

Sexual behavior, use of contraceptive methods and risk factors for HPV infections of students living in Central Italy: implications for vaccination strategies

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Key words

HPV • Vaccination • Risk factors • Sexual behaviour • Use of contraceptive methods

summary

The most frequent risk factors related to the infection/persistence of HPV in the population are an early start of sexual activity, the number of sexual partners, smoking, and the utilization of some contraceptive methods. In Italy, HPV vaccine is offered free of charge to all 12 year-old female adolescents, with a possible extension to other age groups according to Regional policies.

In order to value the suitability of the current HPV vaccination strategies in Italy, an epidemiological study on sexual habits in adolescents and young adults was organized. An anonymous questionnaire on sexual behavior and risk factors for HPV infection was administered to 2300 students aged 13-24 years attending secondary schools and universities in Tuscany during 2008-09. About 12% of the sample declared to be foreign citizen.

The results highlight the early start of sexual activity among young students. Particularly, more than half of the interviewed students declared to be already sexually active. The mean and the median age of the first sexual intercourse was 15.4 ± 1.4 years and 15

years (25th and 75th percentiles = 14-16), respectively. More than 77% of students at age 16 years declared they already had the first sexual intercourse, compared with 0.3% of those < 12 years. Generally, females aged 13-16-years, if sexually active, had sexual contacts with a single partner.

Most students declared to know common contraceptive methods (male condom and contraceptive pill). However, only half of them declared a regular use of male condom. These data confirm the importance of vaccination against HPV for young females before their sexual debut. In addition, the current multi-cohort strategy of HPV vaccination in Tuscany (free of charge in the age range 12-16 years) allows also to catch up those girls that have not yet had their first sexual experiences before 16 years (21.5% according to our study) but also to those girls already sexually active, who very rarely are already infected by all vaccine types at 16 years. Our results also show the importance of sexual health education and of promotion of correct behaviours in schools.

Introduction

The *Human Papillomavirus* (HPV) is generally spread by sexual contacts [1]. The most frequent risk factors correlated with the infection and persistence of HPV in the population are the start of the first sexual contacts at young age, the number of sexual partners, the habit of smoking cigarettes and the utilization of some kinds of contraceptive methods [2, 3].

Two safe and effective vaccines against HPV infections, Gardasil® (Sanofi-Pasteur MSD) and Cervarix® (GlaxoSmithKline), were authorized and marketed in Europe and in Italy [4, 5]. Since January 11, 2007, the Italian Authorities decided to offer the HPV vaccine free of charge to all 12-year-old female adolescents, with a possible progressive extension of vaccination offer to a second cohort of women aged 25/26 years (at the time of the first cervical screening), and, according to availability of resources, to a third cohort of young women between 13 and 25 years [6, 7]. Furthermore, at the end of 2007, each Italian Region agreed to issue specific directives on implementation of vaccination strategies and, during 2008, all Italian Regions organized a vac-

ination program against HPV for all 12 years-old girls [8, 9]. However, in the absence of a unique national recommendation, every Italian Region progressively adopted different strategies of vaccination for additional age groups of females (13-26 years) [9].

The Tuscan Regional Authorities, in addition to the administration of HPV vaccine to 12 years-old girls, introduced active and free of charge vaccination of 16 year-old girls, while 13-15 year-old girls are free to opt for immediate immunization or to wait for the active call at 16 years. No co-payment policy was approved in the Region. Similar extensions of free-of-charge vaccination were deliberated by some other Regions (Basilicata, Piedmont, Valle d'Aosta) [10, 11]. On the other hand, other Regions only decided for the possibility of co-payment for some additional age groups.

An epidemiological study was therefore organized in order to value the suitability of the different vaccination policies in Italy. The presence of previous risk factors for HPV infection in the young population aged 13-24 years was analyzed. Important knowledge is expected from this study in order to provide indications for an op-

timization and, possibly, harmonization of the vaccination strategy at the national level.

