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Dietary intake of selected nutrients and persistence of HPV infection in men

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Abstract

Human papillomavirus (HPV) infection is a common sexually transmitted disease. Although often transitory, persistent oncogenic HPV infection may progress to a precursor lesion and, if not treated, can further increase the risk of cancer. The purpose of this study was to investigate the relation between dietary intake and HPV persistent infection in men of a Brazilian cohort. The study population consisted of 1,248 men from the Brazilian cohort of the HIM (HPV in Men) Study, ages 18 to 70 years, who completed a quantitative food frequency questionnaire. U Mann-Whitney test was used to assess differences in median nutrient intake of selected nutrients. The association of dietary intake and persistent HPV infection was assessed in multivariate logistic models. The prevalence of any HPV infection at baseline was 66.6%. Of 1,248 participants analyzed, 1,211 (97.0%) were HPV positive at one or more times during the 4 years of follow-up and 781 (62.6%) were persistently HPV positive. Men with nonpersistent oncogenic HPV infections had higher median intake of retinol ($p = 0.008$), vitamin A ($p < 0.001$) and folate (DFE; $p = 0.003$) and lower median intake of energy ($p = 0.005$) and lycopene ($p = 0.008$) in comparison to men with persistent oncogenic infections. No significant association was found between selected nutrients and persistent oncogenic HPV infection. For nononcogenic persistent infections, only vitamin B12 intake was significantly associated ($p = 0.003$, test for trend). No association was observed between dietary intake and persistent oncogenic-type HPV infection; however, vitamin B12 intake was inversely associated with nononcogenic HPV persistence.

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Conflict of Interest/Disclosures

AR Giuliano is member of the Scientific and Advisory Boards for Merck Sharp and Dohme. LL Villa is member of the board of Merck Sharp and Dohme for the Quadrivalent HPV vaccine.

Keywords

diet; HPV; men; food frequency questionnaire

Human papillomavirus (HPV) infection is one of the most common sexually transmitted diseases and is generally subclinical and transitory, usually resolved spontaneously by the immune response.[1–3] Although often transitory, persistent oncogenic HPV type infection may progress to a precursor lesion and, if not correctly treated, can further increase the risk of pre-cancer and cancer,[4–6] contributing to diseases such as cervical, vulvar, vaginal, anal, penile and oropharyngeal cancers and genital warts in women and men.[7–9] HPV prevalence is common in sexually active individuals, with male infection significantly contributing to infection and subsequent disease in women.[7]

Prior studies evaluated the association between diet and the risk of HPV acquisition and persistence among women.[10–14]

Nutrients such as folate and vitamins B6 and B12 may have a role in regulating viral integration and gene stability due to their involvement in DNA synthesis, repair and methylation.[11,14] Consuming foods, particularly plant-based foods, that support normal DNA methylation, has the potential to suppress expression of viral oncogenes, promote proper signaling pathways, avoid cell transformation, and reduce the risk of cancer in humans.[14–16] Antioxidant nutrients are capable of modulating immune response and decreasing viral replication and gene expression.[11] Folate, vitamins A, C and E, and the active Vitamin D metabolite are reported to have the ability to inhibit cell proliferation, prevent DNA damage and enhance immunologic functions.[11,14,17,18] Moreover, due to its essential role in the replication of basal and mucosal cells and in the synthesis of protein, vitamin A deficiency could lead to a higher risk of infection and metaplasia.

García-Closas *et al.*(2005)[11] completed a systematic review of the role diet exerts on the risk of persistent HPV and cervical cancer. A possible protective effect against HPV persistence was noted for fruits, vegetables, vitamins C and E, alpha and betacarotene, lycopene, lutein/zeaxanthin and cryptoxanthin. For cervical neoplasia, evidence was probable for folate, retinol and vitamin E and possible for vegetables, vitamins B12 and C, lycopene, lutein/zeaxanthin and cryptoxanthin. However, the authors emphasized the need of more prospective studies evaluating these associations.

Chi *et al.* (2013),[14] in a more recent review, reported that higher intake of nutrients with antioxidant and antiviral functions may prevent the progression of HPV infection to high-grade cervical intraepithelial neoplasia.

