# BURDEN OF GENITAL WARTS IN COLOMBIA: AN OBSERVATIONAL STUDY

# CARGA DAS VERRUGAS GENITAIS NA COLÔMBIA: UM ESTUDO OBSERVACIONAL

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#### ABSTRACT

**Introduction:** Genital warts are benign lesions caused by sexual transmission of human papillomavirus types 6 and 11, with significant impact on healthcare resource use and patients' quality of life. **Objective:** To describe the epidemiology of genital warts in adults visiting a physician office for any reason, physician practice patterns, and healthcare resource use and costs in Colombia. **Methods:** Participants were a convenience sample of 53 physicians in 5 specialties: primary care (15), gynecology (24), urology (12), proctology (1), and dermatology (1). Physicians completed a survey and daily log of all patients 18-60 years old seen over 10 days in their practices in 2016-2017. The physician survey recorded genital warts consultation and management patterns. The daily log recorded patient demographic information and genital warts diagnosis. **Results:** Among 6,393 patients logged by physicians, the genital warts prevalence was 2.03% (95%CI 1.69–2.38) and incidence 1.30% (95%CI 1.02–1.58). Primary care physicians referred most of their genital warts cases for treatment (female: mean 63.3%, SD=44.8; male: mean 58.3%, SD=43.8). Treatment of non-resistant episodes (<6-month duration) lasted an average of 37.4 days (SD=29.4) and required an average of 4.0 (SD=1.9) office visits for females and 3.0 (SD=1.7) for males. The overall mean cost of an episode of care was USD558.13 (SD=507.30). **Conclusion:** Genital warts cases reported by most participant physicians were mainly direct-consult, but patients were typically treated by specialists. Much of the genital warts health care utilization and costs reported could be prevented by immunization with the quadrivalent or nonavalent HPV vaccine.

Keywords: papillomavirus infections; condylomata acuminata; epidemiology; health care costs; cost of illness.

#### RESUMO

**Introdução:** As verrugas genitais são lesões benignas, de transmissão sexual, causadas pelo papilomavírus humano tipos 6 e 11 e que causam impacto significativo no uso de recursos de saúde e na qualidade de vida dos pacientes. **Objetivo:** Descrever a epidemiologia das verrugas genitais em adultos que buscaram atendimento médico ambulatorial por qualquer motivo, incluindo padrões de prática médica, uso de recursos de saúde e custos na Colômbia. **Métodos:** foi utilizada uma amostra de conveniência composta por 53 médicos em 5 especialidades: clínico geral (15), ginecologia (24), urologia (12), proctologia (1) e dermatologia (1). Os médicos completaram um questionário e registros diários de todos os pacientes com idade entre 18 e 60 anos atendidos durante 10 dias em seus consultórios em 2016-2017. O questionário registrou os padrões de prática médica e de tratamento de verrugas genitais. Os registros diários continham informações demográficas do paciente e o diagnóstico de verrugas genitais. **Resultados:** Entre 6.393 atendimentos médicos, a prevalência das verrugas genitais para tratamento (mulheres: média de 63,3%, DP=44,8; homens: média de 58,3%, DP=43,8). O tratamento dos casos não-persistentes (<6 meses de duração) durou em média 37,4 dias (DP=29,4) e requereu uma média de 4,0 (DP=1,9) consultas para mulheres e 3,0 (DP=1,7) para homens. O custo médio geral do tratamento foi de US\$ 558,13 (SD=507,30). **Conclusão:** Os casos de verrugas genitais relatados pela maioria dos médicos participantes derivaram-se principalmente de atendimentos primários e os pacientes foram tratados geralmente por especialistas. Grande parte da utilização de recursos e custos relacionados a verrugas genitais ser evitada pela imunização com a vacina papilomavírus humano 4-valente ou 9-valente.

Palavras-chave: infecções por papillomavirus; condiloma acuminado; epidemiologia; custos de cuidados de saúde; efeitos psicossociais da doença.

# INTRODUCTION

Human papillomavirus (HPV) causes 29.5% of infection-based cancers, including cervical and other cancers, as well as the majority of genital warts (GW)<sup>(1,2)</sup>. GW are benign skin lesions caused primarily by non-oncogenic HPV types 6 and 11<sup>(3)</sup>. Diagnosis is typically made through clinical dermatologic examination and treatment is carried out primarily with topical medications — podophyllin, podophyllotoxin, imiquimod, etc. — or via chemical cauterization<sup>(4)</sup>. Invasive treatment procedures include abrasion, cryotherapy, electrosurgery, laser therapy, and operative surgery<sup>(2)</sup>. The main limitation of current treatments is the high recurrence rate after remission<sup>(5)</sup>.

