the last 4 weeks (variable PST4WKSX). All observations for which the interviewee either refused to answer the question or indicated that they did not know the answer, were recoded as missing. Fig. S1 displays the histogram of monthly number of sexual encounters for women in each age and sexual-behavior group (as defined in the main text). Sample size considerations influenced the decision not to fit age-specific distributions for individuals in the seeking pregnancy and pregnant groups (for several age groups in these groupings data was only available for 15 or fewer survey participants).

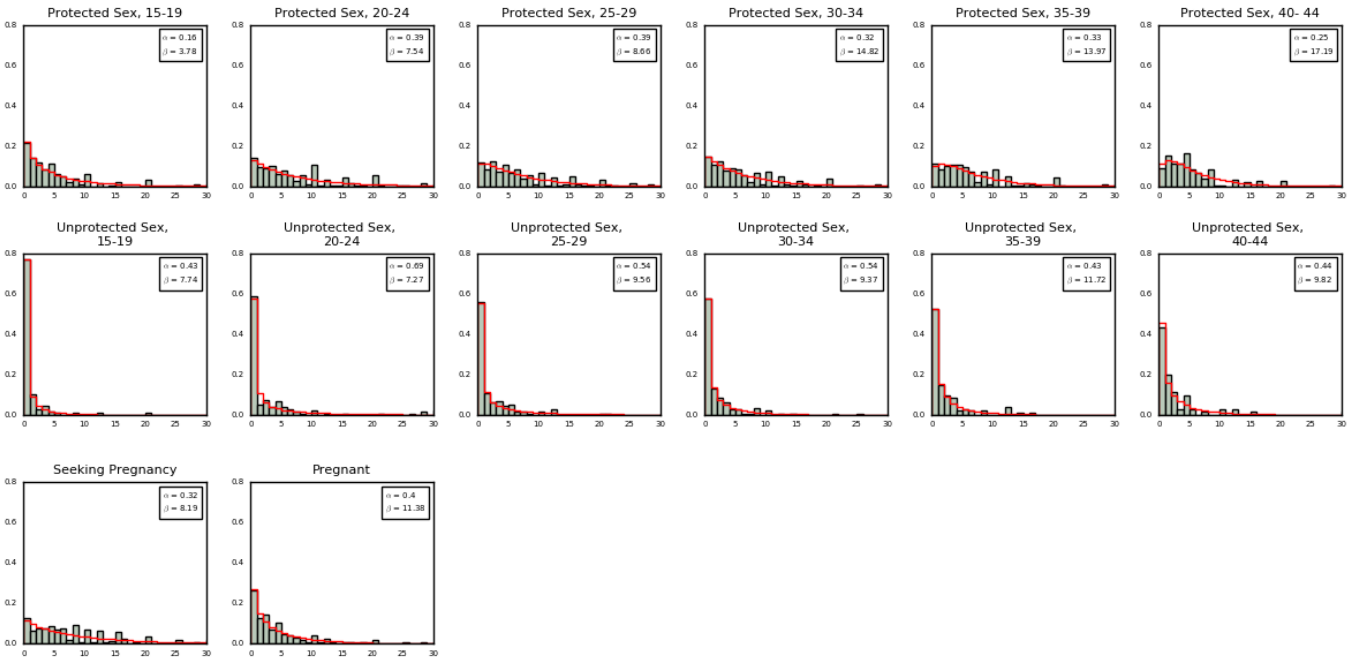

Fig. S1: Distribution of monthly number of sexual encounters by age and sexual-behavior groups based on data from the 2013-2015 National Survey on Family Growth Data. Red curves represent fitted Gamma-Poisson distributions with parameters $\boldsymbol{\alpha}$ and $\boldsymbol{\beta}$.

Determining Alcohol Use Behavior

A series of survey questions were used to understand the drinking patterns of the survey participants. First, interviewees were asked: on average how often in the last year they had beer, wine, liquor, or other alcohol beverages (survey variable DRINK12). Participants could respond that they never drank, or that they drank once or several times per week, month, or year. Individuals that reported any consumption of alcohol in the last year were asked to indicate whether they would prefer to report their drinking over the last 30 days in terms of days per week (variable DRINK30D) or days per month. All estimates of the number of days of drinking per month were rounded to the nearest integer. If the unit selection (per week or per month) and/or the number of drinks per unit time was not ascertained, unknown, or the respondent refused to provide this information then, for this interviewee, the number of days of drinking per month was coded as missing. If the interviewee reported number of days of drinking per week, it was assumed that the same rate of drinking applies for all the weeks in the month. In the case that an individual

reported more than 7 days/week of drinking per week, it was assumed that what they were reporting was the number of days of drinking per month. Fig. S2 displays the histogram of number of days of drinking per month for women in each age and sexual-behavior groups (as defined in the main text). The red curves represent the fitted Gamma-Poisson probability distributions.