Materials and methods

A self-administered questionnaire was designed in order to study the sexual behavior and risk factors for HPV infection in Tuscan students attending the University of Florence (first year students) [12] and 6 secondary schools in Florence and Arezzo. The study population included students between 13 and 24 years old. Parental consent to take part to the enquiry was asked for all participants under the age of 18 years.

After a short presentation on the objectives of this study and on HPV transmission routes (about 30 minutes) by public health physicians who remained available for further questions during questionnaire filling, questionnaires were distributed and anonymously self-filled by students. The questionnaire included 30 closed questions on demographic data of students, family-social status, sexual behaviours (age at the first sexual intercourse, number of sexual partners, known and used contraception methods), reproductive history, smoking habits, previous sexual diseases. The questionnaire was anonymous in order to encourage openness and sincerity in the answers on sensitive topics heavily impacting on personal privacy. Questionnaire data were inputted in a specifically created database (Excel 2010, Microsoft Inc.). Statistical analysis was performed by means of Excel software.

Results

STUDY POPULATION

The survey was carried out from May 2008 to May 2009 and involved 2300 Tuscan students in the age range 13-24 years (1692 females, 73.6%; 594 males, 25.8%; 14 without declared gender, 0.6%). The subjects included in the sample represented 5.3% of people of the same age cohorts living in Florence and Arezzo. The study population was stratified by age group and gender (Tab. I). Considering all students irrespective of gender, the mean age \pm S.D. was 16.6 ± 1.7 years, with a median age

of 16 years. The mean age \pm S.D. was 16.5 ± 1.7 years for females (median: 16 years) and 16.7 ± 1.8 years for males (median: 17 years). About 11.7% (268/2300) of the study population declared to be foreign: 134 students were non-Italian Europeans (Albanians and Romanians were particularly represented), 74 were Asian (mainly Chinese), 34 came from Central and Latin America and 24 from Africa (Moroccans were the most represented group), and 2 subjects did not specified the nationality. The majority (63.2%) of students judged their own health status to be good, 17.0% excellent, 15.8% fairly good, 1.7% bad and 0.7% did not answer. About 88% of students declared that the economic status of their family was satisfactory (8.0% deemed it very good, 31.7% good and 47.8% on average).

SEXUAL ACTIVITY

Table II shows the declared time of start of sexual activity, by age-group and gender: 2 students were excluded because sex and age were not declared. About 50% of all students (1152/2300) declared they already had the first sexual intercourse, 42.6% (982/2300) to be still virgin, and 166/2300 (7.2%) did not answer the question. In particular, 48.4% of females and 54.7% of males had already started their sexual activity. In addition, most of females and males students ≥ 17 -years (68.8% and 70.5%, respectively) declared to be already sexually active.

The mean age \pm S.D. of declared sexual debut was 15.4 ± 1.3 years for females and 15.3 ± 1.5 years for males (median age 15 years for females and males). Considering all students irrespective of gender, the mean age \pm S.D. of the first intercourse was 15.4 ± 1.4 years, with a median age of 15 years (25th and 75th percentiles = 14-16 years).

Figure 1 shows the age of sexual debut of all students by gender, while in Figure 2 we reported the cumulative probability of start of sexual activity by age group and by gender, using data on the age at first intercourse. It is noteworthy that 77.6% of students had already started their sexual activity at 16 years of age (78.5% of females and 75.4% of males), while only 0.1% of females and 0.9% of males are sexually active before 12 years of age (Fig. 2).

Tab. I. Study population stratified by age group and gender (2 students excluded because sex and age were not declared).

Age group (years)	Total number of students (%)	Female (%)	Male (%)	Gender not available (%)
13-16 (%)	1154 (50.2)	861 (50.9)	286 (48.1)	7 (50.0)
17-19 (%)	1024 (44.6)	754 (44.6)	265 (44.6)	5 (35.7)
20-24 (%)	109 (4.7)	69 (4.14)	40 (6.7)	0
Age not available (%)	11 (0.5)	8 (0.5)	3 (0.5)	2 (14.3)
Total number	2298	1692	594	14

Tab. II. Start of sexual activity of students, by age group and gender (2 students excluded because sex and age were not declared).