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<sup>4</sup>Merck & Co., Inc. – Kenilworth (NJ), United States of America. <sup>5</sup>Merck Sharp & Dohme (IA) LLC – Carolina, Puerto Rico. The global prevalence of HPV infection is estimated to be 11.7%<sup>(6)</sup>. Higher rates of HPV infection prevalence have been reported in South America (15.3%), including in Colombia (14.8%) <sup>(7,8)</sup>. GW is an issue for public health systems in Latin America, and the incidence has been consistently increasing in several countries for the last decade<sup>(9)</sup>. While over half of GW resolve spontaneously within a year<sup>(10)</sup>, the other half often requires repeated visits to physicians and referrals to specialists, resulting in additional costs for affected individuals<sup>(11)</sup>. GW can also cause psychological distress for patients<sup>(10,12)</sup>.

In Colombia, there is little published information on the epidemiology and clinical management of GW.

# **OBJECTIVE**

The objective of this study was to describe the prevalence and incidence of GW among women and men between the ages of 18 to 60 years attending to a physician's office for any reason, physician practice patterns, and GW-related health care resource use and costs in Colombia.

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# METHODS

#### Study design

This was an observational, cross-sectional, multicenter study designed to estimate the prevalence and incidence of GW in medical practices, and GW-related health care resource use and costs among adults in Colombia. Physicians who routinely diagnose and/ or treat patients with GW completed a daily log and a survey. In the daily log, physicians recorded the age, gender, and GW status of each patient aged 18-60 years seen in their practice over 10 consecutive workdays. The survey collected information on consultation and management patterns of patients with GW in medical practices.

Before enrollment, the study was approved by the institutional review board or ethics committee at each participating center. Patients' informed consent was not required.

#### Study sample

We recruited a convenience sample of physicians from specialties that normally encounter or manage GW cases: primary care physicians, gynecologists, urologists, proctologists, and dermatologists. Eligible physicians were those who had practiced medicine for at least 6 months, treated or diagnosed GW, and saw at least 75 patients in their office or outpatient clinic (for any reason) in a typical week.

## Definitions

GW cases were defined as gray or flesh-colored growths found in the genital or anal regions, caused by HPV. Genital ulcers caused by herpes virus are not considered GW and thus were not included in this study. Patients should have had visible lesions - an HPVpositive DNA test alone was not sufficient, but biopsy results were not required. A new case (also referred to as a non-resistant case) of GW was defined as a case diagnosed in a patient who had never had a previous GW episode or had not had a GW episode in the past 12 months. New cases of GW included patients who came for follow-up visits for a new episode of GW that had lasted 6 months or less. An existing case was defined as any case of GW not meeting the definition of a new case. Existing cases were classified as recurrent, resistant, or both. A recurrent case was defined as a case of GW where previous episodes of GW (within the last 12 months) had been resolved, with or without treatment. A resistant case was defined as a case of GW that had lasted longer than 6 months, despite treatment.

Prevalence was defined as the number of new and existing GW cases divided by the number of all patients logged during the 10 consecutive workdays. Incidence of GW was defined as the number of new GW cases divided by the number of all patients without an existing case of GW seen during the 10 consecutive workdays. An episode of care consisted of all clinically related services, including physician visits and inpatient and at-home treatments, for one patient from the onset of GW symptoms until treatment was completed. A referral occurred when a physician saw a patient at the request of another physician (same or different specialty), or requested that a patient seek care from another physician.

#### Study instruments and procedures

# Physician's daily log

Physicians were required to record a daily log of all patients aged 18–60 years seen over 10 consecutive workdays. For each patient seen, physicians recorded the patient's age, gender, and current diagnosis of GW (yes or no). If the patient did not have GW, no additional data was collected for that patient. For patients being seen for or diagnosed with GW at the clinic visit, physicians recorded whether the case was new or existing, and categorized the duration of the current episode as  $\leq 6$  months with or without treatment, >6 months without treatment, or >6 months despite treatment. Physicians were instructed to keep to their regular patterns of practice and to record information only for patients seen during the current visit. Completing the physician's log was expected to take no more than 5–10 minutes daily.

#### Physician survey

After finishing the daily log, physicians completed a survey recording their demographic information, specialty, and information on their main practice setting type, affiliation, and geographic location. In addition, the survey queried the gender of patients aged 18–60 years seen in a typical working week, patterns of consultation, treatment, and referral of their GW patients, and reasons for referring GW cases. The survey was self-administered and was expected to take no more than 30 minutes to complete.