Despite the epidemiological support for a role of dietary intake and nutritional status in carcinogenic process, few take into consideration HPV infection and persistence,[11] especially in men. Additionally, the association between specific dietary components and the quantity required to prevent cancer is not well established.[14] Thereby a better understanding of this relation in men is an important component for the prevention of HPV infection-related diseases in both genders.

Considering the possible association of diet and risk of persistent HPV infection, the purpose of this study was to investigate the association between dietary intake of selected nutrients and HPV persistent infection in men of a Brazilian cohort.

Material and Methods

Study population

The HPV in Men (HIM) Study is a multinational prospective study that examines the natural history of HPV infection in men. Participants were eligible for participation if they were aged 18–70 years; residents of southern Florida-USA, São Paulo-Brazil or Cuernavaca-Mexico; reported no previous diagnosis of penile or anal cancers; reported no previous diagnosis of genital or anal warts; had not participated in an HPV vaccine study; reported no previous diagnosis of HIV; reported no current penile discharge or burning during urination; were not being treated for sexually transmitted infection; had not been imprisoned or homeless during the past 6 months; had not received drug treatment during the past 6 months; had no plans to relocate in the next 4 years; and were willing to comply with 10 scheduled visits every 6 months for 4 years.

In Brazil, men were recruited from “Centro de Referênda e Treinamento DST/AIDS-SP,” a large clinic in São Paulo that provides genitourinary services, and the general population through television, radio and newspaper advertisements.

Eligible participants provided written informed consent, and study protocols were approved by institutional review boards at each study site. More detailed description of the study design and population is reported elsewhere.[8,19,20]

Men who provided consent underwent a clinical examination at a visit 2 weeks before the enrolment visit and every 6 months thereafter, for 4 years. To encourage compliance with follow-up, men were given compensation for transport and alimentation for their participation. For this study, only the Brazilian cohort was considered.

The selection of the study sample to test the hypothesis that dietary intake of selected nutrients is associated with persistent HPV infection is described in detail below (Fig. 1).

HPV DNA detection

Samples of penile and scrotal cells were obtained at each visit occurring every 6 months for a median of 4 years of follow-up. DNA was extracted from samples using the QIAamp Mini kit (Qiagen), according to the manufacturer’s instructions. The polymerase chain reaction (PCR) was used to amplify a fragment of the HPV L1 gene. HPV genotyping was conducted with the linear array method on all samples irrespective of the HPV PCR result (Roche Molecular Diagnostics, Alameda, CA) and were categorized as oncogenic (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 66) and nononcogenic HPV types [6, 11, 26, 40, 42, 44, 53, 54, 61, 62, 64, 67, 68, 69, 70, 71, 72, 73, 81, 82, 83, 84, IS39 (a sub-type of 82)] and CP6108 (type 89).

A sample was considered HPV positive if HPV DNA was detected by PCR or if it tested positive for at least 1 of the 37 HPV genotypes. Samples that amplified HPV DNA by PCR but did not test positive for a specific HPV genotype were considered unclassified infections. Individuals who had at least two positive and consecutive tests for the same HPV type were considered as having persistent infection.[21]

Study questionnaires

At each study visit, participants completed a computer assisted self-interview questionnaire to collect information such as age, alcoholic consume, smoking habit, sociodemographic characteristics and HPV risk factors. Physical activity was assessed using a separate questionnaire (International Physical Activity Questionnaire). Weight and height were measured by nursing assistants. Participants were classified according to Body Mass Index (BMI).[22]

Diet questionnaire

Dietary intake was ascertained using a previously validated Quantitative Food Frequency Questionnaire (QFFQ)[23] for the Brazilian population, which provides information regarding usual dietary intake through frequency and consumed portion data.

The questionnaire is composed of 54 food items and was developed based on the dietary intake of a representative sample of the city of São Paulo that had been identified in a population-base study.[24] The detailed methodology for developing the QFFQ used in the HIM Study in Brazil is available in a prior publication.[23] For each food item listed, participants indicated their frequency of consumption (from 0 to 10 times a day, week, month or year) and the portion consumed (small, medium, large or extra large). A spreadsheet containing the nutritional composition of each food item, created using the Nutrition Data System for Research (NDSR, version 2.0, 2007 - University of Minnesota, Minneapolis), was used for calculating the energy and nutrient intake. The QFFQ was validated with correlation coefficients varied from 0.25 to 0.76.[25] For this study, only the first QFFQ applied on the HIM Study in Brazil was considered.

