

This article presents a model-based evaluation of a program designed to reduce HIV transmission from HIV-infected Ethiopian immigrants in Israel. Rather than rely on self-reported variables such as condom use, this study's approach focuses on pregnancy rate reduction, estimated from administrative periodic reporting data, as a measure of unprotected sexual exposure. The models show that among both HIV⁺ women and the female sex partners of HIV⁺ men, the ongoing pregnancy rates estimated during the intervention were significantly lower than the estimated baseline pregnancy rates, suggesting reductions in unprotected sexual exposures among those participating in the program.

A MODEL-BASED EVALUATION OF A CULTURAL MEDIATOR OUTREACH PROGRAM FOR HIV⁺ ETHIOPIAN IMMIGRANTS IN ISRAEL

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In 1991, 20,000 Jewish immigrants from Ethiopia arrived in Israel (Rosen and Rubenstein 1993). To prepare health services to meet their needs, all immigrants were examined and tested after arrival for various health conditions such as HBV, tuberculosis, malaria, intestinal parasites, and HIV. The policy of the State of Israel is to grant Israeli citizenship to immigrants of Jewish origin, without any medical exclusion, and provide them, after arrival, with full medical coverage under the national health system. This policy was applied to the Ethiopian immigrants. All HIV⁺ immigrants were personally informed of their status by a physician, counseled, and referred to the nearby regional HIV center for further counseling, medical and psychosocial follow-up, and care as needed.

That 1.7% of these immigrants were HIV⁺ aroused concerns regarding potential further transmission (Pollack and The Israel AIDS Study Group 1993). Indeed, the high HIV prevalence among Ethiopian immigrants (Kaplan, Kedem, and Pollack 1998) relative to the 0.02% prevalence of HIV reported among non-Ethiopian Israelis (Kaplan, Slater, and Soskolne 1995) led to a controversial policy that excluded Ethiopian Israelis from donating blood (Kaplan 1998).

An outreach intervention targeting HIV seropositives and their sexual partners was developed in 1993 (Shtarkshall and Soskolne 2000). The intervention was delivered by Ethiopian immigrant cultural mediators/case managers (CMs) fluent in both Amharic (the Ethiopian language) and Hebrew. The CMs had to provide individual or couple behavior modification counseling, facilitate access to HIV care and other necessary services, and provide emotional and social support. The program was gradually implemented across the country with the hope of reducing the rate of unprotected sex in the target population to slow the spread of new HIV infections.

This article presents a model-based evaluation of this program. Evaluating this program is a challenge, as the only data available stem from quarterly administrative reports filed by the CMs. Rather than rely on self-reported behavioral measures such as condom use, pregnancy was employed as a marker for unprotected sexual activity because pregnancy, an easily observed outcome, surely indicates unprotected sex. The methodological challenge is thus to infer whether a decline in pregnancy incidence occurred over the course of the program and, if so, whether there are obvious nonprogrammatic factors that compete with the program itself as the primary cause for such a decline.

This article proceeds as follows: We first provide a brief description of the periodic reporting data structure that characterizes the administrative reports available for analysis. We then establish a simple probability model for the probability of observing a pregnancy in a participant's first reporting period;

this probability depends on the baseline pregnancy rate. We next model the probability of observing a pregnancy in any future reporting period; this probability depends on the ongoing pregnancy rate. Applying these models to reporting data, we develop maximum likelihood methods for estimating the baseline and ongoing pregnancy rates. We also present a likelihood ratio test for determining whether there has been a shift in pregnancy incidence. We apply these methods to the data available from the cultural mediator outreach program. The analysis shows that among both HIV⁺ women and the female sex partners of HIV⁺ men, the ongoing pregnancy rates estimated during the intervention were significantly lower than the estimated baseline pregnancy rates, suggesting reductions in unprotected sexual exposures among those participating in the program. We conclude with a discussion of our results and potential limitations of our approach.