#### Data analysis

A descriptive analysis was performed. All daily logs with 7 or more completed workdays were included in the analysis. The 10-day prevalence and incidence of GW were calculated using data from the daily log and expressed as a percentage of patients seen by all physicians combined, by physician specialty, and by patient gender and age group, with confidence intervals calculated by the Clopper-Pearson method. A weighted 10-day prevalence and incidence of all cases seen by physicians in Colombia were calculated by correcting the proportions of physician specialties in the survey to match those nationwide. The weights used were: primary care physicians 0.37, gynecologists 0.24, urologists 0.24, proctologists 0.05, and dermatologists 0.10.

Results of the physician survey were reported for all physicians combined, and by individual medical specialty. Categories of physician characteristics were summarized as percentages of physicians. The percentage of typical patients by gender was reported as mean and standard deviation (SD). Patterns of consultation, referral, diagnosis, and treatment of GW cases were reported as categorical data and were summarized as the median and range of the percentage of patients reported by all physicians combined and by medical specialty. Types of health care resource use were defined as continuous variables and reported as a median and range. Medical services and drug treatments were converted into costs using published, agreedupon price schedules. The cost of an episode of care was the sum of the product of the cost of each category of care (treatment or procedure) times its frequency. Costs of care for non-resistant and resistant cases were estimated for 6- and 12-month periods, respectively. All costs are presented in 2018 Colombian Pesos, and converted to United States Dollars [USD, conversion at the time of analysis was 1 Colombian Peso = .00035 USD]. Analyses were conducted using STATA version 8.2 (StataCorp. 2003. Stata Statistical Software: Release 8. College Station, TX: StataCorp LP).

# RESULTS

## Physicians

A total of 164 physicians were invited to participate in the study: 46 declined the invitation, 14 were found to be ineligible, and 104 agreed to participate. Of the 104 physicians, 53 completed the daily log and the survey: 15 primary care physicians, 24 gynecologists, 12 urologists, 1 proctologist, and 1 dermatologist. Physicians were predominantly male (57%) and 30–50 years old (64%; **Table 1**). The main practice setting was a stand-alone clinic for 57% of physicians and a hospital-based outpatient facility for 42% (**Table 1**). Almost half (41.5%) of physicians' health care facilities were located in a practice service area with >500,000 individuals (data not shown). Patients seen in a normal work week were typically female for primary care physicians (mean, 67%) and gynecologists (100%), but male for urologists (73%); the mean for all physicians was 73% female (**Table 1**).

# Patients

A total of 6,393 patients were seen by all physicians over a 10-day period between September 2016 and April 2017, as recorded in the daily log. Patients were predominantly female — 76.2% overall, but 100.0% for gynecologists, and 26.9% for urologists — and of mean and median age 38.2 and 37.0 years, respectively.

## Prevalence of GW

Of the 6,393 patients, 130 had a GW diagnosis. The overall 10-day prevalence was 2.03% (95%CI 1.69–2.38): 2.01% (95%CI 1.62–2.41) among females and 2.04% (95%CI, 1.33–2.76) among males. The prevalence was lower among patients seen by primary care physicians (0.21%, 95%CI 0.04–0.61) and higher for patients seen by dermatologists (17.28%, 95%CI 9.78–27.30; **Figure 1A**). The prevalence of GW cases was highest in the 18–24 age group (**Figure 1B**). Weighted prevalence of cases expected to be seen by physicians in Colombia was 2.55% (95%CI 2.17–2.94).

## Incidence of GW

Of the 6,393 patients seen over 10 days without an existing diagnosis of GW, there were 83 new cases of GW, for a 10-day incidence of 1.30% (95%CI, 1.02–1.58): 1.29% (95%CI, 0.98–1.61) for females and 1.32% (95%CI 0.74–1.89) for males. The incidence was

Table 1 – Health care use for new (non-resistant) and resistant genital wart episodes, by physician specialty.