Statistical analysis

From at least two 24 hr-recalls (24-HR) applied in a subsample (n = 121) of the Brazilian cohort, administered through a face-to-face interview, and using the Multiple Pass Method,[26] it was possible to estimate calibration equations for FFQ dietary data, reducing measurement errors. Data from the 24HR were entered into the Nutrition Data System for Research and were converted into energy and nutrients. The Multiple Source Method (MSM), a statistical modeling technique, which calculates usual dietary intake, was used to remove within person variation that would otherwise inflate the distribution.[27,28] The 24-HR values were regressed on the intake values from the main dietary questionnaires. BMI, income, education, age, physical activity, among other variables, were included as additional covariates to minimize effects in dietary intake.[29–31] Data from 24-HR and FFQ were previously adjusted for energy intake using the residual method.[32] Dietary folate equivalents values were adjusted according to Brazilian legislation of compulsory enrichment of wheat and corn flours.

Of 1,412 participants in the Brazilian cohort, 1,255 had complete dietary data. Individuals with energy intake lower than 500 kcal ($n = 5$) and individuals without at least two consecutive samples of HPV collected ($n = 2$) were excluded. As a result, 1248 men were assessed regarding HPV infection prevalence (Fig. 1). Median dietary intake of energy and nutrients was described for men with persistent infections (oncogenic and nononcogenic), nonpersistent infections, and among those with no HPV infection. As previously defined, persistence was considered as at least two positive consecutive tests for the same HPV type. U Mann Whitney test was used to assess differences in median nutrient intakes by HPV status group.

To test the hypothesis that dietary intake of selected nutrients is associated with persistent HPV infection, two independent multivariate logistic regression models were developed to assess the risk of both oncogenic and nononcogenic persistence using backwards stepwise elimination. Non-nutrient potential confounding factors were evaluated and retained in models ($p \leq 0.15$). For the oncogenic HPV model, the variables identified by this process were age, marital status, smoking, number of lifetime female sex partners, alcohol consumption in the previous month, and HPV status at enrollment. For non-oncogenic HPV model, variables retained were age, smoking, number of lifetime female sex partners, physical activity, alcohol consumption in the previous month and HPV status at enrollment. Treating categorical nutrient variables as continuous in multivariate logistic regression models allowed the assessment of linear trends. Individuals with no HPV infection and no classified HPV infections were withdrawn from the final logistic models ($n = 170$). All statistical analysis were performed using Stata 12 (Stata Corp., College Station, USA).

Results

The majority of participants (66.6%) were HPV positive at study enrolment: 409 (32.8%) positive for oncogenic HPV, 595 (47.7%) positive for nononcogenic HPV, 268 (21.5%) coinfected with both oncogenic and nononcogenic HPV and 161 (12.9%) positive for nonclassified HPV types (positive for PCR but negative in genotyping). Mean age of study participants at enrolment was 34 years old.

Among the 1,248 men, 1211 (97.0%) had at least one type of HPV infection during the 4 years of follow-up. Persistent HPV infection was observed in 781 (62.6%) individuals, among which 458 (36.7%) had persistent oncogenic infections and 636 (51.0%) persistent nononcogenic infections. The most frequently detected persistent HPV types were 62 (13.2%), 84 (10.4%), CP6108 (9.4%) and 16 (9.1%).

From the potential cofounders initially identified, only increasing age (OR = 0.43 [0.26–0.72]), higher no. of female sex partners in lifetime (OR = 2.5 [1.34–4.67]) and positive HPV status at enrollment (OR= 2.04 [1.49–2.79]) remained statistically significant in the final logistic model for persistent oncogenic HPV. For the persistent nononcogenic HPV model, only higher no. of female sex partners in lifetime (OR = 2.1 [1.12—3.94]), alcohol consumption (OR = 0.7 [0.51–0.94]) and positive HPV status at enrolment (OR = 3.2 [2.38–4.30]) presented significant association in the final model (data not shown).