PERIODIC REPORTING DATA STRUCTURE

The data structure imposed by the administrative reports that are our source of information for this study is illustrated in Figure 1. In the abstract, participants begin to enroll in a program after the starting date, and the study concludes at some fixed ending date (although this is not crucial for what follows). Participants are observed at various points in time, but for administrative reasons, the results of individual participant visits are (unfortunately) not available. Rather, results are only available by reporting period. For any given participant, the most recently observed pregnancy status is reported at the end of each reporting period.

In Figure 1, results for hypothetical visits are shown for 4 participants. Participant A was pregnant upon arrival to the program and is thus reported as pregnant in the first reporting period and excluded from further study. Participant B was not pregnant upon arrival to the program but was observed to be pregnant during a subsequent visit during her initial reporting period. Thus, B is also reported as pregnant in the first reporting period and excluded from further study. Note that Participants A and B would look identical in the periodic reporting database, in that both would be reported as pregnant in their first reporting periods. A pregnant Participant C was observed and reported at the end of her third reporting period after which the study ended, whereas Participant D was not observed to have become pregnant over the two reporting periods during which she was observed before the end of the study. We now turn to probability models for periodic reporting data of the form just described.

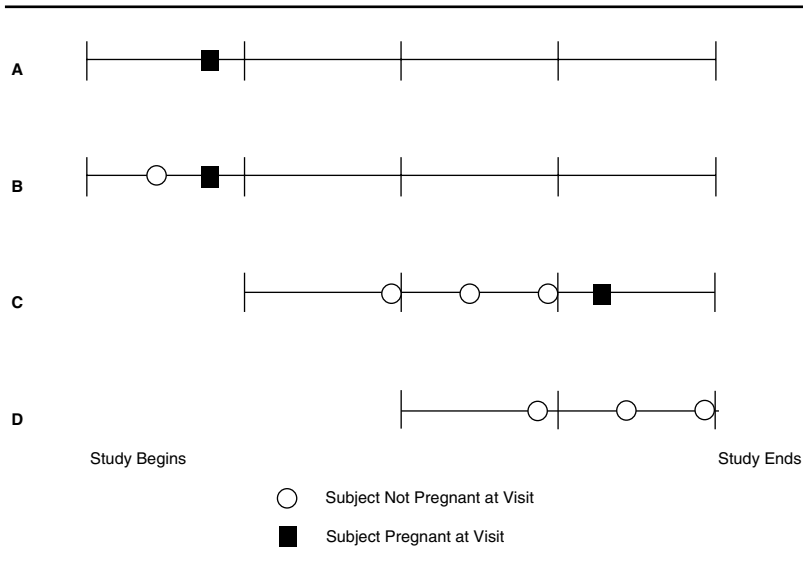


Figure 1: Periodic Reporting Data Structure

ESTIMATING THE BASELINE PREGNANCY INCIDENCE RATE

We assume that the periodic reporting database is organized such that reports are filed once every τ time units (in the cultural mediator program, reports were filed quarterly and thus $\tau = 0.25$ years). We assume that new participants arrive at a constant rate per unit time (and thus arrive at a random time during a reporting period) and that the mean duration of pregnancy in the participant population, which might not equal 9 months on account of abortions or miscarriages, is given by d . Pregnancies are assumed to occur in accord with a homogeneous Poisson process, with the baseline incidence of pregnancy in the (newly arriving) participant population given by r_b pregnancies per woman per unit time. The presumed stable prevalence of pregnancy among newly arriving participants is denoted by π . We assume that there is no relationship between the likelihood that a participant will enroll in the study and pregnancy status (we discuss the importance of this assumption in the last section of this article). Finally, the probability that a participant would be reported as pregnant in the first reporting period is given by p . To estimate the baseline pregnancy incidence rate r_b , we will construct a model for the probability of observing a pregnancy in the first reporting period (p) that depends on r_b in addition to known quantities.

