# Heterosexual Transmission of Human Immunodeficiency Virus (HIV) in Northern California: Results from a Ten-year Study

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To examine rates of and risk factors for heterosexual transmission of human immunodeficiency virus (HIV), the authors conducted a prospective study of infected individuals and their heterosexual partners who have been recruited since 1985. Participants were recruited from health care providers, research studies, and health departments throughout Northern California, and they were interviewed and examined at various study clinic sites. A total of 82 infected women and their male partners and 360 infected men and their female partners were enrolled. Over 90% of the couples were monogamous for the year prior to entry into the study; <3% had a current sexually transmitted disease (STD). The median age of participants was 34 years, and the majority were white. Over 3,000 couple-months of data were available for the follow-up study. Overall, 68 (19%) of the 360 female partners of HIV-infected men (95% confidence interval (CI) 15.0–23.3%) and two (2.4%) of the 82 male partners of HIV-infected women (95% CI 0.3–8.5%) were infected. History of sexually transmitted diseases was most strongly associated with transmission. Male-to-female transmission was approximately eight times more efficient than female-to-male transmission and male-to-female per contact infectivity was estimated to be 0.0009 (95% CI 0.0005–0.001). Over time, the authors observed increased condom use ($p < 0.001$) and no new infections. Infectivity for HIV through heterosexual transmission is low, and STDs may be the most important cofactor for transmission. Significant behavior change over time in serodiscordant couples was observed. *Am J Epidemiol* 1997;146:350–7.

acquired immunodeficiency syndrome; HIV; HIV infections; risk factors; sex partners; transmission

As of June 1996, a total of 44,980 cases (8 percent) of acquired immunodeficiency syndrome (AIDS) among adults and adolescents had been reported to the Centers for Disease Control and Prevention that were attributed to heterosexual contact with a high risk or infected partner (1). This percentage differs markedly from the 4 percent that was reported over 5 years ago (2), and it may reflect a new trend. The year 1993 was the first year that the number of heterosexually acquired AIDS cases in women exceeded that of cases in female injection drug users (3). Similar trends have been observed in regard to infection with human immunodeficiency virus (HIV). For example, in a sequential survey of infection in women at a perinatal clinic in Florida (4), more cases were attributed to heterosexual transmission than to any other risk factor.

Furthermore, anonymous testing of newborns (5) has identified areas of elevated HIV prevalence in the southeastern United States among women, many of whom have been infected heterosexually.

To address this shift in the epidemic toward heterosexually acquired infection, a deeper understanding of risk factors for heterosexual transmission is imperative. We have been able to identify risk factors at the individual level that affect the likelihood of transmission between infected individuals and their heterosexual partners. Elimination or modification of these factors could result in reduced transmission of HIV. In addition, predictions about the epidemic might be refined by identification of such risk factors, because their prevalence signifies potential for future epidemic spread.

## MATERIALS AND METHODS

### Sample

The year 1996 represented the tenth year of our study of the heterosexual transmission of HIV in which we enrolled individuals infected with HIV or who had AIDS along with their opposite sex partners.

Study protocol and data collection methods have been described in detail previously (2, 6). Briefly, couples were recruited without regard to the gender of the index case or to the serostatus of the partner. Although approximately 20 percent of couples (no difference by gender of the index case) thought they knew the serostatus of their partner, many such individuals were incorrect. Individuals with multiple high risk or infected partners (i.e., an "index case" could not be identified) were not eligible to participate. Among couples where both were infected, the direction of transmission was determined from detailed risk histories.

Results presented here include couples enrolled since the beginning of the study. The study protocol has been approved by the University of California, San Francisco Committee on Human Research. During the first 2 years of the study, 1985–1986, we focused on recruitment of infected bisexual men and their female partners. We subsequently expanded recruitment criteria to include couples regardless of risk group or gender of the index case. Infected individuals were recruited from a variety of sources throughout California (alternative test sites, local departments of public health, clinics, physicians, and other research studies). They were counseled to refer their heterosexual partners for HIV testing and counseling and were informed about the study. Baseline data as well as prospective results are presented here. The fundamental design was to compare couples where transmission had occurred with those who remained discordant for HIV infections.