Median nutrient intake and associations with participant demographic and lifestyle characteristics are reported in Table 1. With the exception of folate, the median intake of the majority of nutrients appears higher among white men, those with >12 years of education, and men with a higher monthly income.

Dietary intake values according to HPV infection status are presented in Table 2. For oncogenic HPV infections, men with persistent infections had lower median daily intakes of retinol ($p = 0.0286$), vitamin A* ($p = 0.0002$) and folate equivalents† ($p = 0.0001$), and higher medians of energy ($p = 0.0051$) and lycopene ($p = 0.0237$). No differences in median daily intake were found for nononcogenic infections. Individuals without any HPV infection had higher median intake of α-carotene ($p = 0.0241$), β-carotene ($p = 0.0146$) and lutein/zeaxanthin ($p = 0.0403$).

Table 3 presents the association between specific dietary nutrients and HPV persistence. No significant associations were observed between oncogenic HPV persistence and dietary intake in multivariable adjusted models. Higher intakes of vitamin B12 were significantly associated with lower risk of persistent nononcogenic HPV infections (OR = 0.55 [0.38–0.81]).

Discussion

Persistent HPV infection is an important risk factor for the development of cervical, anal, penile and oropharyngeal cancers.[4–9] In previous studies, carotenoids, retinol, vitamin C, vitamin E and nutrients involved in DNA methylation, such as folate, have been investigated as potential modifiers of HPV persistence and cancer risk among women.[4,11,13,14,33] To our knowledge, no previous studies evaluated the association between HPV persistence and dietary intake in men. Our findings suggest that in this population of Brazilian men dietary vitamin B12 may be protective against nononcogenic HPV persistence. However, no significant association was observed for dietary intake of selected nutrients and oncogenic HPV persistence.

In a comprehensive review, antioxidant nutrients such as carotenoids, retinol and tocopherols were suggested to be protective against cervical dysplasia as they could modulate immune response and decrease viral replication and gene expression. However, there was a lack of prospective studies adequately controlling for HPV infection.[11] A more recent review of dietary prevention of HPV infection and cervical cancer suggested that circulating antioxidants, at high levels, can enhance the clearance of high-risk HPV infections.[14]

Prior studies conducted in women and taking HPV infection and confounders into consideration showed inconsistent results. In a nested case-control study of Brazilian women, β-cryptoxanthin, lutein/zeaxanthin and vitamin C intakes were associated with decreased risk of type specific HPV persistence, but no associations were observed for α and β-carotene.[10] A marginally significant association between median dietary lutein intake and

*Vitamin A = mcg retinol + (mcg beta-carotene equivalents/12).
†Folate equivalents = mcg natural folate + (1.7 × mcg synthetic folate).

HPV persistence was observed in a cohort of young woman.[12] In contrast, inconsistent associations were observed when individual nutrients were examined.[13]

Although no association was observed with dietary folate and vitamin B12, plasma vitamin B12 levels were associated with a reduced risk of HPV persistence in a cohort of young women in Arizona.[4] Methylation of the regulatory region of HPV has been shown to prevent transcription *in vitro,* suggesting that methylation can decrease viral proliferation and prevent maintenance of HPV infection.[11,34] Vitamin B12, as well as folate and vitamin B6, may prevent carcinogenesis through their role in DNA methylation, as they contribute to the synthesis of S-adenosylmethionine.[35,36] Despite relevant biochemical evidence for a role of vitamin B12, the epidemiological literature has not provided consistent evidence of an association with HPV persistence. In our study, dietary vitamin B12 was inversely associated with non-oncogenic HPV infection persistence only, which possibly indicates that other factors may have more influence in the persistence of oncogenic HPV infections. Studies have found an association between viral persistence and multiplicity of HPV infection, as it seems plausible that an underlying immune condition may increase susceptibility to multiple and persistent infections.[5,21]

As there are no prior studies that evaluated the relationship between dietary factors and HPV persistence in men, it is unclear if the results reported here are unique to the study population. As such, more research among men is needed to further elucidate the association between diet and HPV persistence in men.

