

HPV-related quality of life in diagnosed women: A longitudinal study

Journal of Health Psychology
1–15

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DOI: 10.1177/13591053211073642

journals.sagepub.com/home/hpq



**B. Daiana Santos¹, Célia S Moreira² ,
Ana C Teixeira-Santos³, Emília Carvalho⁴
and M. Graça Pereira¹ **

Abstract

This paper explored changes in the HPV-related quality of life (QoL) of 209 women diagnosed with human papillomavirus (HPV) during 1 year of medical monitoring, at three time points (6-month interval between them). Participants completed the HPV Impact Profile (HIP) questionnaire to assess HPV-related QoL. The relationship between HIP scores and time was moderated by the HPV risk type and infection duration: an HPV diagnosis had a stronger negative effect on patients with an HPV high-risk type and on those living with HPV for a long period of time. Age, condom use, motherhood, and type of family were significant predictors.

Keywords

Human Papilloma Virus, HPV, psychosocial impact, quality of life

Introduction

The human papillomavirus (HPV) is the most common causative agent of sexually transmitted viral infections around the world (Casillas-Vega et al., 2017). Around 75% of sexually active women will be infected by HPV at some point in their lives (Tota et al., 2011). HPV global prevalence is estimated to be around 11.7% (Serrano et al., 2018). There are more than 200 HPV genotypes identified (Serrano et al., 2018). They are divided into two groups according to their level of risk of causing cancer. The most frequent high-risk HPV types are the 16 and 18, whereas the most common low-risk types are the 6 and the 11. The high-risk HPV tends to last longer and is associated with precancer (low- and high-grade cervical intraepithelial) lesions and cervical cancer (CC), while low-risk HPV is associated with

benign and premalignant lesions and anogenital warts (Mittal et al., 2017). It is important to notice that CC is the fourth most common type of cancer in women and the fourth one causing death around the world (Serrano et al., 2018).

Transmission of HPV happens through the contact with genital mucosa or skin and it is highly infectious. Most of the infected patients spontaneously clear the infection in a period around 1 or 2 years (Serrano et al., 2018). After

¹University of Minho, Portugal

²University of Porto, Portugal

³University of Luxembourg, Luxembourg

⁴University of São Paulo, Brazil

Corresponding author:

M. Graça Pereira, Psychology Research Centre (CIPsi), School of Psychology, University of Minho, Campus de Gualtar, Braga 4710-057, Portugal.

Email: gracep@psi.uminho.pt

treatment, the clearance period is around 6 months (Juckett and Hartman-Adams, 2010). The prophylactic HPV vaccines have contributed in the reduction of the HPV incidence and the therapeutic ones have shown promising results with positive clinical outcomes (please see Barra et al., 2019, 2020 for reviews). However, less than 2% of the females aging between 9 and 45 years old have taken the prophylactic vaccine and there is no therapeutic vaccine approved in clinical practice, which demonstrates that it will take time until the vaccines are established in clinical practice around the world (Barra et al., 2020). Although screening programs, chemical and surgical treatments, and vaccines for some HPV types have yielded a considerable reduction in HPV prevalence, it is still a health issue that needs much attention (Cummings, 2020; Lin et al., 2010). From the psychosocial perspective, a positive HPV diagnosis has a significant impact on patients' QoL (Wang et al., 2011; Woodhall et al., 2011). Patients infected with HPV have reported concerns about their future, fertility, and health in general (Sharp et al., 2015). An HPV diagnosis causes fear about the infection itself, anguish, and suffering (Nagele et al., 2016). Moreover, as any sexually transmitted infection (STI), the HPV infection is commonly associated with feelings of shame and embarrassment (Maggino et al., 2007). The factors that may influence the emotional aspects of HPV-infected women include worries about a positive result, the awareness of having an STI, and the level of knowledge about the infection (O'Connor et al., 2014). Therefore, a positive HPV diagnosis may cause a significant emotional impact on women, commonly evidencing higher levels of anxiety, depression, and hopelessness (Barnack-Tavlaris et al., 2016). Thus, it is important to assess the psychosocial burden related to the HPV infection and follow patients over time. In fact, the psychosocial status modulates the immune system and consequently may contribute to increase the risk of viral persistence, which has been associated with an increased risk of high-grade lesion and cancer (Buchanan

and Nieland-Fisher, 2001; Sun et al., 1997; Waller et al., 2004).

Hsu et al. (2018) carried out a prospective longitudinal study, having three wave follow-up 1, 6, and 12 months after the diagnosis. They identified that about 20% of the women reported emotional distress and the psychosocial adjustment to HPV was worse at 1 month compared with 6 and 12 months after diagnosis. This finding is important to understand the trajectory of the symptomatology and the temporal windows in which women may need more psychosocial support and professional health.

