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Condom Use and Human Papillomavirus in Men

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Keywords

condoms; human papillomavirus; HPV infection; HPV persistence

In this issue of the *Journal*, an article by Pierce Campbell et al [1] adds new information to the largely inconsistent body of observational studies on the protective effect of condom use against human papillomavirus (HPV) infection. Using data from the HPV Infection in Men (HIM) study [2], a multinational cohort study of the natural history of anogenital HPV in men, the authors examined the effect of self-reported condom use on the incidence and duration of penile HPV infection. Their results suggest reductions in HPV acquisition and duration of HPV infection for some men who reported consistent condom use.

In the HIM study, participants completed a physical examination every 6 months over a 4-year period. At each visit, participants provided DNA specimens and completed a self-administered questionnaire about recent sexual behaviors, including condom use since the prior visit. For this analysis, the authors divided the original cohort into 4 categories based on the risk of HPV exposure, as determined by participants' self-reported sexual behavior. The categories, in order of decreasing exposure risk, were no steady sex partner; nonmonogamous, nonsteady sex partner; nonmonogamous, steady sex partner; and monogamous. Condom use in the previous 6 months was defined at a single time point (the baseline visit) and assessed at 3 levels (always, sometimes, and never). This baseline measure was extrapolated to represent condom use during the entire follow-up period. HPV infection was classified into 3 categories on the basis of HPV type: any HPV type, oncogenic HPV types, and nononcogenic HPV types. In the highest HPV exposure risk category (ie, men with no steady sex partners), those who reported always using condoms in the 6 months before study entry were about 50% less likely to become newly infected with any HPV types in the 12-month follow-up period, compared with men who never used condoms (adjusted hazard ratio [HR], 0.54; 95% confidence interval [CI], .31–.95). Similar reductions were reported when HPV types were stratified by oncogenic risk, but these associations did not reach statistical significance. No significant associations were observed between condom use and HPV incidence in the other 3 HPV exposure risk groups. Evaluating duration of infection, the authors found a faster rate of oncogenic HPV clearance

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only in the group of men who reported always using condoms with their nonsteady sex partners, compared with men who reported never using condoms (adjusted HR, 1.29; 95% CI, 1.03–1.61). Condom use did not impact the duration of infection in the other 3 HPV exposure risk groups, including the group with no steady sex partners, the same group for which consistent use decreased HPV incidence.

Condom use is a frequently examined cofactor in epidemiologic investigations of HPV infection and associated diseases in both men and women. Yet findings from a growing number of studies, including the present one, have been difficult to interpret, partly because many are based on secondary analyses of studies that were not designed to evaluate condom effectiveness [3–20]. Evaluating condom use in observational studies of sexually transmitted infections (STIs), particularly HPV infection, is inherently complex and subject to measurement errors that contribute to the heterogeneity in findings [21, 22]. Importantly, because incorrect or inconsistent use can diminish the protective effects of condoms, investigators must assess whether condoms were used properly during each sex act on the basis of self-reported measures of questionable validity [23]. Other methodological challenges include the inability to establish a clear temporal relationship between the timing of condom use and the onset of new HPV infections [24] in cross-sectional and case-control studies, as well as the failure to account for potential differences in exposure to HPV-infected partners between those who always used condoms and those who never used condoms [25].

This analysis by Pierce Campbell et al is a contribution to the short list of investigations of condom effectiveness against incident HPV infection, but it is subject to many of the same limitations that plague studies of condom effectiveness. A principal concern for interpretation of these results is that the frequency of condom use was assessed at a single time point at the beginning of the study, rather than as a time-dependent measure during each 6-month follow-up interval over the observation period. This could have introduced significant bias because condom use patterns tend to change over time within individuals, as shown in previous studies [26, 27]. Condom use should ideally be assessed during a period that also coincides with the interval during which HPV status is examined.

The lack of assessment of exposure to HPV-infected partners is also a notable limitation. While the cohort was stratified by exposure risk on the basis of self-reported behaviors, the risk groups were not well defined. In the nonmonogamous group, for example, the incidence of HPV infection was similar between those who always used condoms and those who never used condoms, and it was highest among those who sometimes used condoms. In contrast, among men with no steady sex partner, those who reported always using condoms had the lowest incidence, while those who never used condoms had the highest incidence. These findings suggest that the results may be confounded and simply reflect fewer sex partners and less-risky sex among men who reported having a steady sex partner and who never used condoms, compared with those who had no steady sex partner and never used condoms. Another issue to consider in interpreting these results is that, despite the large size of the HIM cohort, small numbers in some of the condom use groups, particularly for consistent users, may have led to imprecise estimates. Previous studies suggest that the types of bias that are likely in this study tend to underestimate condom effectiveness [25, 28, 29]. That

significant inverse associations with both HPV acquisition and clearance were found for condom use in some subgroups in light of the biases is encouraging.

The article by Pierce Campbell et al is one of several evaluations of condom effectiveness to be published using data from the HIM study cohort [4, 7, 8]. A recent article by the same research group presented results from a cross-sectional evaluation of condom effectiveness on prevalent HPV infection in heterosexual men [8], while an earlier cross-sectional analysis evaluated the prevalence of anal HPV among men who reported having sex with men [7]. As with this evaluation, both prior studies suggested a protective effect of condoms among some but not all subgroups. Unfortunately, critical methodological differences, particularly in condom use classification, prevent comparisons across these studies.

Unlike the previous evaluations, the present study is the first to use the HIM cohort to examine condom use and HPV acquisition. To our knowledge, only 2 other cohort studies have examined the effect of condom use on incident HPV infection. The first investigation enrolled a small group of male Danish soldiers and prospectively assessed the incidence of HPV infection at a single time point [20]. The second was a seminal investigation specifically designed to examine the effect of condom use on HPV acquisition in female university students in the United States [11] In that study, daily diaries were used to collect detailed information on condom use and sexual activity, allowing more-accurate measurement of condom use throughout the observation period. Both studies showed a significantly lower incidence of HPV infection among individuals who reported consistent condom use; in the latter study, a 70% reduction in incident HPV infection was found in female partners of men who wore condoms correctly and consistently during each sex act [11]. While the existing biological and epidemiological evidence suggests that condoms may provide at least partial protection against HPV, carefully designed longitudinal investigations such as the one by Winer et al [11] are needed to more conclusively support the role of condoms as an effective prevention strategy against HPV infection.

The availability of highly efficacious vaccines for primary prevention of HPV-associated diseases has revolutionized the field of HPV research. However, additional prevention measures remain necessary to complement vaccination efforts in order to reduce the burden of HPV-associated diseases. Notably, the current vaccines are directed against 2 HPV types that cause 70% of cervical and a large proportion of other HPV-associated cancers, but they do not protect against infection with other HPV types, several of which are known to cause cancer [30, 31]. Therefore, even among fully vaccinated individuals, other prevention strategies will be needed to prevent diseases associated with HPV types not included in the vaccines. Furthermore, the target age group for vaccination is early adolescence, with catch-up vaccination only through the teens or mid twenties in some countries [32].

Condoms are well-established and recommended devices for reducing the risk of human immunodeficiency virus infection in sexually active individuals, with protection against many other STIs also having been demonstrated [33–36]. If condoms are used correctly and consistently, they may reduce the risk of HPV acquisition in select populations. The present findings underscore the importance of additional research to determine the extent to which condom use may protect against HPV and associated diseases.

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