The limitations of this study should also be considered when interpreting these findings. Our results could be affected by measurement error in dietary intake, a common limitation of nutritional epidemiological studies. However, the calibration of dietary intake reported in HIM Study minimizes the impact of possible systematic overestimation or underestimation in dietary intake measurements; however, measurement error of the 24-hr recall is not independent of that of dietary questionnaires. Moreover, there is no information about circulating concentrations of nutrients and it is possible that diet and circulating concentrations measure different exposures, resulting in different relationships with HPV persistence.

In conclusion, results from this study indicate that dietary intake of vitamin B12 is associated with reduced risk of non-oncogenic HPV persistence in men. No associations were found between persistent oncogenic HPV infections and dietary intake of selected nutrients. More studies evaluating the association of HPV persistence and dietary intake in men are needed to further comparisons and a better understanding of this relation.

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What's new?

Can diet influence the persistence of HPV infection? Certain B vitamins, for instance, can promote viral integration, while other nutrients hinder it. This is the first study to investigate whether diet contributes to persistent oncogenic HPV-infection in men. Looking at a Brazilian cohort of men age 18–70, these authors tested the men for HPV over a period of 4 years. At each meeting, they gave them a questionnaire, asking about their diet. Persistent nononcogenic HPV infection was associated with B12 consumption, they found, but they could link none of the nutrients to persistent oncogenic HPV infection.

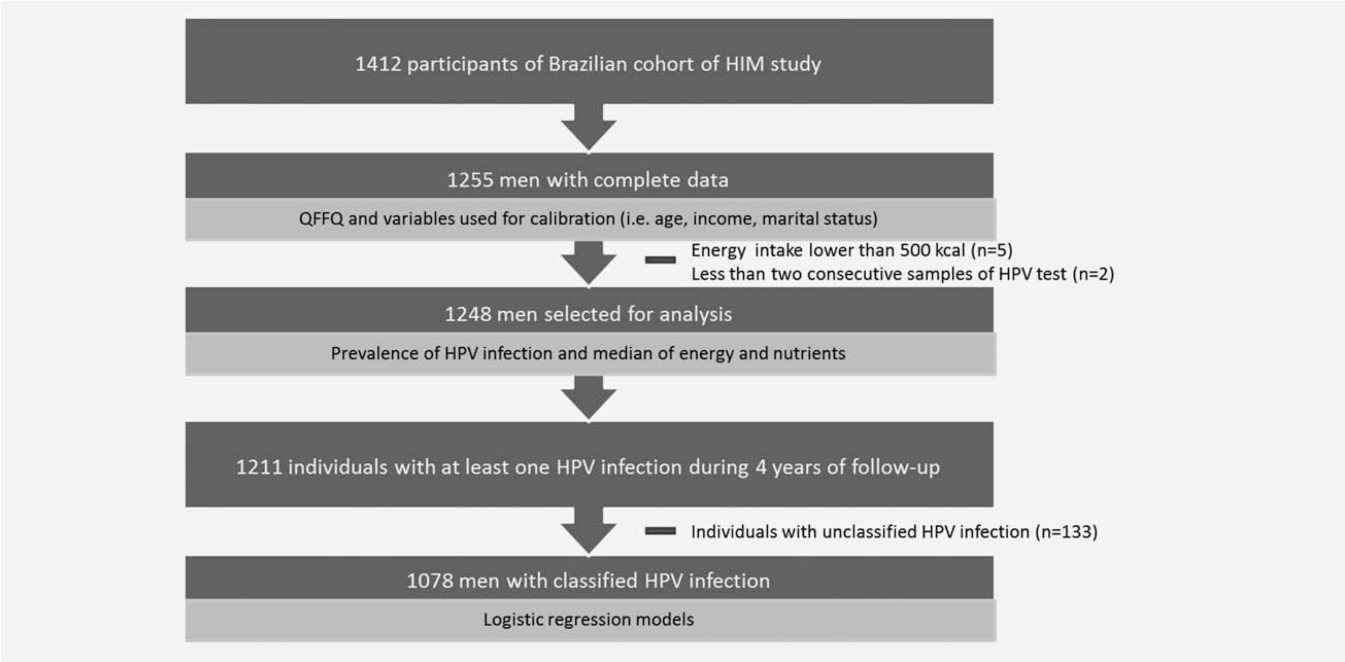

Figure 1.
Selection of sample for statistical analysis. São Paulo, 2015.