There are factors that may interact with the infection and consequently may have an effect on the HPV psychosocial impact. Among them, the regular use of condoms may reduce the risk of infection by HPV, although it does not totally protect (Winer et al., 2006). The use of condoms may increase the perception of security, which in turn makes the intercourse more satisfactory (Pereira et al., 2015). A previous study has shown that no condom use is related to emotional suppression and sexual dissatisfaction in woman with HPV diagnosis (Leite et al., 2019). Age is also another factor associated with the HPV infection since the prevalence decreases after the age of 25 and increases after 50 (Vieira-Baptista et al., 2019). A previous study has shown that the HPV impact on QoL is more substantial in older women (Leite et al., 2019). Additionally, age has been associated with HPV-related negative emotions and worries (Daley et al., 2015; Sharp et al., 2015). Although the disease is asymptomatic or clears up in most women in around 1–2 years, it may partially persist (Tota et al., 2011). As this persistence is associated with an increase in the risk of CC, the duration of the infection should also affect the psychosocial adjustment. As already mentioned, the HPV type is related to the risk of CC development and so, having a high-risk diagnosis may have a larger negative psychosocial impact. There are two other factors that could also interact with the HPV psychosocial impact: motherhood and family structure (Sharp et al., 2015; Wan et al., 2018). Single-parenting

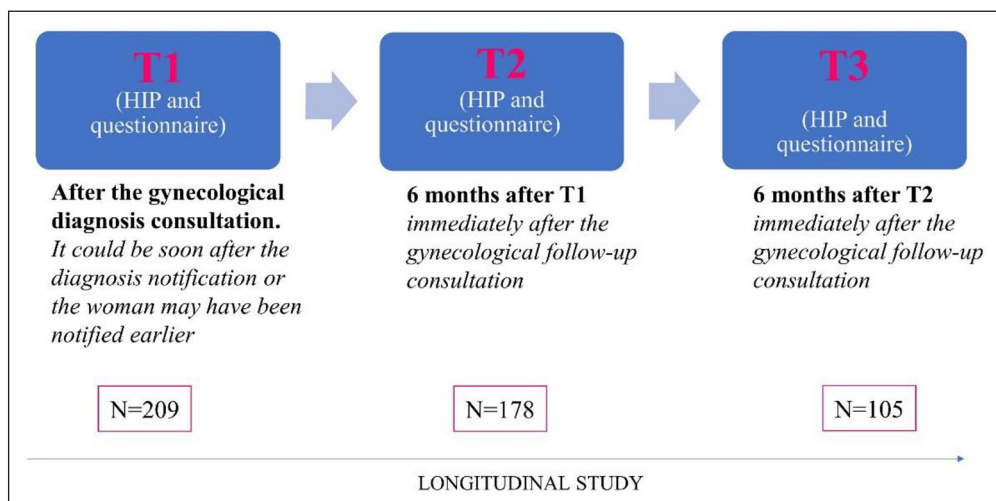


Figure 1. Study design.

was associated with more negative emotions than partner-parenting, while step-parenting was related to an increased stress level and depression symptoms compared to biological parenting (Nomaguchi and Milkie, 2020).

Therefore, the present study aimed to explore the changes, over time, in the HPV-related QoL of women diagnosed with HPV during 1-year of medical monitoring. The effects of sociodemographic variables (age, type of family, and motherhood) and clinical variables (type of HPV, duration of the infection, and use of condoms) were also examined as putative moderators. Our hypothesis was that the participants would start with a higher psychosocial impact at the first assessment and a psychosocial adjustment would be observed throughout the follow-up time points, particularly for women with low risk and short duration HPV. Additionally, moderator effects of the following variables are expected: age, type of family, motherhood, and use of condoms.

Materials and methods

Study design

This study used a longitudinal design (see Figure 1) following the participants for a year,

with three different time points, 6 months apart: T1 (first assessment, immediately after the gynecological diagnosis consultation); T2 (second assessment, immediately after the gynecological follow-up consultation—6 months after T1); T3 (third assessment, immediately after the gynecological follow-up consultation—6 months after T2).

Participants

To calculate the minimum number of participants needed to be recruited into this study, we used the results from the original HIP validation (Mast et al., 2009). More precisely, taking into account that the maximum standard deviation of all HIP subscales is 4.1 in that study, and requiring 95% confidence intervals (two-sided) with a precision of 20% of this maximum, the calculation provided a minimum number of 97 participants. As we knew that attrition would be high, we decided to begin the study with twice that number, that is, with a minimum of 194 participants. Fortunately, it was possible to enroll 209 women diagnosed with HPV ($N_{T1}=209$, $N_{T2}=178$, $N_{T3}=105$). Data were collected in two different hospitals (i.e. Braga Hospital and Alto Minho Local Healthcare Unit), in the northern region of Portugal.

The inclusion criteria of this study were being an adult woman (age ≥ 18) having a positive HPV diagnosis (regardless of the first diagnosis notification time), in a stable monogamous relationship (i.e. sexually active), and attending gynecological consultations at the hospitals where data collection took place. The exclusion criteria were illiteracy, pregnancy, and having another STI in addition to HPV. It is important to mention that, in Portugal, it is recommended that all women aged 25 to 60 years old should be tested for HPV every 5 years if they are sexually active. However, the physician could recommend the screening for younger participants when relevant.