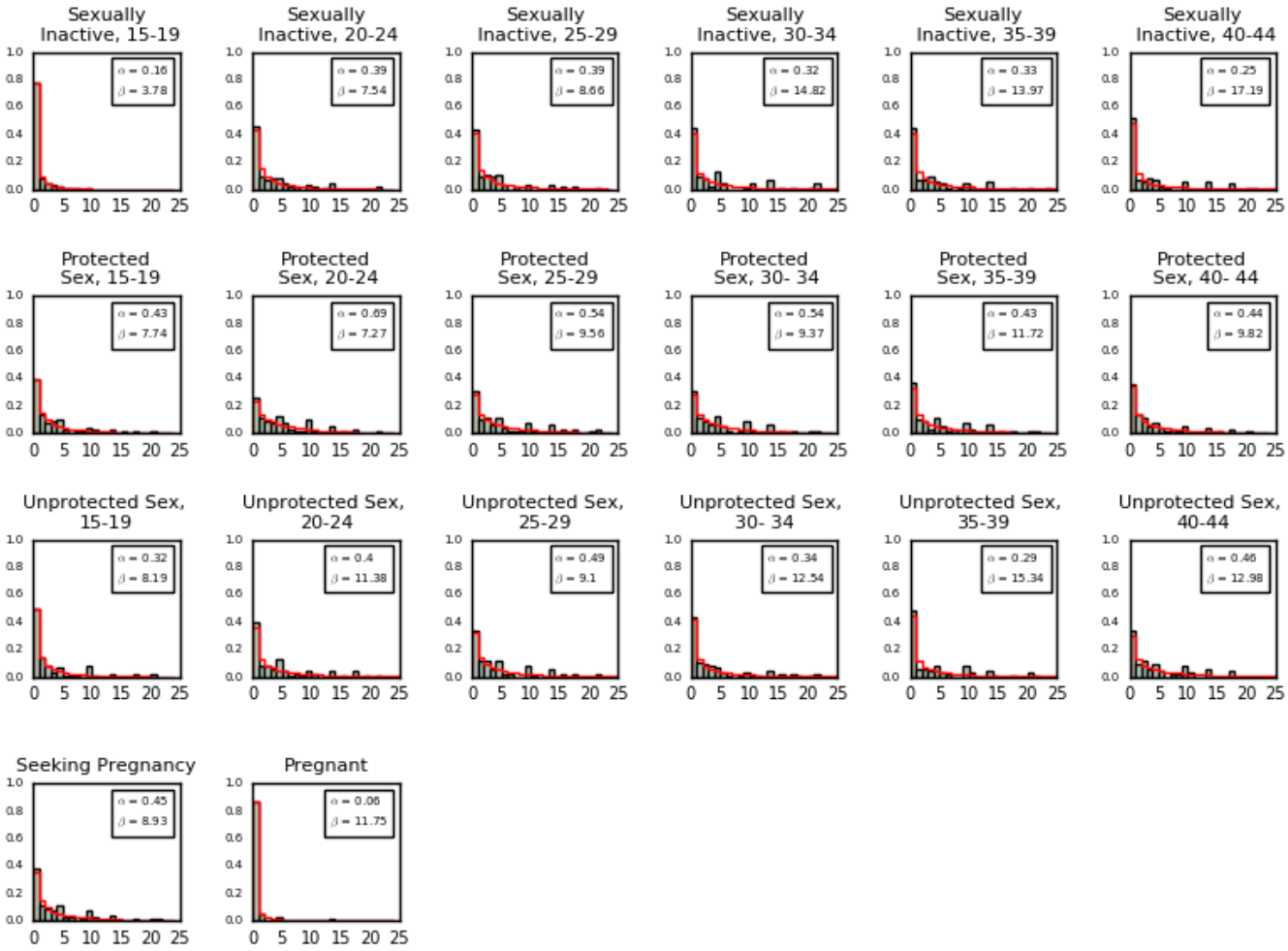

Fig. S2: Distribution of monthly number of alcoholic drinks consumed by age and sexual-behavior groups based on data from the 2013-2015 National Survey on Family Growth. Red curves represent fitted Gamma-Poisson distributions with parameters $\boldsymbol{\alpha}$ and $\boldsymbol{\beta}$.

Contraceptive Use and Effectiveness

Individuals who indicated that they or their partner were naturally or surgically sterile were considered not on contraception and not at risk of becoming pregnant. These individuals make up the 'sterile' sexual activity group (Fig. 1). Individuals who reported using any contraceptive method (including methods such as withdrawal or the rhythm method) were classified as using contraceptives. Table S3 shows the proportion of non-sterile, non-pregnant US women age 15 – 44 using contraception who use each contraceptive method (estimated from the NSFG survey) along with the probability of failure after 1 year of using each contraceptive [2, 3].

Table S3: Contraceptive use statistics among non-sterile, non-pregnant U.S. women who use contraception, ages 15-44.

Contraceptive Method	Proportion of women using each contraceptive method	Probability of failure after 1 year of use [2, 3]
Hormonal Implant	4.36%	0.05%
Depo-Provera	7.24%	6%
Birth Control Pill	34.90%	9%
Vaginal Ring	2.70%	9%
IUD, coil, or loop	16.61%	0.05%
Partner's Condom Use	22.22%	18%
Withdrawal	9.42%	22%
Rhythm Method	1.92%	24%
Contraceptive patch	0.46%	9%
Diaphragm	0.12%	12%
Spermicide	0.05%	28%
	100%	

Correlation between Sexual Activity, Alcohol Consumption, and the Choice of Contraceptive Method

The sample size of NSFG doesn't allow us to characterize the joint probability distributions of sexual activity, alcohol consumption, and contraceptive methods but to capture the correlation between these input parameters, we characterized separate probability distributions for sexual activity and alcohol consumption for sexual behavior groups a simulated woman may belong to (Fig. S1 and Fig. S2). To further investigate the validity of this approach, we calculated the correlations between the monthly number of sexual counters and the monthly number of alcoholic drinks by age and sexual behavior groups (Tables below). These tables indicate that the correlation between the number of sexual encounters and the number of alcoholic drinks among different age and sexual behavior groups is low.

Table S4: Correlation between the monthly number of sexual encounters and the monthly number of alcoholic drinks by age groups

Age Group	**Correlation**	**p-value**
[15, 19]	0.1237	0.0145
[20, 24]	0.0914	0.0113
[25, 29]	0.0200	0.5483
[30, 34]	0.0907	0.0052
[35, 39]	0.0223	0.5326
[40, 44]	0.0486	0.1992

Table S5: Correlation between the monthly number of sexual encounters and the monthly number of alcoholic drinks by sexual behavior group

Sexual Behavior Group	Correlation	p-value
Protected Sex	0.0775	0.0003
Unprotected Sex	0.0061	0.8734
Pregnant	0.1385	0.0299
Seeking pregnancy	0.0545	0.4017
Sterile	0.0520	0.0832

To evaluate whether the distribution of number of alcoholic drinks different by contraception method among women using contraception we produced the violin plots of monthly number of drinks by contraceptive methods as displayed below. While there are some variations across different contraceptive methods (left panel), the number of observations for several contraceptive methods were too small to properly characterize a separate distribution for each contraceptive method. Instead, we also looked at the number of monthly drinks among women who use effective versus ineffective contraceptives (right panel). This figure suggests that the distribution of the number of drinks among these two groups are similar.