	Total		Primary care		Gynecologists		Urologists		Proctologist		Dermatologist	
	Male (N=29)	Female (N=53)	Male (N=15)	Female (N=15)	Male (N=0)	Female (N=24)	Male (N=12)	Female (N=12)	Male (N=1)	Female (N=1)	Male (N=1)	Female (N=1)
Non-resistant cases												
Treatment duration (days)												
Mean (SD)	34.4 (27.9)	37.4 (29.4)	38.6 (29.6)	41.9 (34.6)	-	36.3 (24.2)	25.8 (21.4)	24.1 (18.2)	20.0 (-)	20.0 (-)	90.0 (-)	120.0 (-)
Median (range)	30.0 (1–90)	30.0 (1–120)	30.0 (7–90)	30.0 (7–120)	-	30.0 (8–90)	25.0 (1–70)	25.0 (1–60)	20.0 (-)	20.0 (-)	90.0 (-)	120.0 (-)
Office visits												
Mean (SD)	3.0 (1.7)	4.0 (1.9)	3.4 (2.2)	4.1 (2.3)	-	4.3 (2.0)	2.6 (1.1)	2.9 (0.4)	2.0 (-)	2.0 (-)	4.0 (-)	5.0 (-)
Median (range)	3.0 (0–10)	3.0 (0–10)	3.0 (0–10)	4.0 (0–10)	-	4.0 (2–10)	3.0 (1–5)	3.0 (2–3)	2.0 (-)	2.0 (-)	4.0 (-)	5.0 (-)
Hospital and/or ED visits												
Mean (SD)	0.3 (0.7)	0.4 (0.6)	0.1 (0.4)	0.3 (0.5)	-	0.3 (0.5)	0.5 (0.9)	0.8 (1.0)	0.0 (-)	0.0 (-)	0.0 (-)	0.0 (-)
Median (range)	0.0 (0–3)	0.0 (0–3)	0.0 (0–1)	0.0 (0–1)	-	0.0 (0–1)	0.0 (0–3)	0.5 (0–3)	0.0 (-)	0.0 (-)	0.0 (-)	0.0 (-)
Recurrences*												
Mean (SD)	1.5 (0.8)	1.5 (0.9)	1.3 (0.7)	1.4 (0.8)	-	1.6 (1.0)	1.8 (0.8)	1.4 (0.7)	1.0 (-)	1.0 (-)	1.0 (-)	1.0 (-)
Median (range)	2.0 (0–3)	1.0 (0–5)	1.0 (0–2)	1.0 (0–3)	-	1.5 (0–5)	2.0 (0–3)	1.5 (0–2)	1.0 (-)	1.0 (-)	1.0 (-)	1.0 (-)
Resistant cases												
Office visits												
Mean (SD)	2.7 (2.1)	3.7 (2.7)	1.7 (1.2)	1.9 (1.4)	-	4.8 (2.9)	3.5 (2.3)	3.4 (2.7)	4.0 (-)	4.0 (-)	7.0 (-)	6.0 (-)
Median (range)	2.5 (0–8)	3.0 (0–12)	1.0 (0–4)	1.0 (0–4)	-	4.0 (0–12)	3.0 (0–8)	3.0 (0–8)	4.0 (-)	4.0 (-)	7.0 (-)	6.0 (-)

ED: emergency department; SD: standard deviation; \*number of recurrences per year for patients with recurrent episodes.

lower among primary care physicians (0.14%, 95%CI 0.02–0.50) and higher for patients seen by dermatologists (3.70%, 95%CI 0.00–7.82; **Figure 2A**). The incidence of GW cases was higher in the 18–24 age group (**Figure 2B**). The weighted incidence of cases expected to be seen by physicians in Colombia was 1.13% (95%CI 0.87–1.39).

## **Physician practice patterns**

#### Consultation patterns

Physicians reported that more of their female (mean 66.5%, SD=36.9) and male GW patients (mean 67.0%, SD=40) were direct consultations rather than referrals — though about half of patients seen by urologists were referrals (female: mean 39.2%, SD=10.0;

male: mean 50.8%, SD=32.8). Primary care physicians referred most of their GW cases for treatment (female: mean 63.3%, SD=44.8; male: mean 58.3%, SD=43.8) whereas gynecologists and urologists treated most of their GW patients themselves — a mean of 79.8% (SD=29.2) of female cases (gynecologists) and 97.0% (SD=6.2) of male cases (urologists).

#### Diagnostic techniques

Physicians used a basic physical or visual examination to diagnose almost all new and recurrent non-resistant GW cases for both males (new: mean 95.6%, SD=18.5; recurrent: mean 95.3%, SD=19.5) and females (new: mean 91.7%, SD=22; recurrent: 92.1%, SD=21.3) patients. Gynecologists also used colposcopy for an mean of 39.0% (SD=45.5) of new and 50.0% (SD=46.2) of recurrent



DERM: dermatologist; GYN: gynecologist; PCP: primary care physician; PROCT: proctologist; URO: urologist. Figure 1 – 10-day prevalence of GW in physicians' offices by (A) physician specialty and (B) patient age group.

(female) patients, while urologists also used acetic acid, biopsy, and histological exam to diagnose a mean of 30.4% (SD=37.5), 33.1% (SD=34.8), and 35.0% (35.7), respectively, of new male cases and 33.6% (SD=37.4), 26.3% (SD=23.3), and 35.4% (SD=26.9) of their recurrent male patients, respectively.

## In-office procedures

None of the primary care physicians reported using any in-office treatments or procedures for new or resistant GW cases. Gynecologists used cryotherapy for a few of their new GW cases (mean 6.0%, SD=20.3) but used surgical removal in an average of 30.0% (SD=38.7) of their resistant GW cases. Urologists used electrosurgery/electrocautery for an average of 63.1% (SD=31.4) of their new male GW cases and in 44.5% (SD=45.9) of resistant male cases, and surgical removal in an operating room for an average of 34.5% (SD=34.8) of their new male cases and 42.5% (SD=44.3) of resistant male cases.