Data collection procedures

The procedure for informing the participant about the diagnosis was the same in the two hospitals where the study took place. All patients did the first screening in the primary health care service, including the Pap smear collection. Patients received a letter at home notifying about her test result and, in case of a positive result, they were notified to make a new appointment with the gynecologist at the hospital. The HPV test results delivered to the patients included the following information: patient data; date of the test; and HPV type. In the gynecological appointment more exams could be required, such as a colposcopy. In the context of this study, patients diagnosed with HPV were followed by the gynecologist, in the hospital, every 6 months until being discharged from medical appointments.

Regarding the recruitment, the gynecologists identified patients meeting the inclusion criteria and, immediately after the pathological consultation of the lower genital tract, all eligible women were referred to the researcher. Two hundred and nine women were invited to participate in the study and all of them accepted the invitation. Patients signed a written consent form after being properly informed about the nature of the study and data confidentiality. Participation was voluntary and the study was performed in accordance with the Declaration

of Helsinki. The study was approved by the Ethics Committee of Braga Hospital and by the Ethics Committee for Health of the Local Health Unit of Alto Minho. Authorization was also requested from the National Commission for Data Protection.

Sociodemographic and clinical information was collected from all participants in an interview with the same researcher at all the three time points. The HPV-related QoL questionnaire was self-applied. Patient records were also consulted.

Materials

Patients were assessed through the HIP questionnaire (Mast et al., 2009, Portuguese version by Santos et al., 2019), which is a measure associated with QoL (Qi et al., 2014). Currently, it is the only measure assessing a full spectrum of HPV psychosocial effects (Mast et al., 2009; Santos et al., 2019). The Portuguese version presents good psychometric properties and comprises 23 items, scoring in a Likert scale from 0 to 10, in which 0 means "Not at all" and 10 means "Extremely." It is divided into six subscales: Worries/Concerns (e.g. "I am worried about having abnormal Pap test results"); Emotional Impact (e.g. "When I think about my recent gynecology exam or test results, I feel depressed"); Sexual Impact (e.g. "After my recent gynecology exam or test results, I am having less sex"); Future Treatment/Transmission (e.g. "I am worried that there are no treatments to cure cervical cancer"); Positive Emotions (e.g. "When I think about my recent gynecology exam or test results, I feel good about myself"); and Negative Emotions (e.g. "I felt disgusted by my recent gynecology exam or test results"). Higher scores indicate worse QoL, therefore, scores in "Positive Emotions" were inverted. The Cronbach alphas indicated good internal consistency of the questionnaire (0.86 for the Worries/Concerns subscale, 0.79 for the Emotional Impact, 0.69 for the Sexual Impact, 0.86 for the Future Treatment/Transmission, 0.83 for the Positive Emotions, 0.83 for the Negative Emotions, and 0.92 for the total scale).

Outcomes

The predictors included in the analysis were age, family type, motherhood, HPV risk type, infection duration (i.e. first HPV appointment or not, at T1), and use of condoms. Age was coded in years (continuous variable). It was considered as a fixed variable over time, reflecting the age at T1. The infection duration was a categorical variable. Patients were classified in the category “short duration” when the first HPV diagnosis notification happened in less than half a year, meaning that at T1 they were attending the first appointment with the gynecologist in the hospital. The “long duration” category comprises the participants having the diagnosis for more than half a year and so, at T1 they were, at least, in the second appointment at the gynecological service of the hospital, which was confirmed in the medical records. The other variables were categorical ones, as follows: the HPV risk type (low or high); the regular condom use (yes or no); motherhood (yes or no)—regardless of the children being at home or not; and type of family (nuclear, extended, single-parent, reconstructed). Nuclear family included a couple and their children (if any), while the extended ones included other relatives (e.g. aunts, uncles, grandparents). The term “single-parent” was used when the woman lived only with their children, while “reconstructed family” was used when the couple have had one or more previous relationships from which at least one of them resulted in children. The type of family was treated in a dichotomous way during the analysis, that is, each type was tested separately: nuclear family (yes vs no), extended family (yes vs no), single parent (yes vs no), and reconstructed family (yes vs no).

The sample was divided into four classes according to the risk type and infection duration: (C1) low-risk, short infection duration ($M_{T1}=2.4$ months, $range_{T1}=[1,6]$); (C2) high-risk, short infection duration ($M_{T1}=2.6$ months, $range_{T1}=[1,6]$); (C3) low-risk, long infection duration ($M_{T1}=26.3$ months, $range_{T1}=[7, 108]$); and (C4) high-risk, long infection duration ($M_{T1}=24.3$ months, $range_{T1}=[7, 156]$). To

facilitate the interpretation of the results, whenever the interactions of risk type and infection duration with time were significant, we analyzed the effects of time in the four classes resulting from the interaction “type*duration.” Over time, a patient could change between classes because the HPV diagnosis (high/low risk) could change over the consultations. Therefore, the patients’ HPV risk type was a variable that was not constant over time (i.e. a woman could be in the category “low-risk” at baseline but be classified as “high-risk” at follow-up or vice-versa, according to the natural course of the disease and, consequently, the new diagnosis given by the gynecologist at the follow-up appointment). Supplemental Table 1 shows the number of participants in each class at each timepoint.