Sexual Activity	Total students	Females				Males				Gender not available	
		13-16	17-19	20-24	Age not available	13-16	17-19	20-24	Age not available	13-16	17-19
Yes (%) (95% CI)	1152 (50.1) (48.0-52.2)	251 (29.2) (26.1-32.2)	507 (67.2) (63.8-70.7)	59 (85.5) (77.0-94.0)	2 (25.0)	109 (38.1) (32.4-43.9)	180 (67.9) (62.2-73.7)	35 (87.5) (77.0-98.0)	1	3	5
No (%) (95% CI)	982 (42.6) (40.6-44.8)	551 (64.0) (60.7-67.3)	216 (28.6) (25.4-31.9)	6 (8.7) (1.9-15.5)	6 (75.0)	137 (47.9) (42.0-53.8)	59 (22.3) (17.2-27.4)	1 (2.5)	2	2	
Not Available (%) (95% CI)	166 (7.2) (6.1-8.3)	59(6.9) (5.1-8.6)	31 (4.1) (2.7-5.6)	4 (5.8) (0.2-11.4)	0	40 (14.0) (9.9-18.1)	26 (9.8) (6.2-13.5)	4 (10.0) (0.5-19.5)		2	
Total	2300	861	754	69	8	286	265	40	3	7	5

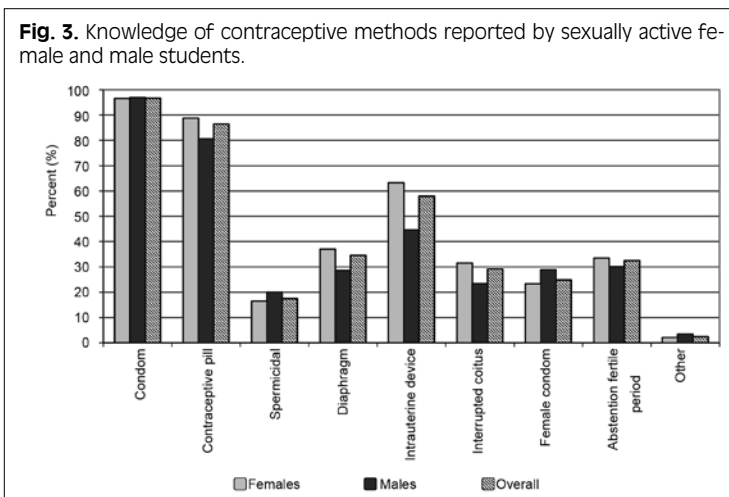
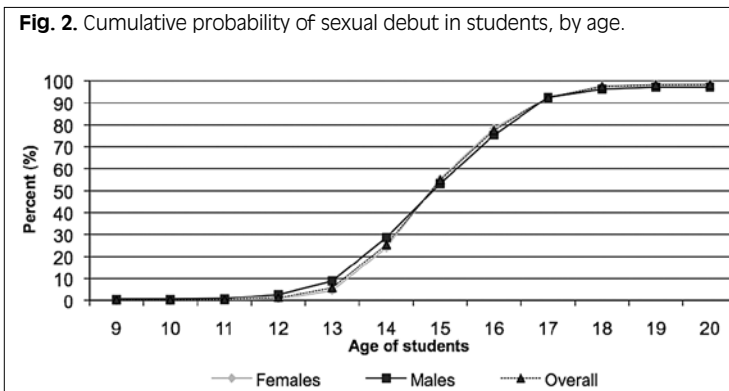
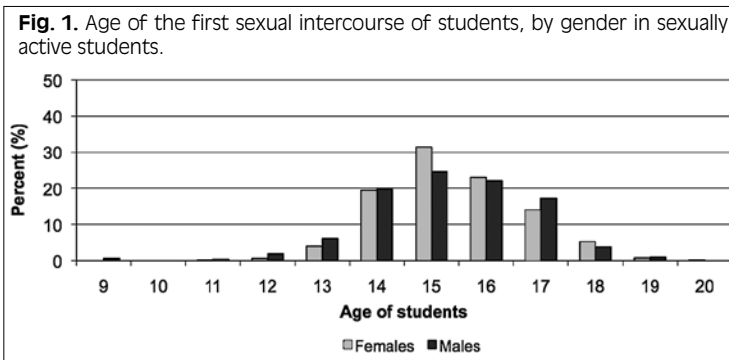