First, via the “prevalence = incidence \times duration” law (Mausner and Kramer 1985), the steady-state pregnancy level in the population of newly arriving participants follows

$$\pi = (1 - \pi)r_b d, \quad (1)$$

which solves to yield

$$\pi = \frac{r_b d}{1 + r_b d}. \quad (2)$$

However, it would be wrong to equate π to p , the probability of observing a pregnancy in the first reporting period, and solve for r_b . The reason is that the reporting data are aggregated over reporting periods of length τ . Thus, really what is observed in the first reporting period is the sum of two values: the number of women who are pregnant upon arrival and the number of women who were not pregnant upon arrival but became pregnant within the first reporting period (consider Participants A and B in the example of Figure 1). Mathematically, this implies the following more general equation for the probability of observing a pregnancy in an arriving participant during the initial reporting period of length τ :

$$\begin{aligned} p &= \underbrace{\pi}_{\text{Pregnant on arrival}} + \underbrace{\int_0^\tau \frac{1}{\tau} (1 - \pi)(1 - e^{-r_b(\tau-x)}) dx}_{\text{Arrived and became pregnant during initial reporting period}} \\ &= \pi + (1 - \pi) \left[1 - \frac{1 - e^{-r_b \tau}}{r_b \tau} \right] \\ &= \frac{r_b d}{1 + r_b d} + \frac{1}{1 + r_b d} \left[1 - \frac{1 - e^{-r_b \tau}}{r_b \tau} \right]. \end{aligned} \quad (3)$$

Given the observed mean duration of a pregnancy in this population (d) and the reporting period duration (τ), we equate the *observed* fraction of initial reporting periods in which pregnancies were observed to p and solve Equation 3 to obtain the (maximum likelihood) estimate of the pregnancy incidence rate r_b . A confidence interval for r_b can be easily constructed by applying Equation 3 to the endpoints of the standard confidence interval for the proportion p .

ESTIMATING THE ONGOING PREGNANCY RATE

Now consider each of the participants who were not reported pregnant in their initial reporting periods and hence followed during subsequent periods.

We assume that pregnancies again occur in accord with a homogeneous Poisson process, but now with the ongoing pregnancy incidence rate r_o . We assume that participants are followed either until they become pregnant or until the ending time of the study, whichever comes first (although the analysis below carries for arbitrary right-censoring, in which case there is no need for a fixed time at which the study terminates). Suppose that when the study ends, the i th client has been observed for k_i reporting periods *beyond* the initial period. The probability that the i th participant became pregnant during the k_i th reporting period is then given by

$$e^{-r_o(k_i-1)\tau} \times (1 - e^{-r_o\tau}), \quad (4)$$

whereas the probability that such a participant was not yet pregnant equals $e^{-r_o k_i \tau}$.

Note that the probability ρ that a participant becomes pregnant over the duration of a reporting period is given by

$$\rho = 1 - e^{-r_o\tau}. \quad (5)$$

This enables us to write the probability that the i th participant became pregnant during the k_i th reporting period (Equation 4) as the geometric probability

$$\rho(1 - \rho)^{k_i-1}, \quad (6)$$

whereas the probability that such a participant was not yet pregnant can be written as $(1 - \rho)^{k_i}$.

Let the indicator $\delta_i = 1$ if the i th participant is reported pregnant in her k_i th reporting period (beyond the first); otherwise, $\delta_i = 0$. The overall likelihood of observing the ongoing reporting data is then given by the familiar binomial form

$$\prod_i [\rho(1 - \rho)^{k_i-1}]^{\delta_i} \times [(1 - \rho)^{k_i}]^{1-\delta_i} = \rho^{\sum_i \delta_i} (1 - \rho)^{\sum_i (k_i - \delta_i)}. \quad (7)$$

Maximizing the likelihood function in Equation 7 yields the maximum likelihood estimate

$$\hat{\rho} = \frac{\sum_i \delta_i}{\sum_i k_i} = \frac{\# \text{ ongoing pregnancies}}{\# \text{ reporting periods}}. \quad (8)$$

From this, one easily recovers the maximum likelihood estimate for the ongoing pregnancy incidence rate as

$$\hat{r}_o = -\frac{1}{\tau} \log(1 - \hat{\rho}). \quad (9)$$

A confidence interval for r_o can be easily constructed using the endpoints of the usual interval for $\hat{\rho}$.

