

radical therapy and who were excluded from the trial. We accept that endoscopic ultrasonography has a role in the staging of disease in such patients and have incorporated it into the baseline assessments required for the follow-up study (United Kingdom National Cancer Research Institute Upper Gastrointestinal Clinical Studies Group ST03 trial), in which patients with resectable gastric cancer will be randomly assigned to perioperative chemotherapy with epirubicin, cisplatin, and capecitabine with or without the antivascular endothelial growth factor antibody bevacizumab.

The survival outcomes of the study have been analyzed and reported on an intention-to-treat basis. The study was powered for overall treatment effect, and we would not expect to find significant results in any subgroup — for example, one defined according to tumor site. Nevertheless, we found no evidence of heterogeneity of treatment effect between the tumor sites (gastric vs. esophagogastric junctional vs. lower esophageal). Under these circumstances, it is generally accepted that the best estimate of treatment effect for an individual patient is the overall effect, rather than the subgroup estimate.<sup>1</sup>

We do not believe that subgroup analyses to evaluate separately the outcomes among patients who received preoperative chemotherapy only, as compared with either those who completed all six cycles or those assigned to surgery alone, would be helpful. The results would be difficult to interpret, because the patients in the perioperative-chemotherapy group who did not complete protocol treatment would not have done so because of early death or disease progression, which would significantly bias such an analysis.

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## Condom Use and the Risk of HPV Infection

**TO THE EDITOR:** The inverse relationship between the frequency of condom use and the incidence of human papillomavirus (HPV) infection, reported by Winer et al. (June 22 issue),<sup>1</sup> may be due to variation in the prevalence of HPV infection among sex partners with different levels of condom use. Men who use condoms more frequently may be more aware of the possibility of sexually transmitted infections and may be less likely to have sexual contact with high-risk groups, such as sex workers. The prevalence of HPV infection among men with a high level of condom use may be lower than among men with a low level of use. Therefore, such men would have a lower risk of transmitting HPV to female sex partners, even in the absence of a protective effect of condom use.

The incidence of an infectious disease is determined by the prevalence of the disease in the population, the probability of transmission per sexual contact, and the number of sexual contacts

per unit of time.<sup>2</sup> Therefore, in this case, an inverse association between the incidence of HPV infection and the level of condom use would be observed if there was an inverse association between the prevalence of HPV infection among sex partners and the level of condom use, even if condom use did not affect the probability of transmission.

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**TO THE EDITOR:** Winer et al. and Steiner and Cates (in the accompanying Perspective article)<sup>1</sup> discuss the importance of data regarding the use of condoms in the prevention of sexually transmitted

diseases. It must be emphasized that specific methodologic recommendations exist for data collection. For example, reporting on the number and type of sex acts provides more accurate information than simply reporting on the number of sex partners. A recent review<sup>2</sup> suggests that although measures of condom use have modestly improved over time, many recommendations have not been implemented. Furthermore, because a gold standard does not exist, data collection must be tailored and comprehensive. This need is particularly important with high-risk groups.

In a study funded by the National Institute on Drug Abuse,<sup>3</sup> 445 women who were actively using drugs and not in treatment reported engaging in an average of 54 sex acts during a 4-month period. Of those encounters, the respondents reported the use of condoms in only 31% of instances of vaginal intercourse, 12% of instances of fellatio, and 4% of instances of cunnilingus. Sex workers used protection more often than did other women but were more likely to engage in folk practices to prevent sexually transmitted diseases, such as having sex only with healthy-looking people. Researchers must integrate recommendations regarding the collection of data on condom use, since accurate data are critical for the development of tailored prevention messages.

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**THE AUTHORS REPLY:** Liang and Cottler et al. address some of the methodologic challenges of conducting studies of the effectiveness of condom use. We agree with Cottler and colleagues that specific measures should be taken to ensure that data collection is accurate and study-specific. In our study, for example, we were able to generate more precise estimates of the frequency of condom use by collecting data on daily sexual behav-

ior every 2 weeks. Furthermore, although the number of instances of vaginal intercourse was not an independent predictor of HPV acquisition in our study (probably because our subjects reported having fewer instances of vaginal intercourse with new partners than with longer-term partners), measurements that incorporate numbers rather than proportions of protected acts, as compared with unprotected acts, may be appropriate for studies in other populations or of other sexually transmitted diseases.

As Steiner and Cates note, the inherent subjectivity of self-reported data on sexual behavior is also a concern. Computer-assisted questionnaires may be more effective than face-to-face interviews at eliciting more truthful reporting of sensitive behavior,<sup>1</sup> and biologic markers may be used to confirm the validity of self-reported data on sexual behavior.<sup>2</sup> Steiner and Cates also stress that a failure to account for the differential risk of exposure to sexually transmitted diseases may lead to the underestimation of the effectiveness of condom use. Indeed, the women in our study tended to report more frequent condom use with "riskier" partners; controlling for the number of new partners and the number of previous partners reported by male partners strengthened the observed inverse association between condom use and HPV acquisition. The latter variable was a useful surrogate indicator of a male partner's infection status, since no infections were detected in women reporting previously virginal male partners. Given these observations and the fact that HPV infections are not concentrated in high-risk populations (in a study of low-risk men attending the same university, for example, the prevalence of HPV infection was 33%<sup>3</sup>), Liang's suggestion that differential risk exposure could have led to an overestimate of the effectiveness of condom use seems unlikely.

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