The dependent variables were the total score in the HIP and its subdomains: Worries/Concerns; Emotional Impact; Sexual Impact; Future Treatment/Transmission; Positive Emotions; and Negative Emotions. The outcomes were obtained by averaging items.

Finally, “time” is the continuous variable that assumes values one, two, and three, according to the corresponding assessment moment. This variable also represents the time in months since the beginning of the study, that is, assuming values 0, 6, and 12, due to the variable transformation $Time_months = 6 \times (time - 1)$.

Statistical analysis

Statistical analyses were performed using Rstudio, R version 3.6.2, through packages “lme4” (Bates et al., 2015), “lmerTest” (Kuznetsova et al., 2017), and “ggplot2” (Wickham, 2009).

Differences in sociodemographic variables between women who ceased the participation and those who remained were examined through regression modeling. For age, a linear regression model was performed, while for the dichotomous variables, logistic regression models were conducted.

Longitudinal changes on patients’ QoL (overall HIP score and subdomains) were assessed through mixed effects models. In each

model, the following variables were included as covariates or factors: time; age; infection duration (short or long); risk type (low or high); condom use (yes or no); motherhood (yes or no); and type of family (nuclear, extended, single parent, reconstructed).

Different models were considered for the overall HPV-related QoL and for each subdomain, including each target variable as a dependent variable. In each case, the final model was selected using the following procedure: first, an unconditional growth model (i.e. the time as unique predictor) was specified in order to assess the general effect of time (over T1, T2, and T3) in the target variable. Then, the predictor effect of each covariate and factor was separately tested in the initial model. Possible interactions between variables were considered. Finally, multiple predictors were assessed together, in a single model.

Data sharing statement

The current article includes the complete raw data-set collected in the study including the participants' data set, syntax file and log files for analysis. All of the data files will be uploaded to the Figshare repository.

Results

Sample characteristics

The age of the participants ranged from 20 to 65 ($M=39.7$, $SD=10.35$). Of the total sample, 36.8% ($N=77$) had a secondary education degree (at least 10 years of formal education) and 20.6% ($N=43$) held an academic degree. Regarding marital status at T1, 43.5% ($N=91$) of women were married, 43.5% ($N=91$) were single, and 12.9% ($N=27$) were cohabiting couples; 69.9% ($N=146$) had children and 86.1% ($N=180$) belonged to a nuclear family. In terms of the risk type, 62.7% ($N=131$) of women presented high-risk HPV at T1, 42.1% ($N=75$) at T2, and 14.3% ($N=15$) at T3.

Regarding the dropouts, most women left the study due to medical discharge or hospital

change. The participants who left the study after T1 did not significantly differ from those who continued in the study, from a sociodemographic and clinical point of view (i.e. age, infection duration, risk type, marital status, education, the use of condom, children, and the family type). From T2 to T3, participants only differ in the risk type. As expected, women with low risk were most of the dropouts, due to clinical discharge. More specifically, 57% of women at low risk at T2 left at T3; while only 19% of women at high risk in T2 left the study at T3. See Supplemental Table 2 for descriptive statistics in each assessment.

HPV-related QoL

The analysis of the HPV-related QoL in the three assessments confirmed the strong moderator effects of the risk type and infection duration over time, that is, moderator effects of the relationship between HPV-related QoL and time. This means that HPV-related QoL differently evolved over time for patients with different risk types and different infection durations. Graphs illustrating these moderator effects in the HPV-related QoL over time are presented in Supplemental Figure 1. The raw data were also used to depict graphs of changes in the general HPV-related QoL and in its subscales across time for each class (see Figure 2). In general, for women with HPV infection, the evolution of the negative impact over time strongly depends on the risk type and on the infection duration.

HIP overall scale

For the overall scale, 33.0% of the total variation was attributed to differences between patients. The analyses showed significant effects of time (i.e. T1, T2, T3) in the overall HIP score (estimate = -2.53 , $p < 0.001$), which means that, in general, the psychosocial negative impact of the HPV diagnosis was stronger at T1 than in the other time points. None of the other covariates and factors (i.e. age; risk type; infection duration; condom use; motherhood;