Table 1.

Distribution of median intake of nutrients according to demographic and lifestyle variables (São Paulo, 2015)

Variable	No	Retinol (μg)	Lycopene (μg)	Vitamin A (μg)	α-Caroteno (μg)	β-Carotene (μg)	β-Cryptoxanthin (μg)	Lutein + zeaxanthin (μg)	Folate (DFE)[1] (μg)	Vitamin D (μg)	Vitamin E (mg)	Vitamin B12 (μg)	Vitamin C (mg)
Ethnicity													
White	773	406.46[2]	2629.45[2]	705.99[2]	393.72[2]	2555.39[2]	244.42[2]	1806.77[2]	711.74[2]	3.67	7.28[2]	5.70	92.78[2]
Nonwhite	475	396.08	2564.78	682.97	373.78	2375.88	171.73	1741.09	725.90	3.63	7.22	5.67	71.12
Education													
≤12 years	719	395.16[2]	2557.66[2]	681.97[2]	369.23[2]	2252.36[2]	199.42[2]	1689.41[2]	733.19[2]	3.60[2]	7.24	5.70	79.48[2]
>12 years	526	412.01	2655.35	716.46	424.57	2966.77	254.55	1948.48	696.94	3.73	7.27	5.69	93.12
Monthly Income, R$ (US$)													
≤3,000,00 (≤932)	951	400.74[2]	2573.34[2]	686.77[2]	366.26[2]	2321.44[2]	197.69[2]	1679.29[2]	732.48[2]	3.63[2]	7.26	5.67[2]	79.41[2]
>3,000,00 (>932)	297	409.46	2669.27	723.19	552.14	3372.93	390.93	2200.57	668.30	3.73	7.25	5.81	114.33
Marital status													
Single	628	407.39[2]	2644.89[2]	678.09[2]	385.55	2513.76	216.09	1773.44	685.17[2]	3.65	7.32[2]	5.49[2]	85.71
With partner	620	397.87	2549.21	713.08	381.66	2434.75	218.31	1786.60	759.05	3.65	7.21	5.96	84.19
Smoking habit													
Current smoker	1024	393.55[2]	2637.69	685.44	385.13	2433.29	205.41	1773.92	677.82[2]	3.60[2]	7.30	5.64	66.48[2]
Nonsmoker	224	404.63	2588.81	699.51	382.39	2488.56	220.04	1779.66	725.46	3.66	7.25	5.71	88.47
No. of female sex partners during lifetime													
0	111	407.57	2607.45[2]	673.29[2]	374.46[2]	2430.46[2]	213.52	1730.66[2]	705.18	3.62[2]	7.32	5.55[2]	86.77
1	69	415.37	2661.48	718.24	387.80	2561.93	214.56	1882.46	733.99	3.71	7.39	5.69	85.34
2–9	361	400.33	2583.55	678.34	382.40	2420.29	215.37	1760.57	722.09	3.59	7.26	5.70	85.17
10–19	242	401.29	2609.00	695.15	379.73	2481.44	216.00	1754.56	720.73	3.69	7.28	5.69	83.40
20–49	269	397.73	2602.55	704.77	392.82	2511.02	226.46	1817.42	707.60	3.64	7.22	5.76	85.99
50+	103	408.59	2721.47	727.38	413.45	2722.78	233.61	1858.80	703.95	3.84	7.23	5.71	89.24
No. of male sex partners during past 3 months													
0	1091	400.81[2]	2589.47	698.56	382.38	2465.21	217.70	1771.32	720.71[2]	3.66	7.24	5.71[2]	85.34