DETECTING A SHIFT IN PREGNANCY INCIDENCE

Let $p(r_b)$ be the probability of observing a pregnancy in a participant's first reporting period in the database, given a baseline pregnancy incidence rate r_b (i.e., Equation 3). Then the likelihood of observing x out of n participants with pregnancies in the first reporting period is simply proportional to

$$p(r_b)^x (1 - p(r_b))^{n-x}. \quad (10)$$

Now consider two possibilities: that the baseline and ongoing pregnancy incidence rates are equal, or alternatively, that they are different. The null model hypothesizes that both the baseline and ongoing pregnancy incidence rates equal r . Let $\rho(r) = 1 - e^{-r\tau}$. The overall likelihood function for the null model is then given by

$$\mathcal{L}_0 = p(r)^x (1 - p(r))^{n-x} \times \rho(r)^{\sum_i \delta_i} (1 - \rho(r))^{\sum_i (k_i - \delta_i)}. \quad (11)$$

Maximizing \mathcal{L}_0 by choosing the appropriate value of r yields the maximum likelihood pregnancy incidence rate, given the data and the hypothesis that the pregnancy incidence did not change over time.

Alternatively, suppose that the baseline and ongoing pregnancy incidence are different. As before, let r_b denote the baseline pregnancy incidence and r_o denote ongoing pregnancy incidence. The corresponding likelihood function for this alternative hypothesis is given by

$$\mathcal{L}_1 = p(r_b)^x (1 - p(r_b))^{n-x} \times \rho(r_o)^{\sum_i \delta_i} (1 - \rho(r_o))^{\sum_i (k_i - \delta_i)}. \quad (12)$$

Maximizing \mathcal{L}_1 by choosing the appropriate values of r_b and r_o yields the baseline and ongoing maximum likelihood pregnancy estimates discussed previously in Equations 3 and 9, respectively.

To test whether there has been a shift in pregnancy incidence, we employ the standard likelihood ratio test (Cox and Hinkley 1974). We compute the quantity

$$\chi^2 = 2 \log(\mathcal{L}_1 / \mathcal{L}_0) \quad (13)$$

and determine the associated p -value using the tail probability of the χ^2 distribution with one degree of freedom.

APPLICATION TO THE CULTURAL MEDIATOR OUTREACH PROGRAM FOR HIV⁺ ETHIOPIAN IMMIGRANTS IN ISRAEL

As stated earlier, evaluation data were retrieved from the CMs' quarterly administrative report forms (and thus the reporting period duration, τ , equals 3 months). Pregnancy status was recorded at each visit for female clients or the female sex partners of male clients. A total of 145 female and 176 male clients enrolled in the intervention over 2 years, generating 408 and 409 ongoing quarterly reports, respectively. Of interest is whether there was a reduction in pregnancy incidence among female clients and among the female sex partners of male clients from baseline (i.e., preprogram) levels because one would expect such a reduction if the intervention successfully reduced the rate of unprotected sexual exposures over time.

Table 1 reports the estimates of baseline and ongoing pregnancy rates as determined by our methods, along with the likelihood ratio test of Equation 13. In computing the baseline estimates, we set the average duration of pregnancy, d , equal to 7 months, because although roughly two thirds of the women in this (HIV⁺) population carry their pregnancies to term, the other one third abort an average of 3 months into pregnancy, yielding an average duration of $2/3 \times 9 + 1/3 \times 3 = 7$ months. Among female clients, pregnancy incidence fell from 19.58 per 100 person years (95% confidence interval [CI] = 10.63-29.53) to 9.93 per 100 person years (95% CI = 3.81 – 16.12), a marginally significant decline ($\chi^2_{df=1} = 3.00$, p -value = .083). Among the female sex partners of men, pregnancy incidence fell from 12.04 per 100 person years (95% CI = 5.79-18.69) to 3.93 per 100 person years (95% CI = 0.10-7.80), a decline of greater significance ($\chi^2_{df=1} = 4.55$, p -value = .033).