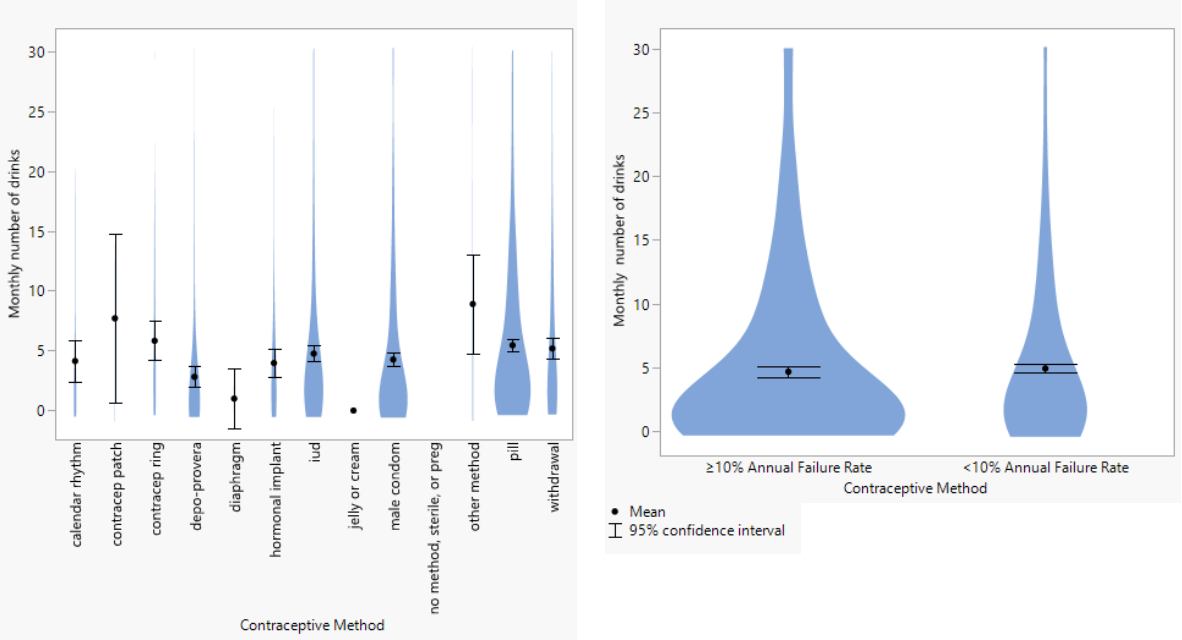

Fig. S3: Violin plots of monthly number of drinks by contraceptive methods.

Time Until Becoming Aware of a Pregnancy

The average time until a woman becomes aware of pregnancy was calculated separately for pregnancies that were "intended" versus "unintended". We considered a pregnancy intended if a participant described their pregnancy (survey variable WANTRESP) as "later, overdue" or "right time", and unintended if the participate described their pregnancy as "too soon, mistimed" or "unwanted". Pregnancies for which the respondent indicated that, in the time

right before they became pregnant, they did not know or did not care whether they had a child were coded as missing data on pregnancy intent.

After determining which pregnancies were intended or unintended, we calculated the time to awareness of pregnancy (survey variable LEARNPRG). This variable reflects the number of weeks pregnant the respondent was when she realized she was pregnant. This data was collected for all completed pregnancies (i.e. pregnancies that did not end with an induced abortion or with unnamed baby placed for adoption). LEARNPRG is a recode so it reflects responses to a range of questions, the most significant of which is the following question: "How many weeks pregnant were you when you learned that you were pregnant this (nth) time?" which was asked of the relevant respondent for each completed pregnancy. If the necessary information could not be extracted from the response to this question, the respondent was asked to indicate, if known, the trimester during which she became aware of her pregnancy. If pregnancy awareness occurred during the first trimester, the time to awareness was assumed to be 10 weeks. If it occurred during the second trimester, time to awareness was assumed to be 18 weeks. Finally, if the respondent indicated that pregnancy awareness occurred during the third trimester, the time to pregnancy awareness was assumed to be 30 weeks.

Fig. S4 displays the histogram of weeks until becoming aware of a planned or unplanned pregnancy. The red curves represent the fitted Johnson Su probability distributions. We note that pregnancies are gestationally dated based on the first day of the last menstrual period. Since pregnancy cannot occur until ovulation and implantation does not occur for 6-12 days after ovulation, [4, 5] actual pregnancies occur on average 3 weeks after the last menstrual period. Therefore, we determine the time until the detection of a pregnancy as $\max\{0, T-\tau\}$, where T is a random draw from the probability distributions in Fig. S4 and τ is the weeks since the end of the last menstrual period.