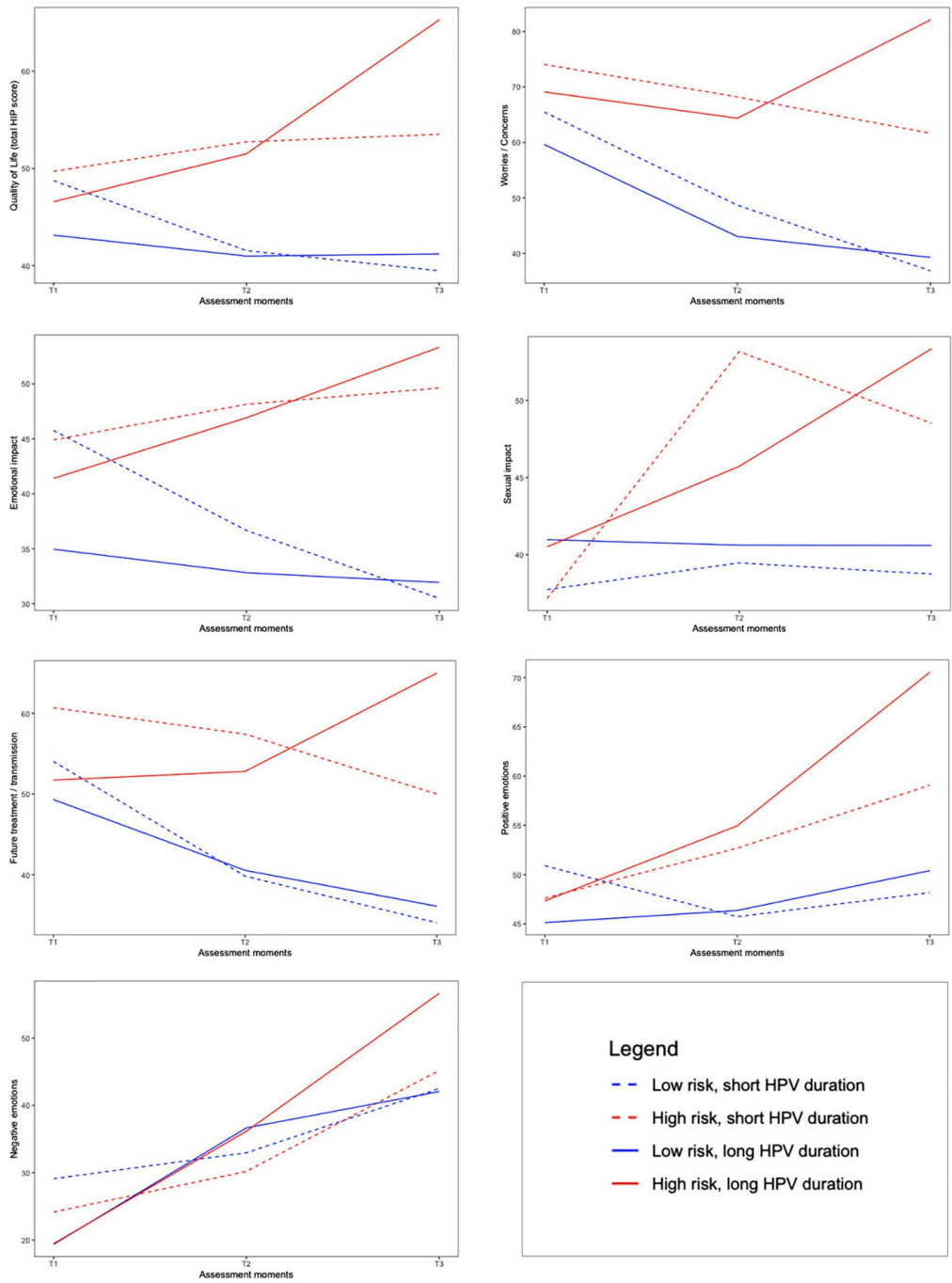


Figure 2. General changing trends of the quality of life and its subscales over time, using raw data and highlighting differences between risk types and HPV durations

and family type) showed significant effects when separately included in the initial model.

When considering interactions with time, both the risk type and the infection duration showed significant effects (See Supplemental Table 3 for complete information about the models). These findings showed that both variables moderate the psychosocial impact of HPV over time. More specifically, patients with low-risk and short infection duration (C1) showed a lower HPV-related QoL over time (estimate_{C1} = -5.08, $p < 0.001$). On the other hand, patients with high-risk and long infection duration (C4) experienced an increase in the negative psychosocial impact over time (estimate_{C4} = 5.72, $p = 0.002$). Time had no significant effects for patients with low-risk and long infection duration (estimate_{C3} = -0.69, $p = 0.597$), as well as for patients with high-risk and short infection duration (estimate_{C2} = 1.62, $p = 0.376$).

HIP: Worries/concerns

In the “worries/concerns” domain, 12.6% of the total variation was attributed to differences between patients. Worries and concerns significantly decreased over time (estimate = -13.58, $p < 0.001$).

Age (estimate = -0.24, $p = 0.045$) and the risk type (estimate = 15.73, $p < 0.001$) were also significant predictors of worries and concerns. Specifically, younger patients showed higher levels of worries and concerns, and the same was observed in patients having a high-risk diagnosis. The variable “motherhood” was also significant (estimate = -6.84, $p = 0.009$), meaning that having children was associated with lower levels of worries and concerns.

Significant interactions between time and both the risk type and infection duration were observed. Only patients with high-risk and long infection duration (C4) did not present a significant change over time (estimate_{C4} = -2.07, $p = 0.460$). All the other subgroups (classes) had a decrease in the worries and concerns over time (estimate_{C1} = -14.65, $p < 0.001$; estimate_{C2} = -6.98, $p = 0.012$; estimate_{C3} = -9.66,

$p < 0.001$). After controlling for these two interactions, only “motherhood” kept its significance, and was then retained in the final model for this domain.