The sample analyzed here excludes some couples who were included in our previous report (2). At that time, partners were considered not to be injection drug users if they reported not having injected drugs since 1978, the year in which HIV is believed to have been introduced into Northern California. To reduce the likelihood of misclassification of transmission due to needle sharing as sexual transmission, we eliminated partners who reported *any* prior history of injection drug use. In addition, for all those couples enrolled since 1990, we tested for drug use by a urine toxicology test and excluded couples where the partner had a positive test but claimed not to have used drugs.

## Procedures and measures

At the recruitment visit, the serostatus of the partner was ascertained along with a risk history. We considered demographic factors such as race, ethnicity, age, and date of enrollment, as well as duration of the relationship. Factors related to the index case included

risk group and disease stage. Health history included male circumcision, reproductive history (parity, hysterectomy, menstrual history, douching, tampon use, contraceptive history), history of a sexually transmitted disease (STD), and substance use including alcohol, drug use, and smoking. General sexual history included age at first intercourse, number of other partners (past and current), and number of known high risk partners (injection drug users, bisexual men, men who were infected with HIV) since 1978. We also ascertained sexual activities with the index case for the 6 months prior to entry into the study, as well as over the relationship, including sex during menstruation; anal and oral intercourse; condom use; number of contacts (frequency of unprotected sexual intercourse); and adverse effects of sexual activities such as pain, itching, or dryness during or after intercourse, and postcoital bleeding.

In order to estimate the number of "exposed" contacts, we excluded all contacts that occurred before 1978. We based estimated dates of index case infection on the assumed mode of acquisition (e.g., transfusion recipients were generally infected before injection drug users). Models including numbers of exposed contacts were fit using several different estimates of this quantity in order to examine sensitivity of results to assumptions about when index cases were infected. In regression analyses, we used the natural logarithm of number of contacts to reduce the influence of extreme observations and because this transformation is suggested by simple models of transmission (7).

Physical examinations for both partners were initiated in 1990. The examination consisted of a standard review of systems; laboratory tests of lymphocyte subsets; serologic tests for HIV, syphilis, and hepatitis B; and cultures for gonorrhea and chlamydia. Because the prevalence of current STDs was so low (<3 percent for men and women), we could not include this variable in statistical analysis. However, given the retrospective nature of the cross-sectional aspect of our design (e.g., transmission occurred prior to entry in the study), past infection is probably a more appropriate measure for the cross-sectional analyses.

A prospective phase of the study began in 1990. After entry, serodiscordant couples who remained together were seen every 6 months for an interview covering the interval since the last visit and a physical examination with the same laboratory tests described above. Although the interviews were administered individually, at each visit, the couple was counseled together regarding safe sexual practices. Details of the counseling session have been published elsewhere (8). Briefly, counseling focused on behavioral obstacles to

use of condoms and included attention to social, financial, and legal issues associated with HIV infection. In addition to the scheduled counseling, study staff were available to participants at any time by telephone via an 800-number. Other sources of social support included a "buddy" system in which individual participants were matched with other participants, and phone numbers and addresses were exchanged. Quarterly social gatherings, information nights, and a quarterly newsletter were also initiated. Because of issues of anonymity and confidentiality, approximately one-third of the couples participated in the buddy system, information nights, or social gatherings, whereas almost all participants used the 800-number.

## Data analyses

Estimates of overall rates of infection and associated 95 percent confidence intervals were based on the binomial distribution. Risk factors for transmission of HIV from male index cases to female partners were investigated singly using the odds ratio as a measure of association in conjunction with exact tests for association and trend. Distributions of risk factors were also compared by gender of the index case using exact contingency table methods (9).

Risk factors were also investigated jointly using logistic regression (10). The final regression model includes factors which were significantly associated with transmission in bivariate analysis, as well as those considered important based on biologic plausibility or previous analyses. Exploratory models were fit to investigate possible interaction and confounding effects between risk factors.

In addition, an adjusted odds ratio comparing transmission rates by gender of the index case, controlled for reported level of condom use, was computed together with 95 percent confidence intervals, using a conditional maximum likelihood estimate. The infectivity constant (per-contact transmission risk) for male-to-female transmission was estimated using maximum likelihood methods taking account of the fact that infection times of both index cases and all infected partners occurred prior to recruitment and are known only to lie in broad intervals (11). These intervals were defined by the reported lengths of exposure for couples and the earliest possible time of infection for the index cases. The plausibility of the assumption that the infectivity is constant was evaluated using methods described in Shiboski and Jewell (12) and Shiboski (13).