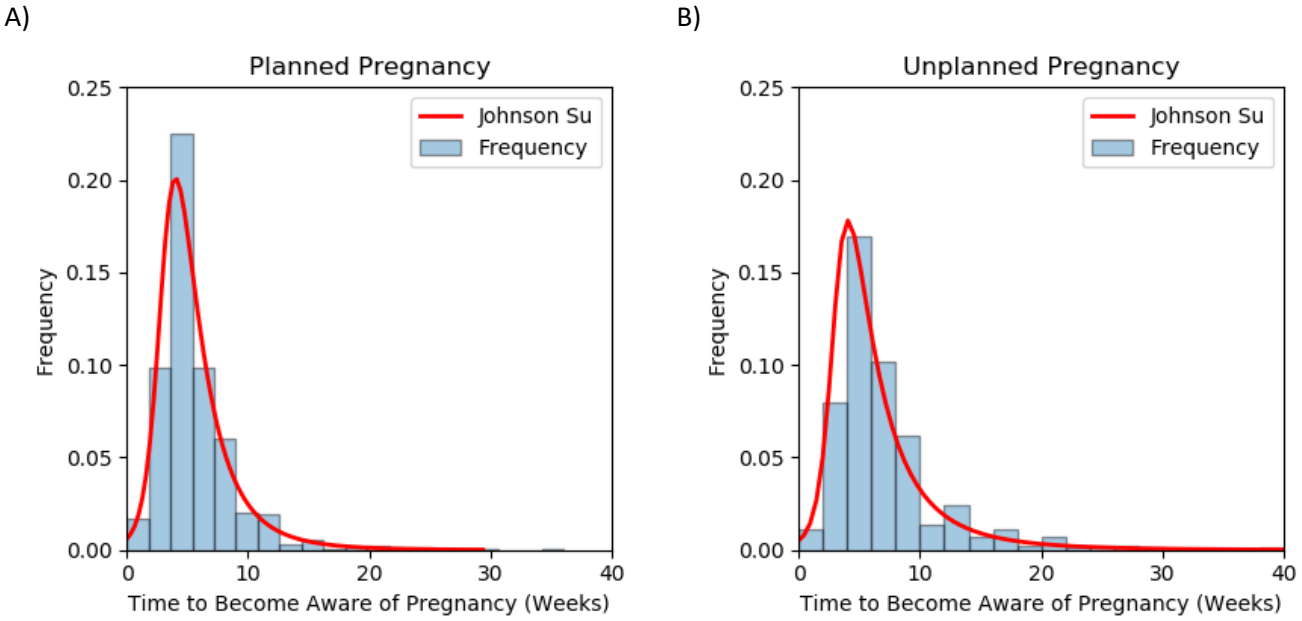

Fig. S4: Distribution of time to become aware of a planned pregnancy (panel A) and of an unplanned pregnancy (panel B) along with the fitted Johnson Su distributions (red curves) based on data from the 2013-2015 National Survey on Family Growth Data.

To evaluate whether the distributions of time to become aware of a pregnancy varies by age and contraception method, we produced the violin plots of time until becoming aware of a planned or unplanned pregnancy conditional on age and contraceptive methods, as shown below. Time until becoming aware of a pregnancy across all age groups had similar distribution (top row). The distribution of time until becoming aware of a pregnancy varied slightly over different contraceptive methods (bottom row) but the variation was not significant to warrant assuming different probability distributions in the model. Furthermore, the data to identify these distributions were spars as only 15% of 4705 woman with planned pregnancy and 45% of 4540 woman with unplanned pregnancy reported their choice of contraceptive method. Therefore, we model the time until becoming aware of a pregnancy using one distribution for unwanted pregnancies and one distribution for planned pregnancies (Fig. S4).

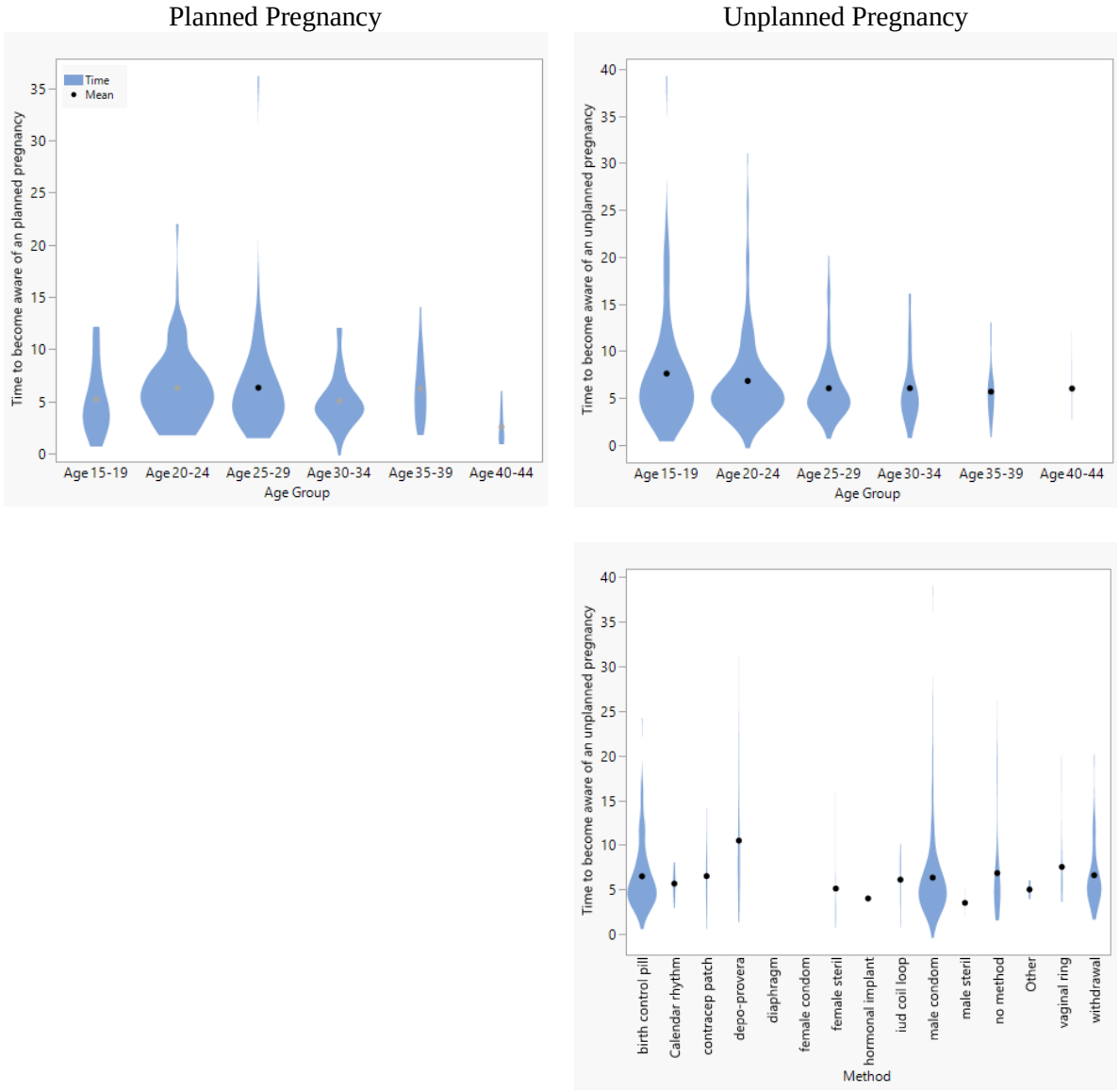

Fig. S5: Violin plots of time until becoming aware of a planned or unplanned pregnancy conditional on age (top row) and on the choice of contraceptive methods (bottom row).