HIP: Emotional impact

In the “emotional impact” domain, 41.9% of the total variation was attributed to differences between patients. A significant effect of the time (estimate = -4.54, $p < 0.001$) was observed. In general, the emotional impact was stronger at T1. Only the HPV type showed a significant effect (estimate = 9.51, $p < 0.001$), meaning that women at high risk had, in general, a larger negative emotional impact. Moreover, the interaction between time and the risk type also showed significant effects: over time, the low-risk group was able to reduce the initial negative emotional impact (estimate = -4.92, $p < 0.001$), but the high-risk group was not (estimate = 3.38, $p = 0.075$). The evolutionary trend over time was significantly different for these two groups (estimate = 8.30, $p < 0.001$). The infection duration was not significant in this analysis.

HIP: Sexual impact

In the “sexual impact” domain, 34.2% of the total variation was attributed to differences between patients. When considering the whole sample, there was no significant statistical evidence of changing over time (estimate = 1.02, $p = 0.294$). However, the interaction between time and the risk type was significant (estimate = 6.88, $p = 0.003$). More precisely, for patients from the low risk group, there was no significant sexual impact over time (estimate = 0.06, $p = 0.967$), while the high-risk group increased the negative sexual impact over time (estimate = 6.93, $p < 0.001$). When other covariates and factors were included in the model along with this interaction, a significant effect emerged only for age (estimate = 0.25, $p = 0.019$). These findings showed a more negative sexual impact was observed in older women. The infection duration was not significant.

HIP: Future treatment/transmission

In the “future treatment/transmission” domain, 31.4% of the total variation was attributed to differences between patients. In general, future treatment and transmission concerns are expected to decrease over time (estimate = -8.47, $p < 0.001$). Age (estimate = -0.50, $p < 0.001$) and motherhood (estimate = -7.87, $p = 0.008$) were associated with a smaller impact in this domain; while high-risk HPV (estimate = 10.41, $p < 0.001$), and reconstructed families (estimate = 17.30, $p = 0.027$) were related to more concerns regarding future treatment and transmission. Condom use was associated with higher future treatment and transmission concerns, although its significance was borderline (estimate = 6.05, $p = 0.056$).

When interactions with time were tested, the moderator effects of the HPV-risk type and infection duration were significant. In general, higher levels of concerns regarding future treatment/transmission were observed at T1. For low-risk groups, these concerns decreased over time (estimate_{C1} = -10.56, $p < 0.001$; estimate_{C3} = -6.02, $p = 0.005$); however, for high-risk groups, these concerns persisted throughout the treatment (estimate_{C2} = -4.69, $p = 0.115$; estimate_{C4} = 2.06, $p = 0.499$). When controlling these interactions, each of the previous predictors (including condom use) remained significant in the model (see Supplemental Table 4).

HIP: Positive emotions

In the “positive emotions” domain, 41.9% of the total variation was attributed to differences between patients. When considering the whole sample, there was no significant statistical evidence of changing over time (estimate = 1.21, $p = 0.125$). However, significant moderator effects of the HPV type and infection duration were found. Positive emotions significantly decreased over time for the high-risk groups, especially for patients infected for a long period of time (estimate_{C2} = 4.26, $p = 0.041$; estimate_{C4} = 8.55, $p < 0.001$). No significant changes in positive emotions were observed

for the low-risk groups over time (estimate_{C1} = -1.96, $p = 0.222$; estimate_{C3} = 2.74, $p = 0.069$). Nevertheless, these two low-risk groups showed a different evolutionary trend over time, with the long-term infection group experiencing fewer positive emotions (estimate = 4.70, $p = 0.033$).

HIP: Negative emotions

For the “negative emotions” domain, 13.8% of the total variation was attributed to differences between patients. Negative emotions increased significantly over time (estimate = 10.83, $p < 0.001$). The infection duration showed significant moderator effects in interaction with time (estimate = 4.78, $p = 0.008$). However, the HPV-risk type did not show a significant effect (estimate = 3.45, $p = 0.110$). In general, negative emotions are expected to increase for all participants throughout the treatment, although with different magnitudes depending on the infection duration, being more serious for women with a long-term infection (estimate_{short} = 8.21, estimate_{long} = 12.99; both with significance $p < 0.001$).

By controlling this interaction of infection duration with time, it was possible to observe significant effects of condom use and family type (reconstructed family). Condom use was linked with lower levels of negative emotions (estimate = -5.13, $p = 0.021$), while reconstructed families were more likely to present higher degrees of negative emotions (estimate = 11.74, $p = 0.033$).

Table 1 summarizes the time coefficient estimates in interaction with HPV-risk type and infection duration in the general HIP score and in each subdomain, while Supplemental Table 4 presents a summary of the models for each significant predictor and their fit indices.

Discussion

In accordance with our hypotheses, the overall HPV-related QoL was worse at T1 than in the other time points. This was expected as the HPV infection commonly disappears after 1 to 2 years after diagnosis. It is in line with

Table 1. Summary of time coefficient estimates of the interaction between HPV risk and duration in the overall scale and all subscales (linear case).