Table III shows the data on the number of previous sexual partners, by age group and gender. A high percentage of females aged 13-16-years (58.2%) had had only one sexual partner, while students older than 17 years had generally had more than two previous partners.

Among female participants who replied to be already sexually active, 27/819 (3.3%) declared they had become pregnant at least once during their life: in almost all cases (74%) the pregnancy ended with an abortion.

KNOWLEDGE AND UTILIZATION OF CONTRACEPTIVE METHODS

Male condom and contraceptive pill were the most well-known contraceptive methods reported by sexually active students (96.7% and 86.5%, respectively) (Fig. 3). Other contraceptive methods (spermicidal, diaphragm, female condom, interrupted coitus and abstinence during fertile period) were known by less than 35% of sexually active students, with the exception of intrauterine devices (58.0%).

About 74% of students declared they used a contraceptive method during the first sexual intercourse (usually the male condom). Table IV and Table V show, respectively, the utilization of male condom and contraceptive pill among sexually active students during the last year and the year before the last one, by gender. In Table V, in the male group the contraceptive pill is obviously used by the partner.

Particularly, during the last year, about 57% of sexually active students declared the utilization of male condom every time or almost all times during their sexual activity, and about 19% of students used the contraceptive pill: these percentages were significantly higher than those declared for the previous year ($p < 0.01$).

Tab. III. Distribution of number of partners, by gender and age-group, in sexually active students (11 students excluded because sex or age were not declared).

Number of partners	Total students	Females			Males		
		13-16 years	17-19 years	20-24 years	13-16 years	17-19 years	20-24 years
1 (%) (95% CI)	436 (38.2) (35.3-41.1)	146 (58.2) (51.9-64.4)	197 (38.9) (34.5-43.2)	17 (28.8) (17.0-40.6)	38 (34.9) (25.7-44.0)	35 (19.4) (13.5-25.3)	3 (8.6)
2-5 (%) (95% CI)	458 (40.1) (37.2-43.0)	70 (27.9) (22.2-33.5)	228 (45.0) (40.6-49.4)	31 (52.5) (39.5-65.5)	38 (34.9) (25.7-44.0)	74 (41.1) (33.8-48.4)	17 (48.6) (31.7-65.5)
>5 (%) (95% CI)	130 (11.4) (9.5-13.3)	14 (5.6) (2.7-8.5)	49 (9.7) (7.0-12.3)	10 (16.9) (7.2-26.7)	14 (12.8) (6.4-19.3)	34 (18.9) (13.1-24.7)	9 (25.7) (10.9-40.5)
Not available (%) (95% CI)	117 (10.3) (8.5-12.1)	21 (8.4) (4.9-11.9)	33 (6.5) (4.3-8.7)	1 (1.7)	19 (17.4) (10.2-24.7)	37 (20.6) (14.5-26.6)	6 (17.1) (4.4-29.9)

Tab. IV. Utilization of male condom among sensually active students during the previous and last year by gender.