Age-Specific Percentage of Pregnancies That Resulted in Miscarriage or Abortion in the Past 5 Years

To calculate the age-specific percentage of pregnancies that resulted in a miscarriage or abortion, the following assumptions are made:

1. All pregnancies resulted in live birth, miscarriage or abortion. Therefore, for each female survey participant, summing up the relevant survey variables (i.e. CASIBIRTH, CASILOSS, and CASIABOR) yields the number of all pregnancies they had in the 5 years prior to the interview date.
2. In the absence of information about when a specific pregnancy occurred, it is assumed that all pregnancies occurred halfway through the five-year window (i.e. age at interview minus 2.5 years).
3. Responses with values 97, 98, 99 or nonsensical values are coded as missing (e.g. Two individuals reported 11 or more livebirths and one individual reported 90 miscarriages over 5 years; all of these responses were determined to be illogical and were recoded as missing).

Table S6 shows the percentage of pregnancies over the past 5 years that results in miscarriage or abortion for participants of the 2013-2015 NSFG.

Table S6: Percentage of pregnancies over the past 5 years that results in miscarriage or abortion for female participants of the 2013-2015 National Survey on Family Growth

Age Group	Miscarried	Aborted
[15, 19]	29.3%	22.1%
[20, 24]	19.0%	12.0%
[25, 29]	21.8%	10.7%
[30, 34]	21.5%	7.5%
[35, 39]	23.9%	7.9%
[40, 44]	26.6%	5.6%

S2. Modeling the Change in A Woman's Sexual-Behavior Group Over Time

To initialize the simulation model, the initial age group of each individual is determined according to the probabilities listed in Table S1. The initial individual's age is then calculated as $15 + 5(U + a - 1) - w$, where U is a random number uniformly distributed over $[0,1)$, $a \in 1, 2, \ldots, 6$ is the age group of this individual (Table S1), and w is the simulation warm-up period (for our analysis, we chose $w = 5$ years). Given the initial age group of the individual, her initial sexual-behavior group is determined according to the probabilities listed in Table S2. If the sampled sexual-behavior group is 'Pregnant', the time (in years) until giving birth is calculated as $U \times 9/12$, where U is a random number uniformly distributed over $[0,1)$.

Throughout the simulation, the individual may become pregnant according to the model that is described in the following section. Non-sterile women who are not pregnant may move to a new sexual-behavior group whenever they age one year. This transition is determined according to an age-dependent Markov model (Fig. 1, left panel). In the absence of data to directly inform the transition probability matrices of this Markov model, we estimated these

probability matrices by ensuring that the proportion of women in each age and sexual-behavior group remain consistent with the 2013-2015 National Survey on Family Growth (NSFG) data during 6 years of simulation.

To illustrate, Fig. S6 confirms that the distribution of women in our simulated cohort across different age and sexual-behavior groups remains consistent with what observed in the NSFG data after 5 years of simulation.

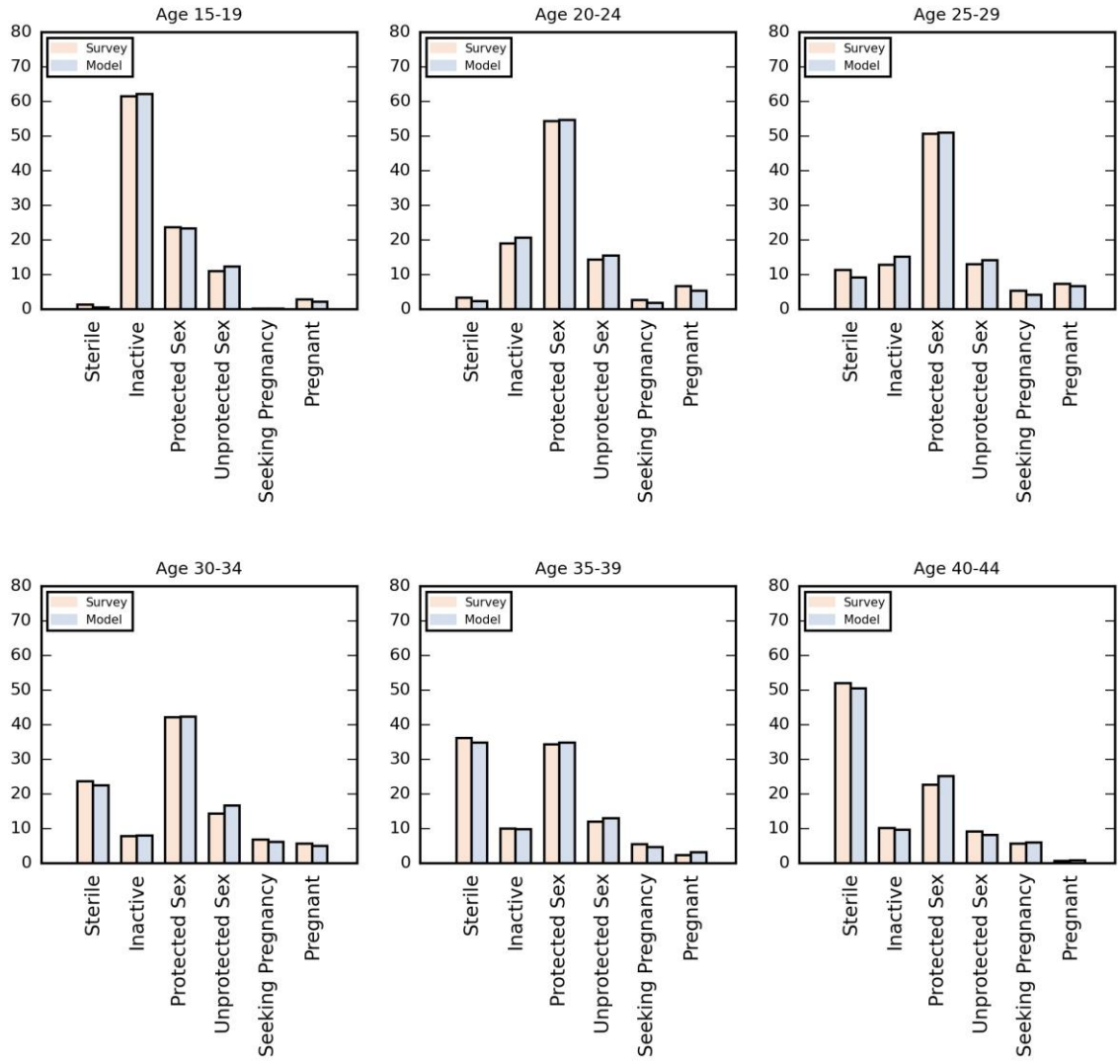

Fig. S6: Percentage of women in age groups that belong to each sexual-activity group as informed by the 2013-2015 National Survey on Family Growth (NSFG) data (Table S1, blue bars in these figures) and produced by our simulation model (orange bars) at the beginning of the projection period (after a 5-year warm-up period).