## RESULTS

### Patient characteristics

We report here on 360 female non-injection drug using partners of infected men and 82 non-injection drug using partners of infected women. Thirteen couples were eliminated because of evidence that the partner had used drugs prior to 1978 and three couples were eliminated because of evidence of current drug use by the partner. The median number of sexual partners since 1978 was three among men and nine among women. More than 90 percent of participants had no other partners during the year before they entered the study. For women, median age was 33 years (range 17–71 years), while for men it was 35 years (range 22–62 years). Sixty-six percent of the women were white, 18 percent Latina, 11 percent African American, and 4 percent of other ethnic origin (primarily Asian). Sixty-eight percent of the men were white, 18 percent Latino, 11 percent African American, and 3 percent of other ethnic origin. More than 95 percent of couples in the study were concordant for race. The median duration of the relationship for the couples was 4 years (range, 1 month to 46 years).

Regardless of gender, approximately 20 percent of index cases were injection drug users, and 14 percent had acquired their infection from contaminated blood products or transfusions. Most (51/82; 62 percent) of the female index cases were infected by previous heterosexual partners. In contrast, only 12 percent (44/360) of the male index cases reported havingbeen infected via heterosexual transmission ($p < 0.001$). A majority of these male cases (53 percent) were bisexual.

The characteristics of newly recruited couples changed over time. In order to examine this change, we compared couples recruited during the first half of the study ($n = 212$) with those recruited later ($n = 230$) (table 1). Over time, we recruited fewer partners of bisexual men (52 percent in the first half of the study vs. 34 percent second half) and fewer white couples (80 percent first half vs. 57 percent second half, $p < 0.001$ for both). In addition, significantly more couples (79 percent) had used condoms prior to entry in the study in the second half of the study compared with couples recruited earlier (54 percent, $p < 0.001$). There were no differences in the age distribution over time.

### Cross-sectional results

Overall, 68 (19 percent) of the 360 female partners of male index cases were infected (95 percent confidence interval (CI) 15.0–23.3 percent) and two (2.4 percent) of the 82 male partners of female index cases

TABLE 1.   Sample characteristics of 442 Northern California heterosexual couples including one partner with acquired immunodeficiency syndrome (AIDS) or human immunodeficiency virus (HIV) recruited from 1985 to 1996*

| Characteristic | Year of recruitment | | | | p value |
| | <1990 (n = 212) | | ≥1990 (n = 230) | | |
| | No. | % | No. | % | |
|---|---|---|---|---|---|
| Condom use at entry | 114 | 54 | 181 | 79 | <0.001 |
| **Risk group of index** | | | | | |
| Bisexual | 111 | 52 | 78 | 34 | |
| Hemophiliac or transfusion-associated | 46 | 22 | 15 | 7 | |
| Injection drug use | 30 | 14 | 65 | 28 | |
| Heterosexual | 25 | 12 | 70 | 31 | <0.001 |
| **Partner race†** | | | | | |
| White | 169 | 80 | 131 | 57 | |
| Black | 20 | 9 | 54 | 24 | |
| Latino(a) | 18 | 9 | 34 | 15 | |
| Other‡ | 5 | 2 | 10 | 4 | <0.001 |
| **Age (years)** | | | | | |
| <30 | 58 | 27 | 60 | 26 | |
| 30–34 | 64 | 30 | 64 | 28 | |
| 35–40 | 39 | 19 | 59 | 26 | |
| >40 | 50 | 24 | 46 | 20 | 0.31 |

\* Numbers and percentages may be affected by missing values.
† Although these data represent the race of the partner, more than 95 percent of couples were concordant for race.
‡ Asian, American Indian, or Pacific Islander.

(95 percent CI 0.3–8.5 percent). Table 2 shows crude odds ratios for risk factors for male-to-female transmission that were significant at $p \geq 0.05$ in bivariate analysis in this study or in previous reports (2, 6, 14). The practice of anal sex had the greatest measure of effect (odds ratio (OR) = 2.6). In addition, having a partner who acquired his infection through activities associated with injection drug use (OR = 1.9), reports of postcoital bleeding (OR = 2.3), and female partner who had history of a previous STD (OR = 2.0) were all significant. We found only marginal significance

for enrollment in the study prior to 1990 (OR = 1.9), not using condoms (OR = 1.7), and >300 unprotected penile-vaginal or penile-anal contacts (the median number of contacts) (OR = 1.6), all of which had been found to be significant in previous analyses (2, 6, 14).