It is interesting to note that the baseline pregnancy rates among female clients were quite similar to fertility rates among Ethiopian immigrants in Israel: 21 per 100 person years in the 25- to 29-year-old age bracket and 19 per 100 person years in the 30- to 34-year-old age bracket (Israel Central Bureau of Statistics 1997). These comparison figures were computed by recording the number of reported births in 1996 among all Jewish women in Israel who were born in Ethiopia.

DISCUSSION

We have framed our evaluation of the cultural mediator program in terms of detecting a shift in pregnancy incidence using the periodic administrative reports that were available for study. Our focus on pregnancy incidence

TABLE 1:

	<i>Women</i>	<i>Female Partners of Men</i>
Number in group	145	176 (men)
Number of initial pregnancies	18	14
Baseline probability of pregnancy	18/145 = 0.1241	14/176 = 0.0795
Baseline incidence/100 person years (95% confidence interval [CI])	19.58 (10.63-29.53)	12.04 (5.79-18.69)
Incident pregnancies	10	4
Total reporting periods	408	409
Ongoing incidence/100 person years (95% CI)	9.93 (3.81-16.12)	3.93 (0.10-7.80)
Null model incidence/100 person years (95% CI)	14.37 (9.63-20.51)	8.18 (4.94-12.63)
χ^2	3.00	4.55
<i>p-value</i>	.083	.033

avoids the possible social desirability bias that could accompany self-reported measures such as condom use.

We have presented models for estimating both baseline and ongoing pregnancy incidence from such data and also shown how to test statistically to see if a shift in incidence has occurred. To the extent that periodic reporting data are employed in administrative record keeping, our methods are perhaps of independent interest in the estimation of event incidence rates. Of particular note is our model for estimating the prior pregnancy incidence rate solely from first-quarter reporting data.

We applied our methods to the cultural mediator prevention program targeting HIV⁺ Ethiopian immigrants to Israel. The results indicate that there has been a significant decline in pregnancy incidence among both female clients and the female sex partners of male clients in this intervention, which in turn suggests that the rate of unprotected sexual exposures has declined as intended.

Our evaluation is not a controlled trial but rather an observational "before-and-after" study viewed through the lens of probability models for periodic reporting data. Indeed, given that the program targeted all HIV⁺ Ethiopian immigrants to Israel, a controlled trial was simply not feasible. Nonetheless, as with any observational study, one must worry about the limitations of the analysis and the results obtained.

One possible concern with our approach is that participants who are already pregnant might enroll at a different rate from participants who are not

pregnant. For example, if the prenatal services provided by the program were both desired and otherwise difficult to obtain, pregnant participants might be more likely to enroll. Such a selection bias would lead to overestimating the baseline pregnancy rate because the fraction of arriving participants would exceed the natural prevalence of pregnancy in the participant population. In turn, overestimating the baseline pregnancy incidence would make it easier to “detect” a downward shift in pregnancy incidence when in fact no such shift occurred. However, in our application, we are reasonably certain that no such bias is present. First, all Ethiopian immigrants to Israel were tested for HIV, and the HIV intervention discussed targeted *all* HIV⁺ Ethiopians. Second, as reported earlier, the baseline pregnancy rates estimated for women in the intervention program were nearly identical to the rates observed for Ethiopian women in the population at large in the same age range.

That the reported pregnancy rates among the female sex partners of HIV⁺ men in the program were lower than among female clients might reflect reporting bias. The female partners of HIV⁺ male clients were not examined, and the men in the study might have become aware that pregnancy is an “undesired” outcome (and be less likely to report pregnancies that did occur as a result). Although the intervention espoused the use of condoms and avoidance of unprotected sex, the HIV prevention messages did *not* explicitly advocate pregnancy avoidance so as not to offend the clients (for fertility is highly valued in this community). In addition, the information on pregnancies was provided not only by the clients but also by other sources such as health care clinics or welfare services. Female partners were also seen throughout the program as the CMs worked with the clients and their family members. Therefore, we do not believe that there was serious underreporting of pregnancies among the female partners of the men in the program.