In the absence of reliable data to model a woman's choice of contraceptive method over time, we made the following simplifying, yet reasonable, assumption. A simulated woman who is in "protected sex" group does not change her contraceptive method unless she moves out of this group. If she later moves back to this group (i.e. from "inactive", "seeking pregnancy", "unprotected sex", or "pregnant" to "protected sex"), her choice of contraceptive will be reassigned according to the data in Table S3. Since our simulation period is relatively short (5 years of warm-up and 1 years of projection), we believe this assumption does not play a significant role in our conclusions.

At the beginning of each week, the probability that a simulated woman would get pregnant during the following week is calculated based on her level of sexual activity and her choice of contraceptives (as described in the following section). It is assumed that the women in the sexual-behavior group 'Sexually-Inactive' or 'Sterile' will not get pregnant (Fig. 1). If a woman gets pregnant, she remains unaware about her pregnancy for a certain period that is determined by a random draw from the lognormal distributions in Fig. S4 (if the pregnancy was planned, the lognormal distribution in Fig. S4A is used; otherwise the lognormal distribution in Fig. S4B is used). At this time, it is determined if the pregnancy is destined to be miscarried based the age-specific probabilities in Table S6. If the pregnancy was unintended, we assumed it will be aborted with 12% probability. This choice of probability led our model to produce estimates for the age-specific proportion of pregnancies aborted that matches those of informed by the 2013-2015 NSFG data (Fig. S7E). We assume that if a woman is destined to have a miscarriage, it occurs on average 8 weeks after conception, and that a pregnant woman who will not experience miscarriage or abortion will give birth 38 weeks after conception.

S3. Calculating the Probability of Getting Pregnant during a Week

We assume that a simulated woman may only become pregnancy during 1 week out of a 4 week cycle consistent with the existing evidence that suggests nearly all pregnancies can be attributed to intercourse during the week leading to the day of ovulation [6-8]. To calculate the probability that a woman gets pregnant over the next week, we first use the fitted probability distributions in Fig. S1 to determine the number of sexual encounters she would have over the next week, k. To this end, we note that a realization K from the fitted probability distributions in Fig. S1 represents the number of sexual encounter over the next month (or approximately over the next four weeks). To get the weekly number of sexual encounters we assume that these K encounters are distributed uniformly over the next 4 weeks according to a multinomial distribution with number of trials equal to K and event probabilities equal to $1/4$. Once the number of sexual encounters during the next week is determined, say k, the probability that a woman in age group i who uses the contraceptive method j becomes pregnant over the next week is calculated as:

$$1 - \left(1 - p_i(1 - \epsilon_j)\right)^k, \tag{1}$$

(i.e. the complement of the probability that none of the sexual encounters results in pregnancy) where p_i is the probability that a woman in age group i could get pregnant after a sexual intercourse when no contraception is used, and ε_j is the effectiveness of contraception method j. Parameters p_i's are informed by existing estimates[9, 10] and adjusted to match the U.S. age-specific annual birth rates in the U.S. (Fig. 2A in the main text). Contraceptive effectiveness parameters ε_j are estimated through the approach described below.

S4. Estimating the Effectiveness of Contraception Methods in Each Sexual Encounter, ϵ_j

The probability of failure after one year of use for different contraceptive methods are provided in Table S3. To use these data to estimate the effectiveness of each contraceptives in each sexual encounter (i.e. ϵ_j in Eq. 1), we use the following approach. Let $A_{i,j}$ denote the event that a woman in age group i who uses contraception method j becomes

pregnant during period Δt, and let the random variable K_i denote the number of sexual encounters during this period. The probability of event $A_{i,j}$ can be calculated by conditioning on the number of sexual encounters (i.e. K_i):

$$\Pr\{A_{i,j}\} = \sum_{k=0}^{\infty} \Pr\{A_{i,j} | K_i = k\} P_{K_i}(k)\,. \tag{2}$$

If we assume that the number of sexual encounters for a woman in age group i during a period Δt (i.e. the random variable K_i in Eq. 2) follows a Poisson distribution with rate $\lambda_i \Delta t$, then:

$$\Pr\{A_{i,j}\} = \sum_{k=0}^{\infty} \left[1 - \left(1 - p_i(1-\epsilon_j)\right)^k\right] \frac{(\lambda_i \Delta t)^k e^{-\lambda_i \Delta t}}{k!} \tag{3}$$

$$= \sum_{k=0}^{\infty} \frac{(\lambda_i \Delta t)^k e^{-\lambda_i \Delta t}}{k!} - \sum_{k=0}^{\infty} \left(1 - p_i(1-\epsilon_j)\right)^k \frac{(\lambda_i \Delta t)^k e^{-\lambda_i \Delta t}}{k!} \tag{4}$$

$$= 1 - e^{-p_i(1-\epsilon_j)\Delta t \lambda_i}. \tag{5}$$

Eq. 5 is obtained by noting that $\sum_{k=0}^{\infty} \frac{(\lambda_i \Delta t)^k e^{-\lambda_i \Delta t}}{k!} = 1$ (a property of Poisson distributions) and that $\sum_{k=0}^{\infty} \left(1 - p_i(1-\epsilon_j)\right)^k \frac{(\lambda_i \Delta t)^k e^{-\lambda_i \Delta t}}{k!}$ is the z-transform[1] of Poison distribution for $z = 1 - p_i(1-\epsilon_j)$, and hence, is equal to $e^{-p_i(1-\epsilon_j)\Delta t \lambda_i}$.

We let α_j denote the probability of unintended pregnancy within a year for each contraception method, as listed in Table S3. As shown above, the probability a woman in age group i who uses contraception method j becomes pregnant during a period Δt can be calculated as $1 - e^{-p_i(1-\epsilon_j)\Delta t \lambda_i}$. Therefore, to estimate the effectiveness of the contraception method j for an average female population member, we can set $1 - e^{-p(1-\epsilon_j)52\lambda} = \alpha_j$ where λ is the average weekly number of sexual encounters (informed by survey data) and p is the probability that an average female population member could get pregnant after a sexual intercourse when no contraception is used. This leads to $\epsilon_j = 1 + \frac{1}{p\lambda 52} \ln(1 - \alpha_j)$ as an estimate for the effectiveness of contraception method j. To calculate ϵ_j, we set $p = \sum_i \pi_i p_i$, where π_i is the proportion of female population members that belong to age group i.