Table 2 also presents the adjusted odds ratios (and 95 percent CIs) from a logistic regression model including the same variables. In the multivariate model, the effect of postcoital bleeding was attenuated and nonsignificant. In contrast, the effect attributed to lack of condoms increased. The effect of number of con-

TABLE 2.   Risk factors for male-to-female transmission of human immunodeficiency virus (HIV) among 360 heterosexual couples recruited in Northern California from 1985 to 1996

| Risk factor | Infected | | Odds ratio | 95% CI* | Adjusted odds ratio† | 95% CI |
| | No. | % | | | | |
|---|---|---|---|---|---|---|
| Index injection drug user | 77 | 27 | 1.9 | 1.0–3.54 | 2.0 | 1.0–4.2 |
| Enrolled before 1990 | 91 | 12 | 1.9 | 0.94–1.07 | 1.0 | 0.98–1.0 |
| No condoms | 131 | 24 | 1.7 | 0.95–3.01 | 2.1 | 1.1–4.1 |
| Anal sex | 115 | 30 | 2.6 | 1.45–4.56 | 2.1 | 1.1–4.1 |
| Post-coital bleeding | 57 | 32 | 2.3 | 1.13–4.56 | 1.7 | 0.8–3.5 |
| Sexually transmitted disease history | 163 | 25 | 2.0 | 1.14–3.65 | 2.6 | 1.4–5.1 |
| No. of contacts >300 (median)‡ | 163 | 23 | 1.6 | 0.90–3.0 | 1.3 | 0.98–1.6 |

\* CI, confidence interval.
† Adjusted odds ratio from multivariate model.
‡ The adjusted odds ratio for number of contacts is based on the logarithm of the exposed contact count which is estimated as described in the text.

tacts (included as a continuous variable) was somewhat reduced and only marginally significant; nevertheless, its omission from the model induced large changes in the effects estimated for the other independent variables. All of the other factors found significant in bivariate analysis remained significant, with history of an STD (OR = 2.6, 95 percent CI 1.4–5.1) having the strongest effect. The positive predictive value of risk factors was limited, however. For example, transmission occurred in 5 of 69 couples (7 percent) with no risk factors, but was avoided in two of four couples with all four independent significant risk factors, and 60 percent of 37 couples with three risk factors (data not shown). In exploratory analyses, we observed no significant interactions between variables. The constant per-contact infectivity for male-to-female transmission was estimated to be 0.0009 (95 percent CI 0.0005–0.001). However, diagnostic tests indicated that there may be some departure from constant infectivity. Models that allow infectivity to vary with time following index case infection, or across partnerships (i.e., heterogeneity of infectiousness and/or susceptibility) may provide better fits. Nonetheless, the constant per-contact infectivity that we observed corresponds closely to that seen in other studies (15), and thus may be interpreted to be an average rate.

Because there were only two instances of female-to-male transmission, we could not examine risk factors for these events statistically. However, there are noteworthy findings from these case histories. In the first case, which has been described previously (2), both partners reported numerous instances of postcoital bleeding from the genital area, In the second case, the woman appears to have infected her partner with both HIV and chlamydia within a short period (both partners reported that they had been tested 6 months before entry into the study, and, at that time, the woman's male partner was not infected with either disease, whereas she was infected with both).

In order to better explain differences in transmission rates according to gender of the index case, we compared the distribution of risk factors associated with heterosexual transmission according to gender of the index case. In addition to factors significantly associated with transmission in our study, we also considered factors found to be significant in other studies, such as CD4 level and disease stage (asymptomatic, symptomatic, AIDS diagnosis). In our previous report (2), female index cases were less likely to be symptomatic than male index cases, but this association no longer holds. In our current analyses, the only significant difference was that more study couples with female index cases consistently used condoms at study

entry (85 percent) compared with couples with male index cases (63 percent) ($p < 0.001$). The crude odds ratio that compared male-to-female with female-to-male transmission was 9.29 (95 percent CI 2.38–79.91, $p < 0.001$). After controlling for consistent condom use, this odds ratio was reduced to 7.77 (95 percent CI 1.97–67.3, $p < 0.001$).