HPV risk	HPV infection duration*	HPV infection QoL	Overall Worries / Concerns	Emotional impact	Sexual impact	Future treat./ transmission	Positive emotions	Negative emotions
Low	Short	↘ -5.08 ***	↘ -14.65 ***	↘ -4.92 ***	→ 0.06 ^{ns}	↘ -10.56 ***	→ -1.96 ^{ns}	↗ 8.21 ***
	Long	→ -0.69 ^{ns}	↘ -9.66 ***			↘ -6.02 **	↗ 2.74 [^]	↗ 12.99 ***
High	Short	→ 1.62 ^{ns}	↘ -6.98 *	↗ 3.38 [^]	↗ 6.93 ***	→ -4.69 ^{ns}	↗ 4.26 *	↗ 8.21 ***
	Long	↗ 5.72 **	→ -2.07 ^{ns}			↗ 2.06 ^{ns}	↗ 8.55 ***	↗ 12.99 ***

Note. Treat. = treatment. HPV infection duration (i.e., first HPV appointment or not, at T1) was not significant for emotional impact and sexual impact analyses. Higher levels indicate a stronger psychosocial impact over time. ↘ Significant linear decreasing trend over time, ↗ Significant linear increasing trend over time, ↗ Marginally significant (significant at the 0.10 level) linear increasing trend over time, → No significant linear trend over time. Significance: ns $p \geq .10$;

[^] $p < .10$, * $p < .05$,

** $p < .01$, *** $p < .001$.

the literature, Hsu et al. (2018) reported that the initial impact of a positive HPV diagnosis is larger than in a later assessment, 6 or 12 months later. However, in cases of high-risk and long-duration HPV, the overall HPV-related QoL decreased over time. This result was expected since the persistence of HPV in women is associated with an increase in the risk of developing CC and, therefore, they may experience greater suffering, anxiety, and concerns about the disease which, in turn, has negative effects on patients' QoL (Heinonen et al., 2013; Kwan et al., 2011; Tota et al., 2011). Women with low-risk HPV normally have an asymptomatic condition, with no big impact on daily lives and, consequently, a decrease in the HPV psychosocial impact over time. On the other hand, high-risk HPV may have more invasive treatments, which may have a large impact in their perception of QoL.

In the "worries/concerns" domain, in general, the impact was higher at T1. However, once more, women with high-risk and long-duration HPV did not present an adjustment in this domain over time. It is known that women with HPV commonly have concerns about the future, fertility, and health in general, as well as fears related to CC (Sharp et al., 2015). This study complements those findings by evidencing a moderator

effect of the HPV type (low/high risk) and infection duration in this modality regarding the evolution of worries and concerns. Supporting previous literature (Hsu et al., 2018), age had a significant effect, that is, young women are more vulnerable to the impact of a positive diagnosis, which may be due to the fact that HPV is a condition much more prevalent in young woman, with increased severity of cervical lesions in this group (Hao et al., 2020; Vieira-Baptista et al., 2019).

Regarding the "emotional impact," two significant different types of trajectories were observed: women with low-risk HPV had a good adjustment over time; however, women with high-risk HPV showed an inverse tendency, with a marginally significant negative impact over time. These results resonate with previous research in which women living with HPV experienced higher levels of stress, anxiety, and worries about the infection progress (Kosenko et al., 2012). As any STI, the HPV represents a social threat and can cause shame, which in turn might contribute to potentiate women's emotional impact, including anxiety and depression (Flynn et al., 2017).

The "sexual impact" was significantly different for women with high- and low-risk types. More precisely, women with a low-risk HPV

diagnosis did not show significant changes over time; however, women with a high-risk diagnosis exhibited an increased negative impact in this domain over time. The HPV infection has a negative impact on women's interpersonal and sexual relationships, yielding fears about sexual transmission, affecting women's self-image and life control perception (Nagele et al., 2016; Wang et al., 2011). However, the evolution of this impact depends on the type of risk involved. The results also showed that, when controlling the type of HPV, age had a significant effect in the patients' sexual impact, with older women being more negatively affected. This finding may be associated with an age-related change in sexuality found in general (Hayes and Dennerstein, 2005).

Concerns about "future treatment/transmission" were higher in the first assessment than in the later time points for women with a low-risk diagnosis. Once more, women with HPV high-risk diagnosis were not able to show this recovery trend over time. Given that the HPV status influence the evolution of the condition, women at high-risk diagnosis were expected to present more concerns about the treatment (Cruickshank et al., 2015). Older women showed lower levels of concerns about future treatment/transmission. This is in line with the fact that younger women present higher concerns about their future, health, and more specifically about their fertility in the future (Sharp et al., 2015). Moreover, women with high-risk HPV in reconstructed families presented more concerns about future treatment/transmission. Even though reconstructed families were a minority in this study, the result is relevant. (Kiecolt-Glaser and Wilson (2017) refer that not all conjugal relationships are favorable to the health, because it may be related to a more unstable relationship which may cause concerns and stress. Additionally, the presence of a partner is not always a symbol of protection. Despite the marginally significant effect, the use of condom was associated with increased concerns about future treatment/transmission. These results may be related to the fact that people using condoms may be more worried about transmission

in general. Or yet, it may be possible that the regular use of condoms may be symbolically associated with mistrust and fear of infidelity (Gavin, 2000; Juarez and Martín, 2006; Van Campenhoudt et al., 1997). Here is also important to highlight that when it was necessary to perform conization of cervix, patients are advised to avoid having sexual activity in the following days and always use the condom after that. This fact may also underline the observed impact of condom on concerns about future treatment/transmission.