[1] z-transform of a discrete random variable X with probability mass function $P_X(x)$ is defined as $G(z) = E[z^X] = \sum_{x=0}^{\infty} z^x P_X(x)$ and for a Poisson distribution with rate $\lambda\Delta$, $G(z) = e^{(z-1)\lambda\Delta t}$.

S5. Model Parameters

Table S7: Model Parameters

Parameter	Value	Source
Cohort size	5,671	To match the number of female participants in 2013-2015 NSFG.
Probability of getting pregnant after a sexual encounter when no contraceptive is used		Informed by existing estimates [9, 10] and adjusted to match the U.S. age-specific annual birth rates (Fig. 2A)
Age group [15, 19]	6.5%	
Age group [20, 24]	3.0%	
Age group [25, 29]	3.5%	
Age group [30, 34]	3.0%	
Age group [35, 39]	2.5%	
Age group [40, 44]	0.5%	
Contraceptive methods		
Choice of method	Empirical distribution	2013-2015 NSFG (Table S3)
Effectiveness	Varies by method	[2] (Table S3)
Weeks until aware of pregnancy		
Planned pregnancy	LogNormal distribution (mean = 5.4, StDev = 3.3)	2013-2015 NSFG (Fig. S4A)
Unplanned pregnancy	LogNormal distribution (mean = 6.6, StDev = 4.8)	2013-2015 NSFG (Fig. S4B)
Probability of miscarriage	Varies by age	2013-2015 NSFG (Table S6)
Excess probability of abortion if pregnancy is unintended	15%	Estimated to match the percentage of pregnancies over the past 5 years that aborted for female participants of the 2013-2015 NSFG (Table S6 and Fig. S7E)
Excess probability of abortion due to alcohol consumption during the month before detection of the pregnancy	50%	Estimated to match the results of [11] where among women seeking pregnancy termination, about 56% reported any alcohol using the month before pregnancy recognition (in our model, 52% (45-58%) of woman who terminate their pregnancy have consumed alcohol during the month prior to pregnancy recognition).
Number of monthly sexual encounters	Gamma-Poisson distributions varies by age and sexual-behavior group	2013-2015 NSFG (Fig. S1)
Number of days consumed alcohol drinks in a month	Gamma-Poisson distributions varies by age and sexual-behavior group	2013-2015 NSFG (Fig. S2)

S6. Additional Validation Figures

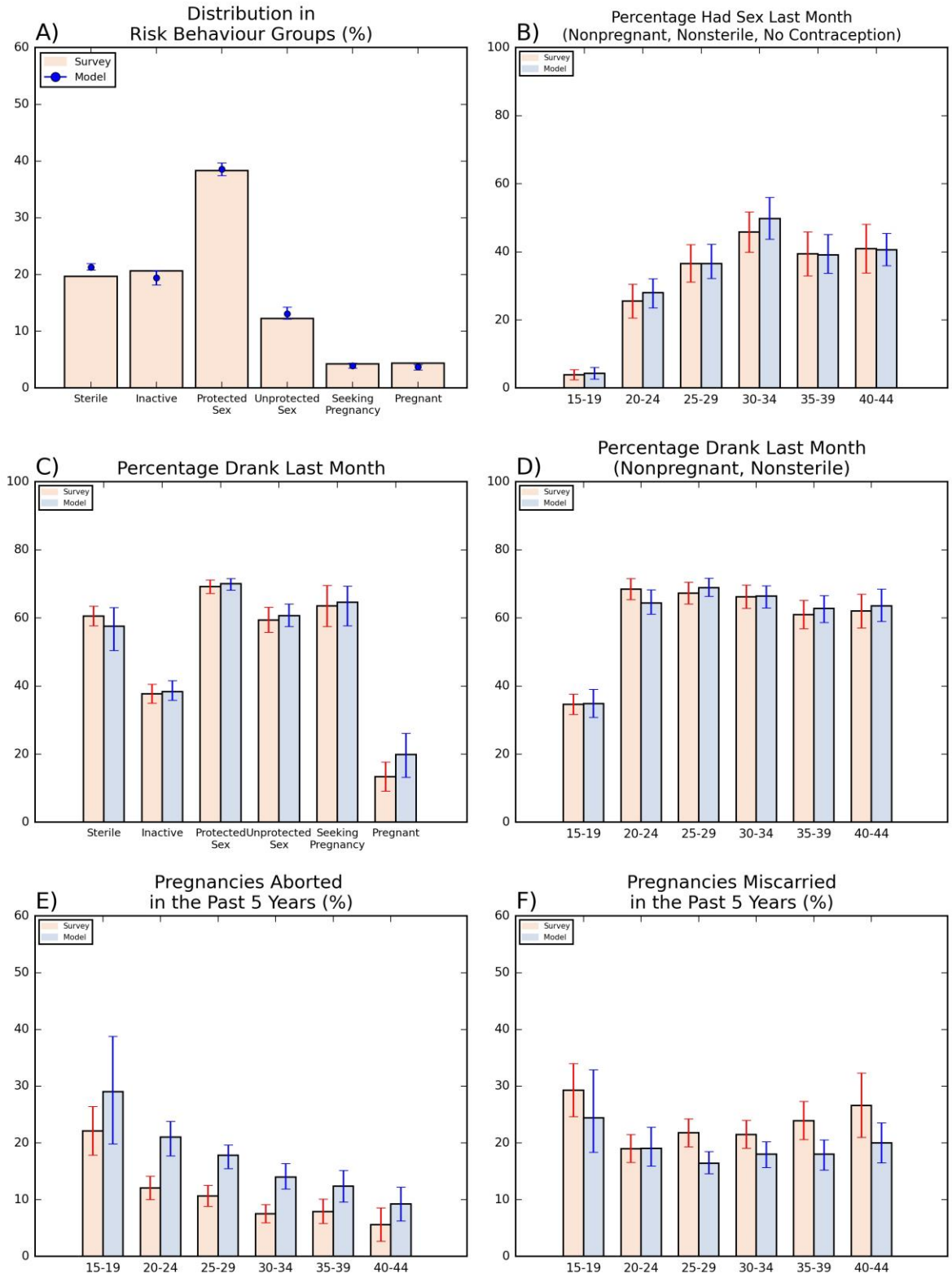

Fig. S7: Additional figure (besides Fig. 2 in the main text) to demonstrate the ability of our model to produce estimates that matches those calculated from the 2013-2015 National Survey on Family Growth Data.