## Prospective results

We followed 175 HIV-discordant couples over time, for a total of approximately 282 couple-years of follow-up (table 3). Because of deaths as well as the break-up of couples, attrition was severe; only 175 couples are represented in table 3. The longest duration of follow-up was 12 visits (6 years). We observed no seroconversions after entry into the study. Table 3 summarizes behavior change over time, comparing behaviors at the entry visit with those reported at the last follow-up visit for that couple. A detailed report of behavior change at each follow-up visit is available elsewhere (8). However, approximately 97 percent of behavior change was reported between baseline and the first follow-up visit. At last follow-up, couples were much more likely to be abstinent or to use condoms consistently, and were much less likely to practice anal intercourse ($p < 0.0005$ for all). Nevertheless, only 75 percent reported consistent condom use in the 6 months prior to their final follow-up visit. Forty-seven couples who remained in follow-up for 3 months to 6 years used condoms intermittently, and no seroconversions occurred among exposed partners.

## DISCUSSION

To our knowledge, our study is the largest and longest study of the heterosexual transmission of HIV in the United States. The consistency of results over the 10-year duration argues for the validity of our results. For example, the practice of anal sex and lack of condom use have remained strong predictors of transmission since the beginning of the study, and we continue to observe that male-to-female transmission is approximately 7–9 times more efficient than female-to-male transmission.

Over time, we recruited more index cases who were injection drug users and more minority couples. Although some of these changes in the recruitment characteristics of the couples over time can be attributed to changes in recruitment strategy, in spite of significant outreach, we did not see the proportion of couples including a bisexual man significantly decrease until mid-1990, close to 3 years after we increased our focus beyond recruitment of female partners of infected men who have sex with men. Condom use at

**TABLE 3. Risk behavior at baseline and most recent (final) follow-up visit among 175 human immunodeficiency virus (HIV)-discordant couples recruited in Northern California from 1985 to 1996 (n = 175 couples with a total of 3,384 couple-months of follow-up)**

|  | Baseline visit (%) | Final follow-up visit (%) |
|---|---|---|
| Abstention | 0 | 14.5* |
| Consistent condom use | 32.2 | 74* |
| Any anal intercourse | 37.9 | 8.1* |

* p < 0.0005 (by McNemar's test for matched pairs).

entry into the study was also more common among couples recruited more recently, probably accounting for the significant association (only in bivariate analyses) between recent enrollment and transmission.

A new finding in this report was increased transmission rates in couples where the partner was an injection drug user, which remained significant even controlling for all other significant risk factors. Although we were rigorous in ruling out drug use in the uninfected partner, we cannot be absolutely certain that we succeeded. In addition, there may be other unidentified cofactors for transmission from injection drug users to their sexual partners.

There are obvious physiologic and anatomical gender differences that could account for higher rates of male-to-female transmission (16). Still, we continue to find lower rates of female-to-male transmission in our study, compared with those found in some other studies with a similar design. The low rates of female-to-male transmission that we observed are consistent with the low rates of cases attributed to heterosexual transmission in Northern California, including comparatively low rates of AIDS cases in women. These trends in AIDS surveillance data have been confirmed in studies of HIV seroprevalence. For example, in women in California, estimated seroprevalence of HIV has remained constant among women at 0.5 percent for almost the last 2 years (17).

Higher rates of heterosexual transmission, particularly from females to males, reported in other studies may be due to a number of factors. Possible explanations include geographic differences in sexual practices, distributions of key cofactors for infection, and misclassification of transmission due to other sources such as needle sharing.

Differences in the prevalence of risk factors among populations from which participants are selected may contribute to different transmission rates. In our study, history of STDs was the most significant predictor of male-to-female transmission (OR = 2.6, p = 0.004). Similarly, in our assessment of female-to-male transmission, the fact that chlamydia was transmitted si-

multaneously or close to transmission of HIV is striking but not statistically significant, probably in part due to low power. In fact, the lack of incident STDs during the course of the study may have contributed to the absence of seroconversions during follow-up. Our findings are consistent with the hypothesis that co-infection with STDs increases susceptibility in the HIV uninfected partner, and increases infectiousness in the HIV-infected partner (18). Higher background rates of STDs would thus account for higher HIV sexual transmission rates.

The prevalence of other cofactors, some of which could not be considered in our study, may also affect transmission rates. Saracco et al. (19) found increased risk associated with use of intrauterine devices. However, the prevalence of this method (<2 percent), as well as other contraceptive methods, was too low in our sample for an effect to be detectable. In other studies, antibodies reactive with V3 apex peptides of HIV, MHC class 1 alleles, and presence of a mutant CCR-5 allele, were associated with decreased susceptibility (20–22). None of these variables were assessed in our study.