Variable	No	Retinol (μg)	Lycopene (μg)	Vitamin A (μg)	α-Caroteno (μg)	β-Carotene (μg)	β-Cryptoxanthin (μg)	Lutein + zeaxanthin (μg)	Folate (DFE)[1] (μg)	Vitamin D (μg)	Vitamin E (mg)	Vitamin B12 (μg)	Vitamin C (mg)
1	58	403.96	2602.10	703.04	393.87	2602.15	215.12	1820.73	694.25	3.58	7.27	5.63	85.13
2	38	420.34	2698.31	668.17	390.54	2491.14	215.72	1845.48	695.49	3.61	7.34	5.61	84.36
≥3	61	417.37	2645.79	689.79	381.02	2637.93	213.52	1745.14	697.11	3.74	7.42	5.54	84.86
Alcohol consumption during last month													
Yes	889	401.16	2614.24[2]	692.38[2]	384.65	2489.71	218.34	1793.75	708.65[2]	3.64	7.25	5.71	85.13
No	358	406.75	2563.33	714.19	377.66	2452.94	215.00	1754.14	732.83	3.68	7.28	5.64	85.35
Circumcision status													
Yes	241	409.31	2633.90	716.99[2]	390.10	2579.86	218.80	1810.98	716.37	3.66	7.32	5.71[2]	84.94
No	985	400.82	2583.55	693.64	381.85	2462.37	216.69	1773.06	718.94	3.65	7.24	5.70	85.60
Physical Activity													
Sedentary/ Insuficiently active	306	396.48	2552.84[2]	674.79[2]	372.47[2]	2423.67[2]	203.54[2]	1727.53[2]	718.99	3.66	7.14[2]	5.77[2]	81.27[2]
Active	542	404.80	2615.48	702.79	389.69	2502.44	223.50	1795.84	716.71	3.63	7.28	5.68	87.03
Very active	400	404.52	2603.59	703.65	383.68	2473.88	218.84	1803.07	719.19	3.67	7.30	5.68	84.61

[1] Values of Dietary Equivalents of folate corrected for Brazilian values.

[2] $p < 0.05$, Kruskall-Wallis test.

Table 2.

Median values of nutrient intake, by HPV infection status (São Paulo, 2015)

	Persistent oncogenic HPV[1]			Persistent nononcogenic HPV[1]			HPV infection[2]		
	Yes (*n* = 458)	No[3] (*n* = 790)	*p*-Value	Yes (*n* = 636)	No[4] (*n* = 612)	*p*-Value	Yes (*n* = 1211)	No (*n* = 37)	*p*-Value
Energy (kcal)	2485.96	2431.83	0.0051	2453.03	2447.79	0.7538	2451.54	2364.54	0.7136
Carbohydrate (g)	294.35	295.48	0.5759	294.97	294.36	0.4171	294.80	296.18	0.6644
Protein (g)	95.10	95.00	0.6016	94.93	95.23	0.0706	95.01	95.99	0.1117
Total fat (g)	89.21	88.79	0.0501	89.03	89.93	0.4605	89.00	89.11	0.7036
Retinol (μg)	397.79	403.23	0.0286	402.57	399.80	0.1979	402.54	404.17	0.6398
Lycopene (μg)	2641.01	2581.58	0.0237	2600.17	2615.54	0.7715	2598.33	2580.96	0.4779
Vitamin A (μg)	681.04	706.40	0.0002	695.65	695.77	0.5728	697.16	753.34	0.1701
α-carotene (μg)	382.15	382.40	0.4731	381.36	385.83	0.3442	381.85	412.60	0.0241
β-carotene (μg)	2438.44	2497.39	0.3532	2448.19	2502.44	0.8543	2835.42	3067.06	0.0146
β-cryptoxanthin (μg)	215.29	218.91	0.8217	216.71	216.29	0.8315	216.66	217.70	0.4904
Lutein + zeaxanthin (μg)	1765.61	1776.97	0.9110	1766.44	1777.78	0.5104	1770.98	1816.27	0.0403
Folate (DFE) (μg)	707.02	720.49	0.0001	718.12	713.00	0.9126	717.17	736.40	0.2094
Vitamin D (μg)	3.64	3.66	0.3364	3.65	3.66	0.2041	3.65	3.76	0.2791
Vitamin E (mg)	7.28	7.24	0.0671	7.26	7.23	0.3904	7.25	7.43	0.0502
Vitamin B12 (μg)	5.65	5.74	0.0533	5.68	5.73	0.0436	5.69	5.74	0.4458
Vitamin C (mg)	84.68	85.51	0.5029	84.91	85.52	0.3740	85.13	87.77	0.3591

[1] Only classified infections considered.