Use of male condom	Previous year				Last year			
	Female	Male	Gender not available	Total	Female	Male	Gender not available	Total
Every time (%) (95% CI)	295 (36.0) (32.7-39.4)	108 (33.2) (28.0-38.5)	4 (50.0)	407 (35.3) (32.5-38.1)	313 (38.2) (34.8-41.6)	123 (37.8) (32.5-43.2)	2 (25.0)	438 (38.0) (35.2-40.9)
Almost all times (%) (95% CI)	136 (16.6) (14.0-19.2)	57 (17.5) (13.3-21.8)	1 (12.5)	194 (16.8) (14.6-19.0)	153 (18.7) (16.0-21.4)	61 (18.8) (14.4-23.1)	1 (12.5)	215 (18.7) (16.4-21.0)
Sometime (%) (95% CI)	82 (10.0) (7.9-12.1)	36 (11.1) (7.6-14.6)	2 (25.0)	120 (10.4) (8.6-12.2)	92 (11.2) (9.0-13.4)	32 (9.8) (6.5-13.2)	2 (25.0)	126 (10.9) (9.1-12.8)
Rarely (%) (95% CI)	37 (4.5) (3.1-6.0)	15 (4.6) (2.3-6.9)	1 (12.5)	53 (4.6) (3.4-5.8)	53 (6.5) (4.8-8.2)	21 (6.5) (3.7-9.2)	1 (12.5)	75 (6.5) (5.1-8.0)
Never (%) (95% CI)	44 (5.4) (3.8-6.9)	23 (7.1) (4.2-9.9)	0	67 (5.8) (4.4-7.2)	63 (7.7) (5.8-9.6)	16 (4.9) (2.5-7.3)	1 (12.5)	80 (6.9) (5.4-8.4)
Non-responder (%) (95% CI)	225 (27.5) (24.4-30.6)	86 (26.5) (21.6-31.4)	0	311 (27.0) (24.4-29.6)	145 (17.7) (15.0-20.4)	72 (22.2) (17.5-26.8)	1 (12.5)	218 (18.9) (16.6-21.2)
Total	819	325	8	1152	819	325	8	1152

Tab. V. Utilization of contraceptive pill among sensually active students during the previous and last year by gender (in the male group the contraceptive pill is used by partner).

Use of contraceptive pill	Previous year				Last year			
	Female	Male	Gender not available	Total	Female	Male	Gender not available	Total
Every time (%) (95% CI)	98 (12.0) (9.7-14.2)	22 (6.8) (4.0-9.6)	1 (12.5)	121 (10.5) (8.7-12.3)	151 (18.4) (15.7-21.1)	26 (8.0) (5.0-11.0)	0	177 (15.4) (13.2-17.5)
Almost all times (%) (95% CI)	17 (2.1) (1.1-3.1)	10 (3.1) (1.2-5.0)	0	27 (2.3) (1.5-3.2)	24 (2.9) (1.8-4.1)	17 (5.2) (2.8-7.7)	1 (12.5)	42 (3.6) (2.5-4.8)
Sometime (%) (95% CI)	14 (1.7) (0.8-2.6)	14 (4.3) (2.1-6.6)	1 (12.5)	29 (2.5) (1.6-3.4)	20 (2.4) (1.4-3.5)	23 (7.1) (4.2-9.9)	1 (12.5)	44 (3.8) (2.7-4.9)
Rarely (%) (95% CI)	17 (2.1) (1.1-3.1)	21 (6.5) (3.7-9.2)	0	38 (3.3) (2.2-4.4)	11 (1.3) (0.5-2.1)	21 (6.5) (3.7-9.2)	0	32 (2.8) (1.8-3.7)
Never (%) (95% CI)	412 (50.3) (46.8-53.8)	162 (49.8) (44.3-55.4)	4 (50.0)	578 (50.2) (47.2-53.1)	454 (55.4) (52.0-58.9)	164 (50.5) (44.9-56.0)	4 (50.0)	622 (54.0) (51.1-56.9)
Non-responder (%) (95% CI)	261 (31.9) (28.6-35.1)	96 (29.5) (24.5-34.6)	2 (25.0)	359 (31.2) (28.4-33.9)	159 (19.4) (16.6-22.2)	74 (22.8) (18.1-27.4)	2 (25.0)	235 (20.4) (18.0-22.8)
Total	819	325	8	1152	819	325	8	1152

OTHER RISK FACTORS FOR HPV INFECTION

About 7% of students (162/2300: 137 females, 22 males and 3 students without gender information) experienced at least one genital infectious disease during their life (the infection by *Candida albicans* being the most frequently declared disease by 63/162 students, 38.9%): 6 students reported a previous infection by HPV.