#### Treatment with topical medications

Primary care physicians typically treated new (non-resistant) and resistant GW cases with at-home topical imiquimod (new: mean of 20.7%; SD=39.7) in males and females (21.0%; SD=39.5), and resistant: mean of 7.1% (SD=26.7) in males and females of GW cases. Gynecologists treated an average of 51.5% (40.6) of new female GW cases and 39.1% (SD=39.8) of in-office resistant cases with tri- or bi-chloroacetic acid and an average of 35.2% (SD=41.6) of new cases with in-office topical imiquimod; gynecologists treated



DERM: dermatologist; GYN: gynecologist; PCP: primary care physician; PROCT: proctologist; URO: urologist. Figure 2 – 10-day prevalence of GW by (A) physician specialty and (B) patient age group.

an average of 45.4% (SD=42.9) of their new and 42.7% (SD=44.2) of resistant female GW cases with at-home imiquimod. Urologists treated an average of 30.9% (SD=34.4) of their new male GW cases with in-office topical imiquimod and an average of 24.5% (SD=31.7) with in-office topical podophyllin lotion or gel; topical imiquimod and topical podophyllin lotion or gel; topical imiquimod and verage of 30.9% (SD=29.4) and 29.5% (SD=32.2) of urologists' new male GW cases, respectively. Urologists typically did not treat resistant cases with in-office topical imiquimod (mean 7.7%, SD=11.2) but provided at-home topical imiquimod to an average of 19.1% (SD=31.4) of resistant male cases.

# Health care use and costs

## Health care use

For new non-resistant episodes of GW, the duration of treatment was on average 37.4 days (SD=29.4 days) for females and 34.4 days (SD=27.9 days) for males. The number of office visits was an average of 4.0 (1.9) for females and 3.0 (SD=1.7) for males, and the number of hospital and/or ED visits ranged from 0 to 3 for female and male patients (**Table 1**). The median number of office visits per year for a resistant case was, on average, 3.7 for female patients (SD=2.7) and 2.7 (SD=2.1) for male ones (**Table 1**).

#### Cost of GW

The most expensive treatment was at-home topical medications, costing USD169.75 (SD=149.96) and USD 205.35 (SD=252.15) per treatment of non-resistant and resistant GW, respectively. The mean total cost of an episode of care for GW (non-resistant or resistant) was USD 558.13 (SD=507.30).

# DISCUSSION

Previous studies have shown that HPV infection is highly prevalent in cervical samples from women in Colombia<sup>(7,13-15)</sup>. In a population-based survey of 1,859 women aged 18–85 years with normal cervical cytology conducted in Colombia, the prevalence of HPV DNA (any type) was higher among women under the age of 20 (26.1%) followed by women aged 20–24 (22.7%) and women aged 30–34 (16.6%)<sup>(7)</sup>. HPV types 6 and 11 were detected in 0.4% and 1.4–5.5% of cervical samples, respectively<sup>(7)</sup>, which account for the majority of GW cases<sup>(16)</sup>. In a single-site study conducted in Colombia from 2009–2010, HPV DNA was detected in approximately 90% of biopsy-confirmed GW cases, with approximately 93 and 86% of the HPV genotypes being types 6 and 11 in women and men respectively<sup>(17)</sup>.

The prevalence and incidence results from this study are similar to those in other countries. The 10-day unweighted prevalence and incidence of GW cases seen by physicians in Colombia was 2.03 and 1.30%, respectively; weighting by specialty, the prevalence increased to 2.55% and the incidence decreased to 1.13%. The prevalence reported here is within the range of values reported in population-based studies conducted in 2001–2012 in countries worldwide,

where the prevalence of GW based on genital examinations ranged from 0.2 to 5.1%, with a median of  $3.2\%^{(2)}$ . The incidence is higher than that reported in studies worldwide, where the overall annual incidence ranged from 160 per 100,000 to 289 per 100,000, with a median of 194.5 per 100,000<sup>(2)</sup>. However, these results are similar to the results seen in other South American countries. Incidence rates of 5.6 and 1.8% were reported during the first and second years, respectively, of sexual activity in a cohort of girls aged 11–19 years old seen at a gynecology clinic in Brazil in 1993–2006<sup>(18)</sup>. In the cohort of men from Brazil, Mexico, and the United States (Florida) included in the prospective observational HPV-in-Men (HIM) study, 4.5% developed GW during a median of 18 months of follow-up<sup>(19)</sup>.