S7. Additional Supporting Results

Table S8: Change in the prevalence of AEPs and unaware AEPs for each additional 1 million U.S. women of reproductive age who adhere to the strategies listed in Table 1.

Strategy	Reduction in the prevalence of AEPs	Reduction in the prevalence of unaware AEPs
A	-1.3 (-1.6--0.9)	-0.8 (-1.1--0.6)
B	-1.2 (-3.3-0.9)	-2.3 (-4.1--0.8)
C	-3.6 (-4.4--2.9)	-1.3 (-1.8--0.8)
D	-2.2 (-2.6--1.8)	-1.3 (-1.6--1.0)
E	-1.6 (-1.9--1.4)	-1.0 (-1.2--0.8)
F	-1.7 (-2.0--1.4)	-1.1 (-1.3--0.9)

Intervals represent the 95% uncertainty intervals.

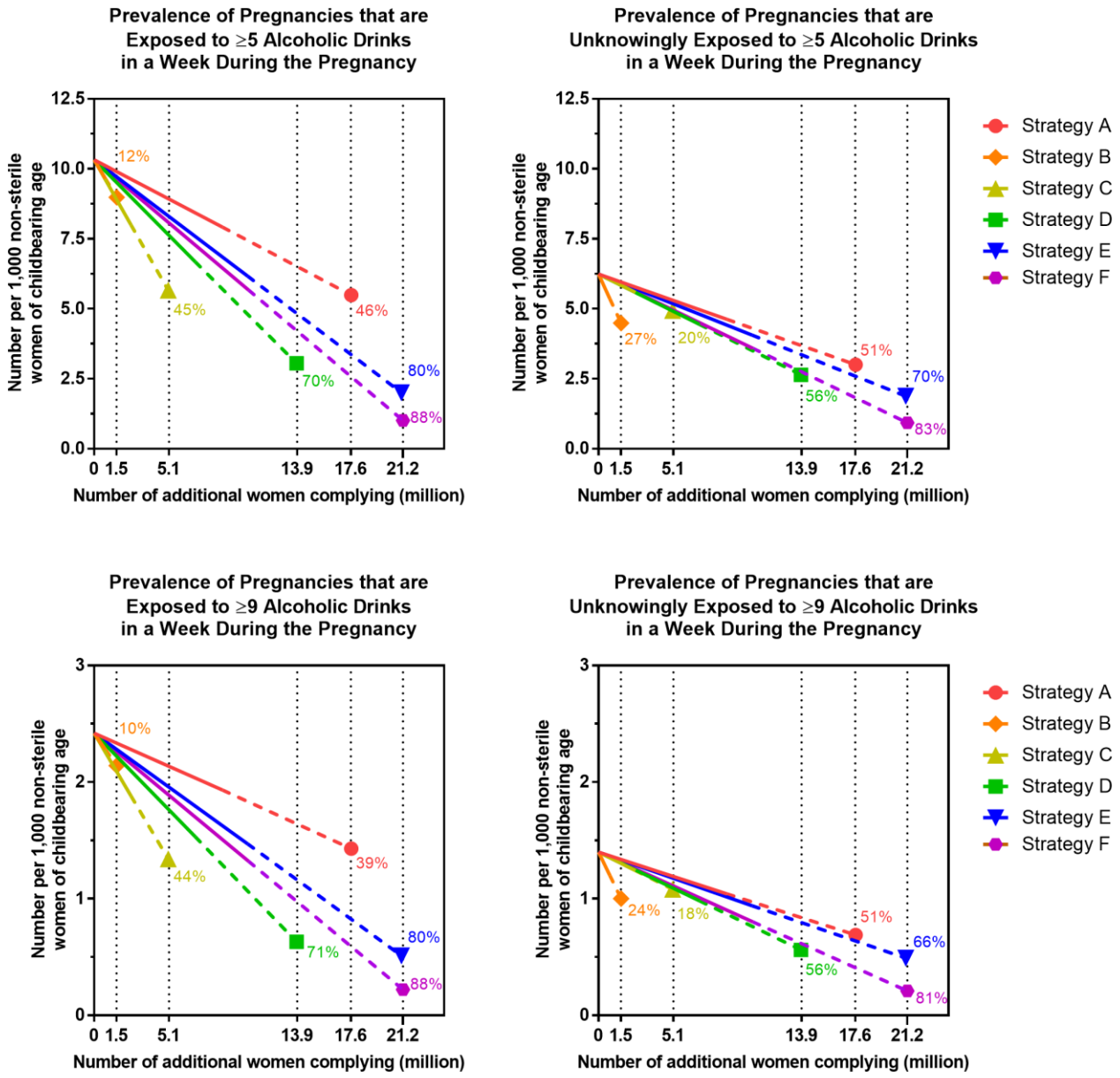

Fig. S8: Change in the prevalence of pregnancies that are exposed to ≥5 or ≥9 alcoholic drinks in a week during the pregnancy under strategies defined in Table 1. The x-axis represents the number of non-sterile, women of reproductive age who: under **strategy A**, switch to effective contraceptives (with less than 10% probability of failure in one year of use) from not using contraceptives at all or using ineffective methods; under **strategy B** detect their pregnancies within a week of a missed period; under **strategy C**, abstain from drinking if seeking pregnancy or pregnant; under **strategy D**, abstain from drinking if pregnant, seeking pregnancy or not using contraceptives with sex; under **strategy E**, comply with strategies A and C; and under strategy F comply with strategies A-C. Solid lines and dotted lines assume up to 0-50% and >50-100% adherence, respectively. Vertical dotted lines represent the maximum number of women that could be reached through each strategy in the U.S. The numbers next to each line represent the maximum percentage reduction in the prevalence of AEP or unaware AEP under each strategy.

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