Finally, misclassification of mode of transmission may be an especially important factor to consider, particularly when interpreting estimates of the rate of female-to-male sexual transmission, because women who are injection drug users themselves are more likely to have a male injection drug user partner than vice versa (23–25). Studies in Europe (26) and the United States (27) which have reported higher rates of female-to-male transmission include relatively higher numbers of female injection drug users and their sexual partners. Tests for drug use somewhat reduce this kind of misclassification. However, we found higher rates of male-to-female transmission from drug users to their sexual partners compared with men who acquired their infection in other ways, an association which was maintained even in multivariate models that controlled for other significant risk factors. This highlights the importance of sexual transmission in areas with prevalent HIV infection among drug users.

In general, we estimate that infectivity for male-to-female transmission is low, approximately 0.0009 per contact, and that infectivity for female-to-male transmission is even lower. While data from this study suggest that the probability of male-to-female transmission appears to vary across couples, our estimate may still be useful as an index of "average" transmission risk for the purpose of comparisons among studies, or in epidemic model construction. Furthermore, our estimation procedure does not require knowledge of the infection time of the index case, which is usually unknown in partner studies; estimation proce-

dures that fail to take this uncertainty into account are potentially subject to serious biases (12). <mark>While our estimation procedure does not require that infection time be observed, it does depend on the assumptions of constant contact rates and parametric forms for the infectivity.</mark> (We assumed that the infectivity was either constant, linearly increasing, or linearly decreasing with time following index case infection.) Direct non-parametric estimation of this quantity is problematic in the absence of information on when the index case became infected (9).

Currently identified risk factors remain imprecise predictors of transmission. Two infected men whose female partners had all of the risk factors that we found to be significant in this study did not transmit the disease. Fewer than 50 percent of such couples with three of the risk factors had transmission events. In contrast, five women with no identified risk factors acquired HIV from their male partners. While some of these results might be attributed to errors in self-report, other factors which affect infectiousness and/or susceptibility may remain to be identified. As with studies of long-term survivors of HIV infection (28), an obvious area for future investigations is to focus on immunologic, genetic, and virologic factors among those individuals with multiple risk factors for whom transmission did not occur, compared with couples where transmission occurred in the absence of known risk factors.

<mark>While lack of transmission in our prospective study may in part be due to such unidentified protective factors, we also observed significant behavior change over time.</mark> In previous reports (8, 14, 29), the proportion of couples who used condoms at their last follow-up prior to analysis was 100 percent; the 75 percent reported here is the lowest proportion that we have observed. The proportion of couples who would use condoms if the study were continued beyond 10 years remains unknown. <mark>Nevertheless, the absence of seroincident infection over the course of the study cannot be entirely attributed to significant behavior change.</mark> No transmission occurred among the 25 percent of couples who did not use condoms consistently at their last follow-up nor among the 47 couples who intermittently practiced unsafe sex during the entire duration of follow-up. <mark>This evidence also argues for low infectivity in the absence of either needle sharing and/or cofactors such as concurrent STDs.</mark>

Because couples were recruited on a volunteer basis, results presented here are not necessarily reflective of trends in the population. Nevertheless, the increase over time in the recruitment of number of couples where the index case was an injection drug user or was infected from a previous heterosexual partner, as well

as the increase in recruitment of minority couples, may reflect the changing nature of the epidemic in Northern California as infection spreads outside homosexual and bisexual communities. <mark>The results from our study, including both the characteristics of participants and observed risk factors for transmission, confirm the significant contribution of both injection drug use and infection with other sexually transmitted diseases.</mark>

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## ERRATUM

### RE: "EPIDEMIOLOGY OF INSULIN-LIKE GROWTH FACTOR-I IN ELDERLY MEN AND WOMEN: THE RANCHO BERNARDO STUDY"

The *Journal* has been informed by Drs. Goodman-Gruen and Barrett-Connor of errors in the abstract of their recently published paper on insulin-like growth factor-I (IGF-I) in elderly men and women (1). Specifically, as published, a sentence in the abstract reads: "IGF-I decreased linearly with age in both sexes, with significantly lower levels in men than women (126.9 $\mu$g/liter vs. 134.1 $\mu$g/liter; $p = 0.03$)." The correct sentence should read: "IGF-I decreased linearly with age in both sexes, with significantly higher levels in men than women (134.1 $\mu$g/liter vs. 126.9 $\mu$g/liter; $p = 0.03$)." The *Journal* regrets these errors.

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