The majority of GW patients seen by physicians - with the exception of urologists - were direct-consultations rather than referrals. Primary care physicians referred most of their GW cases for treatment. Similarly, in other countries, GW cases are managed primarily by specialists. In a study carried out in England, only 5% of GW cases were managed by a general practitioner, 22% were seen by a general practitioner before being referred to a genitourinary medicine clinic, and most GW cases (73%) were seen only in genitourinary medicine clinics(20). Studies in other European countries have been restricted to specialists in gynecology, dermatology, and urology<sup>(21,22)</sup>. In the study set in Spain, only a minority (17%) of GW cases were referred, males most frequently to a general practitioner and females to a gynecologist<sup>(21)</sup>. Other features of the management of GW, including diagnostic techniques, in-office procedures, and at-home medications in Colombia, appear to be similar to those in European countries<sup>(21,22)</sup>. In the current study, physicians relied largely on a basic physical or visual examination to diagnose both new and recurrent GW cases. The most commonly utilized in-office procedures included electrosurgery/electrocautery and surgical removal, and the most commonly prescribed at-home medications were imiquimod and podphyllin lotion or gel. Similarly, electrosurgery was the most frequently utilized in-office procedure in Germany and the most frequently self-administered medications were imiquimod, podophyllotoxin solution, and podophyllotoxin cream<sup>(22)</sup>. In Spain, the majority of patients were prescribed imiquimod or podophyllotoxin<sup>(21)</sup>.

Diagnosis and treatment of GW were associated with a mean total cost of USD 558.13 (SD=507.30) per episode. Costs associated with GW have been assessed in several other countries, but the socioeconomic situations and healthcare systems in these countries are not comparable to those in Colombia. In Mexico, a study using national data reported by health care professionals who care for patients with GW was performed to estimate the health care burden of  $GW^{(23)}$ . The study estimated the cost to treat a single GW episode to be USD 342.06 USD (USD 290.27–USD 435.25), being slightly higher in Colombia.

Two vaccines have been approved by the U.S. Food and Drug Administration that prevent infection with HPV types 6 and 11, the quadrivalent and nonavalent HPV vaccines<sup>(24-26)</sup>. In 2012, the Ministry of Health and the National Institute of Health of Colombia implemented free vaccination against HPV with the quadrivalent vaccine using a three-dose vaccination schedule in school-aged girls from 9 to 17 years old<sup>(27)</sup>, and was updated in 2018 to a two-dose vaccination schedule for girls from 9 to 18 years old. Despite the HPV vaccine's

inclusion in the national immunization schedule, there are potential barriers to the success of the HPV vaccination program<sup>(28)</sup>. First, parents may have concerns that vaccination increases adolescent sexual activity and the risk of sexually transmitted diseases<sup>(29)</sup>. However, in a survey of 1,436 young women conducted in Colombia in 2011–12, sexual risk behaviors (initiation of sexual intercourse, number of lifetime sexual partners, use of alcohol or drugs at last intercourse, condom use, contraception use, and pap smear screening) were not associated with HPV vaccination after adjustment for risk perception, age, educational level, and HPV knowledge<sup>(29)</sup>. Second, a lack of awareness of the HPV vaccine has been reported in Colombia. In a 2009-2010 cross-sectional study of adults with GW in Colombia, 26.4% of males and 48.4% of females were aware of the HPV vaccine<sup>(30)</sup>. Similarly, among a nationally representative sample of 53,521 females aged 13-49 surveyed in the Colombian 2010 National Demographic and Health Survey, only 27% had heard about HPV vaccination<sup>(31)</sup>. Results from the survey indicate that living in rural areas decreased the probability of having heard about HPV vaccination<sup>(31)</sup>.

#### Strengths

This study provides valuable insight on the prevalence and incidence of GW, physician practice patterns, and GW-related health care resource use and costs in Colombia, where little published information is available. The results of study are in line with those in previously published literature, as discussed previously.

#### Limitations

This study has several limitations. The estimates for incidence and prevalence may not be generalizable to individuals with GW who do not seek medical care at physician offices. In addition, GW patients who did not seek treatment were not included in the study, which may underestimate the true prevalence in Colombia. In addition, this study included a convenience sample of physicians rather than a random sample, consisting of physicians who treat and/or diagnose GW and who were willing to participate in the study. Thirty-two percent of the physicians invited participated in the study, including only one proctologist and one dermatologist. This may have resulted in some physicians seeing more GW patients than other physicians of the same specialty, which may overestimate GW prevalence when data for each specialty office are projected at the national level. Additionally, it is possible that some existing cases of GW may have been misclassified as new cases if the patient was not diagnosed with GW within the first six months.

# CONCLUSION

Colombia has a high burden of genital warts, particularly in males under 40 years of age. This study illustrates that GW requires multiple physician visits to treat, are typically treated by specialists, and utilize significant healthcare resources, which is compounded by the frequent recurrence of the disease. Much of the GW health care utilization and costs reported in the current study could be avoided by implementing strategies of education and prevention, in addition to immunization with the quadrivalent or nonavalent HPV vaccine.