Regarding "positive emotions," women diagnosed with a low-risk type did not show significant changes over time. However, positive emotions decreased significantly in women with a high-risk diagnosis, especially in those living with this infection for a long period of time. In general, these results mirror the literature, particularly a longitudinal study that sought to assess the psychological impact of a high-risk HPV diagnosis, in which women with a positive exam presented greater anxiety and concerns about cancer, as well as greater psychosocial burden than women with a negative one (Kwan et al., 2011).

Finally, negative emotions increased significantly over time for the four classes, although with different magnitude depending on the HPV type and infection duration. These results corroborate the literature, since the positive diagnosis, as well as the treatment, is followed by negative emotions. Studies not considering the HPV type showed that women with HPV diagnosis experience several negative emotions, such as fear of developing CC, anxiety, and anger (Barnack-Tavlaris et al., 2016; Thangarajah et al., 2016). Again, women with HPV living in reconstructed families presented increased negative emotions. Literature does not refer specifically to the impact of living in a reconstructed family in women infected with HPV. However, it is known that stepparenting is related to an increased level of stress and depression symptoms (Nomaguchi and Milkie, 2020). However, in future studies, it would be important to control the effects of the relationship quality. In addition to these results, the

regular use of condoms was associated with lower levels of negative emotions. It makes sense that women that consistently use condoms report a lower negative emotional impact, since condoms reduce the risk of transmission (Winer et al., 2006).

To the best of our knowledge, this was the first longitudinal study researching the effect of the interactions between time, the type of HPV, and the diagnosis duration in the HPV-related QoL of women infected, considering different psychosocial domains. The results of the present study showed that the HPV infection may have different impacts on women's quality of life over time. It suggests that it is essential to evaluate factors influencing women's quality of life, considering the HPV risk, infection duration, age, condom use, motherhood, and type of family, in order to help patients within a biopsychosocial approach and offer a tailored treatment, for which a multidisciplinary team will be needed. The limitations of this study include the fact that the sample was collected only in two hospitals in the northern region of Portugal, limiting the external validity of the study, as well as, the exclusive use of self-reported instruments and the non-inclusion of the HPV-infected women's partners. Another limitation could be attrition rates. From T1 to T2 the attrition rate was 15%, however, from T1 to T3 it was 50%. Similarly, a previous longitudinal study with women having an HPV diagnosis reported a high attrition rate of 37.3% (Banister et al., 2013). Most women who stopped participation did it because they were discharged from the gynecological consultations. Inclusively, participants who left the study after T1 did not significantly differ from the remaining in terms of sociodemographic or clinical characteristics and after T2 only differed in terms of the HPV type due to the fact that a large number of women with low-risk HPV cleared the infection and were discharged, so they did not fulfill the studies criteria to keep participating in the T3 timepoint. Thus, dropout does not appear to have substantially affected the results. Finally, another limitation was the small number of participants in some of the family type categories.

Future studies are still necessary to confirm the influence of the family type in QoL and should also include partners, with the aim of evaluating the impact of HPV on their quality of life, as well as studying how the partners' attitudes have an impact on women's quality of life and recovery. Furthermore, it would be important to assess women over a more extended period of time.

Our findings point out the need to create psychological intervention programs, considering the negative impact of HPV on the patients' emotions and quality of life, taking into account the infection type and duration, as well as factors such as age, condom use, motherhood, and family type. It would also be relevant that women with HPV infection could receive psychoeducation sessions about HPV in order to better understand the trajectory of the infection and learn to cope with its emotional impact. For those women struggling with HPV, diagnosis, trajectory and treatment on the couple's sex life, couple's therapy may be offered. Therefore, health care providers should assess the psychosexual impact particularly in women with HPV lesion's treatment and in women experiencing dysfunctional sexuality prior to the diagnosis.

Conclusion

This study showed that the group with low HPV risk and short duration was the only one that presented significant reduction of the diagnosis impact over time in all domains of the HIP. Therefore, special attention should be given to women with the long-term infection and the high-risk type. Those results suggest that it is of the utmost importance to assess the QoL in HPV-infected women, especially regarding the domain of negative emotions. In fact, the emotional impact on women with HPV diagnosis appears to be critical from the very moment they receive the diagnosis.

Acknowledgement

We thank all the volunteers for their participation and the health professionals for the collaboration in this project.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: CSM was partially supported by CMUP, which is financed by national funds through Portuguese Foundation for Science and Technology (FCT), under the project with reference [UIDB/00144/2020].

ORCID iDs

Célia S Moreira  <https://orcid.org/0000-0001-5602-7171>

M Graça Pereira  <https://orcid.org/0000-0001-7987-2562>

Supplemental material

Supplemental material for this article is available online.

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