A third concern is that in computing the baseline pregnancy incidence rate, we consider both arriving prevalent pregnancies and incident pregnancies over the initial reporting period to have been generated by the same baseline pregnancy incidence rate. However, in a context where it is anticipated that pregnancy incidence will decline, such as in the HIV prevention example presented earlier, this actually makes the analysis conservative in that the baseline pregnancy incidence estimated will be lower than what would have been the case had only arriving prevalent pregnancies been considered. On the other hand, unless one believes that ongoing pregnancy incidence should drop suddenly and sharply from baseline (itself a hypothesis favorable to the program), including incident pregnancies in the first reporting period will not introduce much in the way of bias and actually could contribute to a more stable estimate of the baseline rate.

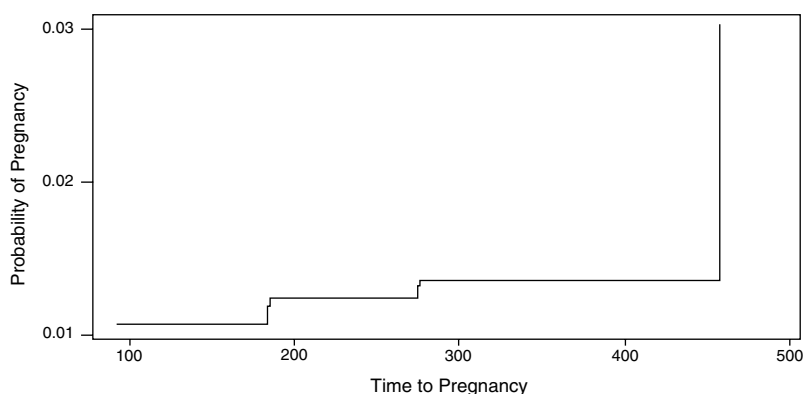


Figure 2: Nonparametric Pregnancy Hazard Estimate

A fourth concern is that heterogeneity in fecundity (ability to conceive) across women in the population could lead to the estimated decline in pregnancy rates. If indeed such heterogeneity was present in our cohort setting, those women most likely to get pregnant would do so early on, leaving behind a sample of women with lower average pregnancy rates (see Kaplan et al. 1992 for further details). However, excluding the initial quarterly report (which includes both women who were pregnant upon arrival as well as incident pregnancies and nonpregnancies), standard survival analysis rejects such a decline in pregnancy incidence over the ensuing reporting periods. For example, Figure 2 shows the discrete nonparametric pregnancy hazard evaluated at the observed dates of pregnancy for the women in the program (Kalbfleisch and Prentice 1980). A similar picture results for the female partners of male clients. Additional parametric analysis (e.g., Weibull-distributed time to pregnancy) fails to reject the constant hazard model associated with our Poisson pregnancy process assumption. Such findings are inconsistent with the notion that heterogeneity in fecundity is responsible for the decline in pregnancy incidence observed.

In sum, it seems plausible that the observed decline in pregnancy incidence reflects reductions in the rate of unprotected sex among program participants.

From 1991 to 1996, the prevalence of HIV among newly arrived Ethiopian immigrants rose to 7% (Kaplan, Kedem, and Pollack 1998). As previously mentioned, one controversial reaction to this was the exclusion of Ethiopian immigrants from blood donation in Israel (Kaplan 1998). The intervention

evaluated above represents a more positive response to this situation. The screening of all recent Ethiopian immigrants created a unique situation in which all HIV⁺ immigrants were known to Israel's Public Health Service and entailed an obligation to curtail further transmission in the community. Although the results reported above are modest, they do suggest progress in the right direction.

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