# Participation of each author

Joaquin Gustavo Luna Rios, Monica Rojas, Glorian Persaud Yen, Alexandra Altland, Miguel Cashat, Homero Antonio Monsanto and Claudia Beltran contributed to the study design, manuscript preparation, and review.

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#### **Conflict of interests**

Joaquin Gustavo Luna Rios received research support from Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA. Monica Rojas and Claudia Beltran are employees of MSD, Colombia. Miguel Cashat is an employee of MSD, Mexico. Glorian Persaud Yen and Alexandra Altland are employees of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ USA. Homero Antonio Monsanto is an employee of MSD, Puerto Rico.

# REFERENCES

- Plummer M, de Martel C, Vignat J, Ferlay J, Bray F, Franceschi S. Global burden of cancers attributable to infections in 2012: a synthetic analysis. Lancet Glob Health. 2016;4(9):e609-6. https://doi.org/10.1016/s2214-109x(16)30143-7
- Patel H, Wagner M, Singhal P, Kothari S. Systematic review of the incidence and prevalence of genital warts. BMC Infect Dis. 2013;13:39. https://doi.org/10.1186/1471-2334-13-39
- Tchernev G. Sexually transmitted papillomavirus infections: epidemiology pathogenesis, clinic, morphology, important differential diagnostic aspects, current diagnostic and treatment options. An Bras Dermatol. 2009;84(4):377-89. https://doi.org/10.1590/S0365-05962009000400009
- Kollipara R, Ekhlassi E, Downing C, Guidry J, Lee M, Tyring SK. Advancements in Pharmacotherapy for Noncancerous Manifestations of HPV. J Clin Med. 2015;4(5):832-46. https://doi.org/10.3390/jcm4050832
- Workowski KA, Bolan GA, Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep. 2015;64(RR-03):1-137.
- Clifford GM, Gallus S, Herrero R, Munoz N, Snijders PJF, Vaccarella S, et al. Worldwide distribution of human papillomavirus types in cytologically normal women in the International Agency for Research on Cancer HPV prevalence surveys: a pooled analysis. Lancet 2005;366:991–998.
- Molano M, Posso H, Weiderpass E, van den Brule AJC, Ronderos M, Franceschi S et al. Prevalence and determinants of HPV infection among Colombian women with normal cytology. *Br J Cancer* 2002;87(3):324–333.
- Perez G, Lazcano-Ponce E, Hernandez-Avila M, García PJ, Munoz N, Villa LL, et al. Safety, immunogenicity, and efficacy of quadrivalent human papillomavirus (types 6, 11, 16, 18) L1 virus-like-particle vaccine in Latin American women. *Int J Cancer*. Mar 15 2008;122(6):1311-1318.
- Koshiol JE, Laurent SA, Pimenta JM. Rate and predictors of new genital warts claims and genital warts-related healthcare utilization among privately insured patients in the United States. Sex Transm Dis. 2004;31(12):748-52. https://doi.org/10.1097/01.olq.0000145851.76025.ad
- Lopaschuk CC. New approach to managing genital warts. Can Fam Physician. 2013;59(7):731-6.
- Buenconsejo L, Kothari-Talwar S, Yee K, Kulkarni A, Lara N, Roset M, et al. Estimating the burden of illness related to genital warts in the Philippines: a nationally representative cross-sectional study. Infect Agent Cancer. 2019;14:26. https://doi.org/10.1186/s13027-019-0240-y