About 68.3% of students (1572/2300) had smoked cigarettes at least once during their life: 70.1% (1186/1692) of females and 63.6% (378/594) of males, respectively. Among those students who had experienced smoking cigarettes at least once during their life, 53.9% (847/1572) were smoking at the time of questionnaire filling. Smoking students smoke an average of 53 cigarettes in one week. The average age of the first smoked cigarette among at least once smokers was 14 years \pm 1.8, while the mean age of start of regular smoke was 15 years \pm 1.6.

VALIDATION OF THE STUDY

About 89.5% of students (2059/2300) judged very easy to fill the questionnaire (90.9% of Italian students and 80.6% of foreigners). In addition, 77.9% of subjects (1792/2300) considered filling this questionnaire useful in order to investigate the sexual behavior of the younger generations and for obtaining information on the transmission of sexual infections (79.4% of Italian students and 67.5% of foreign ones).

Discussion and conclusions

Almost three quarters of students involved in this study were females, that are the target population of HPV vaccination and represent a useful sample to evaluate indirectly the suitability of the current vaccination strategies in Tuscany, Italy.

The results of this study highlight the early start of sexual activity among young students in Tuscany, as shown in other Italian geographic areas involved in this study [13].

Particularly, more than half of interviewed students declared to be already sexually active. The mean and median age of the sexual debut is about 15 years: 77.6% of students at 16 years declared to have had already the first sexual intercourse, compared with 0.3% of students younger than 12 years ($p < 0.01$). These data confirm the importance of vaccination against HPV for young females aged 12-16 years, before their sexual debut.

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Particularly, the current strategy of vaccination against HPV involving more than one cohort, adopted in the Tuscany Region (12-16 year-old females) [11], is likely to provide additional benefits: it will allow also to catch up girls that had not had yet the first sexual experiences until 16 years (21.5%) and/or did not experience previous infections by HPV yet. These considerations are additionally supported by the number of sexual partners declared by students: generally females aged 13-16 years had sexual contacts with only one partner, while students ≥ 17 -years declared they had had at least two partners during their life.

Tuscan students showed good knowledge of the most usual contraceptive methods (particularly, male condom and contraceptive pill). Although male condom use does not provide total protection against HPV infections, it considerably reduces the risk of spreading them [14-17]. However, only half of involved students declared to use male condom (the most widely used contraceptive method) regularly. This low use of condoms may lead to a greater circulation of HPV among adolescents, and consequently, to a higher probability of infection by HPV genotypes at high risk (16 and 18).

Our data are in line with the results obtained in Liguria, where the same questionnaire was administered to a similar target population [13]: in particular an increase in the percentage of sexually active people in the youngest age groups (13-16 years), is more and more evident with time, also comparing our data with those obtained in past studies in Italy and other European Countries [18-25]. Furthermore, the trend towards an earlier sexual debut, is also confirmed by a recent update on sexual behavior in young adults reported in some European countries [26].

For these reasons, and taking into account that HPV vaccination in female adolescents before or immediately after their sexual debut is effective in reducing the overall risk of developing cervical cancer [27], the most suitable vaccination program for Italy seems to be increasing coverage in cohorts involved in the present national vaccination strategy (immunization of 12-years-old girls), complemented by a temporary active offer of vaccination to female adolescents aged 13-16 years, that was already implemented in the Tuscany Region. If economically and logistically feasible, a multi-cohort vaccination strategy, involving a large pool of susceptible females in a short time, would rapidly reduce the circulation of the vaccine-types viruses and, consequently, have a higher clinical impact on diseases related to those high-risk HPV types.

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