[2] Including individuals with nonclassified infections.

[3] Includes individuals with transitory infection for oncogenic HPV and no infection for oncogenic HPV, but at least one positive result for other HPV types.

[4] Includes individuals with transitory infection for nononcogenic HPV and no infection for nononcogenic HPV, but at least one positive result for other HPV types.

Table 3.

Association between energy-adjusted dietary intake and persistent HPV (São Paulo, 2015)

Nutrient	Infection no.		Crude OR (95% CI)	Adjusted OR (95% CI)[1]
	Transient	Persistent		
Oncogenic HPV				
Vitamin A, (μgRAE)[2]				
Quartile 1	143	147	1.00	1.00
Quartile 2	157	116	0.72 (0.51–1.00)	0.77 (0.52–1.15)
Quartile 3	161	103	0.62 (0.44–0.87)	0.78 (0.49–1.24)
Quartile 4	159	92	0.56 (0.40–0.79)	0.73 (0.42–1.25)
Folate equivalents (μg)[3]				
Quartile 1	157	158	1.00	1.00
Quartile 2	143	102	0.71 (0.51–0.99)	0.96 (0.64–1.43)
Quartile 3	165	122	0.74 (0.53–1.01)	1.24(0.80–1.92)
Quartile 4	155	76	0.49 (0.34–0.69)	0.95 (0.54–1.69)
Lycopene (μg)[4]				
Quartile 1	143	93	1.00	1.00
Quartile 2	165	106	0.99 (0.69–1.41)	0.96 (0.64–1.44)
Quartile 3	154	109	1.09 (0.76–1.56)	1.08 (0.71–1.64)
Quartile 4	158	150	1.46(1.03–2.06)	1.33 (0.87–2.01)
Vitamin B12 (μg)[5]				
Quartile 1	190	159	1.00	1.00
Quartile 2	147	123	1.00 (0.73–1.37)	0.94 (0.65–1.37)
Quartile 3	154	92	0.71 (0.51–0.99)	0.72 (0.47–1.09)
Quartile 4	129	84	0.78 (0.55–1.10)	0.98 (0.61–1.58)
Retinol (μg)[6]				
Quartile 1	148	128	1.00	1.00
Quartile 2	160	115	0.83 (0.59–1.16)	0.76 (0.52–1.12)
Quartile 3	150	117	0.90 (0.64–1.26)	0.86 (0.58–1.28)
Quartile 4	162	98	0.70 (0.49–0.99)	0.81 (0.53–1.23)

Nutrient	Infection no.		Crude OR (95% CI)	Adjusted OR (95% CI)[1]
	Transient	Persistent		
Vitamin E (mg)[7]				
Quartile 1	153	98	1.00	1.00
Quartile 2	137	100	1.14(0.79–1.64)	1.01 (0.73–1.65)
Quartile 3	174	130	1.17 (0.83–1.64)	1.14(0.76–1.70)
Quartile 4	156	130	1.30 (0.92–1.83)	1.29 (0.82–2.02)
Nononcogenic HPV				
Vitamin B12 (μg)[8]				
Quartile 1	133	216	1.00	1.00
Quartile 2	108	162	0.92 (0.67–1.28)	0.77 (0.54–1.10)
Quartile 3	100	146	0.90 (0.64–1.25)	0.70 (0.49–1.02)
Quartile 4	101	112	0.68 (0.48–0.96)	0.55 (0.38–0.81)

NOTE. CI, confidence interval; OR, odds ratio.

[1]For oncogenic HPV: Logistic-regression model adjusted simultaneously for energy intake (kcal), age, marital status, smoking, no. of female sex partners in lifetime, and HPV status at enrollment. For nononcogenic HPV: Logistic-regression model adjusted simultaneously for energy intake (kcal), physical activity, age, marital status and HPV status at enrollment.

[2]$p = 0.250$, test for trend.

[3]$p = 0.821$, test for trend.

[4]$p = 0.137$, test for trend.

[5]$P = 0.703$, test for trend.

[6]$p = 0.471$, test for trend.

[7]$p = 0.319$, test for trend.

[8]$p = 0.003$, test for trend.