- 12. Clarke P, Ebel C, Catotti DN, Stewart S. The psychosocial impact of human papillomavirus infection: implications for health care providers. Int J STD AIDS. 1996;7(3):197-200. https://doi.org/10.1258/0956462961917618
- 13. Bedoya AM, Gaviria AM, Baena A, Borrero M, Duarte DF, Combita AL, et al. Age-specific seroprevalence of human papillomavirus 16, 18, 31, and 58 in women of a rural town of Colombia. Int J Gynecol Cancer. 2012;22:303-10.
- Camargo M, Soto-De Leon SC, Sanchez R, Perez-Prados A, Patarroyo ME, Patarroyo MA. Frequency of human papillomavirus infection, coinfection, and association with different risk factors in Colombia. Ann Epidemiol. 2011;21(3):204-13. https://doi.org/10.1016/j.annepidem.2010.11.003
- Murillo R, Molano M, Martinez G, Mejia JC, Gamboa O. HPV prevalence in Colombian women with cervical cancer: implications for vaccination in a developing country. Infect Dis Obstet Gynecol. 2009;2009:653598. https://doi.org/10.1155/2009/653598
- Garland SM, Kjaer SK, Muñoz N, Block SL, Brown DR, DiNubile MJ, et al. Impact and Effectiveness of the Quadrivalent Human Papillomavirus Vaccine: A Systematic Review of 10 Years of Real-world Experience. Clin Infect Dis. 2016;63(4):519-27. https://doi.org/10.1093/cid/ciw354
- Hernandez-Suarez G, Pineros M, Vargas JC, Orjuela L, Hernandez F, Peroza C, et al. Human papillomavirus genotypes in genital warts in Latin America: a cross-sectional study in Bogota, Colombia. Int J STD AIDS. 2013;24(7):567-72. https://doi.org/10.1177/0956462412474538
- Monteiro DL, Sodré DC, Russomano FB, Trajano AJ, Silva KS. Incidence of genital warts in adolescents and their association with cervical intraepithelial lesions. Eur J Obstet Gynecol Reprod Biol. 2013;168(1):80-2. https://doi.org/10.1016/j.ejogrb.2012.12.032
- Anic GM, Lee JH, Villa LL, Lazcano-Ponce E, Gage C, Silva RJC, et al. Risk factors for incident condyloma in a multinational cohort of men: the HIM study. J Infect Dis. 2012;205(5):789-93. https://doi. org/10.1093%2Finfdis%2Fjir851
- Desai S, Wetten S, Woodhall SC, Peters L, Hughes G, Soldan K. Genital warts and cost of care in England. Sex Transm Infect. 2011;87(6):464-8. https://dx.doi.org/10.1136%2Fsti.2010.048421
- Castellsagué X, Cohet C, Puig-Tintoré LM, Acebes LO, Salinas J, Martin MS, et al. Epidemiology and cost of treatment of genital warts in Spain. Eur J Public Health. 2009;19(1):106-10. https://doi.org/10.1093/eurpub/ ckn127
- Hillemanns P, Breugelmans JG, Gieseking F, Bénard S, Lamure E, Littlewood KJ, et al. Estimation of the incidence of genital warts and the cost of illness in Germany: a cross-sectional study. BMC Infect Dis. 2008;8(1):76. https://doi.org/10.1186/1471-2334-8-76

- Domenech-Viñolas M, León-Maldonado L, Ramírez-Palacios P, Flores YN, Granados-García V, Brown B, et al. Incidence, psychosocial burden, and economic impact of genital warts in Mexico. Salud Publica Mex. 2018;60(6):624-32. https://doi.org/10.21149/10008
- Villa LL. Overview of the clinical development and results of a quadrivalent HPV (types 6, 11, 16, 18) vaccine. Int J Infect Dis. 2007;11(Suppl. 2):S17-S25. https://doi.org/10.1016/S1201-9712(07)60017-4
- Giuliano AR, Palefsky JM, Goldstone S, Moreira Jr. ED, Penny ME, Aranda C, et al. Efficacy of quadrivalent HPV vaccine against HPV Infection and disease in males. N Engl J Med. 2011;364(5):401-11. https:// doi.org/10.1056/nejmoa0909537
- Muñoz N, Kjaer SK, Sigurdsson K, Iversen OE, Hernandez-Avila M, Wheeler CM, et al. Impact of human papillomavirus (HPV)-6/11/16/18 vaccine on all HPV-associated genital diseases in young women. *J Natl Cancer Inst.* Mar 03 2010;102(5):325-339.
- República de Colombia. Ministerio de Salud y Protección Social. Lineamientos Técnicos y operativos para la vacunación contra el Virus Del Papiloma Humano (VPH). Colombia: Ministerio de Salud y Protección Social; 2012.
- Castro C. Highlights from the first ecancer-Liga Colombiana contra el Cancer conference, 17-18November2016, Bogota, Colombia. Ecancermedicalscience. 2017;11:730. https://doi.org/10.3332/ecancer.2017.730
- Ruiz-Sternberg AM, Pinzón-Rondón AM. Risk perception and sexual behavior in HPV-vaccinated and unvaccinated young Colombian women. Int J Gynaecol Obstet. 2014;126(3):205-8. https://doi.org/10.1016/j.ijgo.2014.03.033
- Piñeros M, Hernández-Suárez G, Orjuela L, Vargas JC, Pérez G. HPV knowledge and impact of genital warts on self-esteem and sexual life in Colombian patients. BMC Public Health. 2013;13:272. https://doi. org/10.1186/1471-2458-13-272
- Bermedo-Carrasco S, Feng CX, Peña-Sánchez JN, Lepnurm R. Predictors of having heard about human papillomavirus vaccination: Critical aspects for cervical cancer prevention among Colombian women. Gac Sanit. 2015;29(2):112-7. https://doi.org/10.1016/j.gaceta.2014.09.005

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