Transmission and treatment of cutaneous warts in general practice

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CHAPTER 3

Warts transmitted in families and schools: a prospective cohort

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ABSTRACT

Background

Cutaneous warts are very common in primary schoolchildren. However, knowledge on the routes of transmission of human papillomavirus (HPV) causing warts is scarce.

Objective

This study examines the association between the degree of HPV exposure and incidence of warts in primary schoolchildren to support evidence-based recommendations on wart prevention.

Methods

In this prospective cohort study, the hands and feet of all children in grades 1-7 (aged 4-12 years) of three Dutch primary schools were inspected for the presence of warts at baseline and after 11-18 months follow-up. Data on the degree of HPV exposure included information obtained from parental questionnaires: pre-existent warts, warts in family, prevalence of warts at baseline in the class, and use of public places (e.g. swimming pools).

Results

Of the 1134 eligible children 97% participated, response rate from parental questionnaires was 77%, and loss to follow-up 9%. The incidence for developing warts was 29 per 100 person-years at risk (95% CI 26-32). Children with a Caucasian skin type had an increased risk of developing warts (HR 2.3, 95% CI 1.3-3.9). Having family members with warts (HR 2.08, 95% CI 1.52-2.86) and wart prevalence in the class (HR 1.20 per 10% increase, 95% CI 1.03-1.41) were independent environmental risk factors.

Conclusions

The degree of HPV exposure in the family and school class contributes to the development of warts in schoolchildren. Preventive recommendations should focus more on limiting HPV transmission in families and school classes, rather than in public places.

INTRODUCTION

Cutaneous warts are benign papillomas of the skin. Warts are highly prevalent in the general population, especially among primary schoolchildren, for whom the prevalence ranges from 4-33% [1-3]. Although about 67% of warts resolve within 2 years without treatment [4], general practitioners are often consulted for treatment because of physical or psychological discomfort [5]. Based on registries in the UK and the Netherlands, the annual episode incidence rate of cutaneous warts for the age group 5-14 years in family practice ranges from 3-5 per 100 children [6;7]. However, incidence rates in the general population are unknown. Cutaneous warts are caused by infection with human papillomavirus (HPV), which is transmitted by direct contact with contaminated skin or indirectly via objects carrying the virus [8;9]. Increased exposure to HPV theoretically increases the risk of developing warts [10]. Based on studies exploring which risk factors are most important [3;11-18], recommendations to prevent warts focus on limiting the personal spread of HPV and transmission in public places. For example, the use of communal showers is considered to be a risk factor for acquiring plantar warts because wet floors are assumed to be HPV reservoirs [12]. Based on this assumption, the following type of recommendations are issued: 'Wear flip-flops in communal showers'[19], 'Cover the wart with a waterproof plaster when swimming', or 'Do not go barefoot into public places'[20]. However, data from studies on risk factors for warts are contradictory and all studies have a cross-sectional design, thus precluding determination of causal relationships. This prospective cohort study examines the incidence rate of warts in primary schoolchildren and assesses whether the degree of exposure to HPV contributes to the risk of developing warts, to provide evidence-based recommendations for wart prevention.

METHODS

Study cohort

A trained medical student inspected the hands and feet of all children in grades 1-7 from three primary schools (in/around the city of Leiden, the Netherlands) for the presence of warts. Details of the baseline examination are already published [3]. One year later, another trained medical student inspected the hands and feet of all children who were also examined at baseline (now in grades 2-8), again for the presence of warts. Parents were asked to give informed consent before both examinations. Apart from this, children were free to refuse participation during examinations. Due to practical reasons and taking into consideration the school class agenda, the follow-up period ranged from 11-18 months. The study was approved by the Medical Ethical Committee of the Leiden University Medical Center, as well as by the boards of the participating schools.

Development of warts

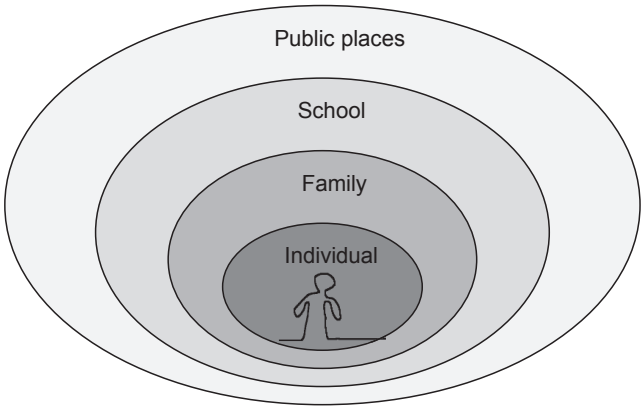
At baseline and follow-up, the type and number of warts were recorded on standard forms with schematic representation of hands and feet. A distinction was made between plantar warts (located on the soles of the feet) and common warts (located on the dorsal side of the feet or hands). Over 5% of all baseline and follow-up examinations were supervised by an experienced general practitioner, with no discordance in wart diagnosis. The examiners were unaware of the answers given in the parental questionnaires.

HPV exposure

Personal factors were recorded during baseline examination: age, sex, and skin type; the latter was coded according to Fitzpatrick to stratify into Caucasian and non-Caucasian subgroups [21]. The degree of exposure to HPV was ranked according to a conceptual model (Figure 3.1), which we operationalised by defining potential environmental risk factors for warts [3]. Information on the presence of these risk factors was obtained during baseline examination and through parental questionnaires prior to baseline examinations:

- *Individual factors*: pre-existent warts (yes vs. no);
- *Family factors*: the presence of a family member with warts (yes vs. no), walking barefoot at home (yes vs. no); [1;3;15-18]
- *School factors*: School (school A vs. B vs. C), and the prevalence of warts in school class at baseline (per 10% increase) [3], presence of warts in at least one of three closest school friends (yes vs. no);
- *Public factors*: use of public swimming pools (yes vs. no), use of public showers (yes vs. no), and practicing sports barefoot (yes vs. no) [11;14;16-18].

Figure 3.1. Conceptual model of HPV exposure [3]. The theoretical degree of HPV exposure decreases from the core outwards.



Statistical analyses

Incidence rates with 95% confidence interval (CI) were calculated, dividing the incident cases by the sum of the person-time of children at risk. An incident case was defined as a child who had developed one or more new warts at follow-up examination, irrespective of pre-existent warts. Also calculated were incidence rates stratified for plantar and common warts, and the incidence rate of new warts in children without warts at baseline.
Cox proportional-hazards model was used to identify risk factors for developing warts. First, univariate analysis was performed for the risk factors to estimate hazard ratios (HR) with 95% CI, in which $p<0.05$ was considered as significant risk factor. Multivariate analysis was performed to assess whether the degree of exposure to HPV contributed to the risk of developing warts. We included age, sex, and skin type as personal factors, as well as environmental risk factors representing the various degrees of HPV exposure: pre-existent (individual factor), presence of family members with warts (family factor), presence of warts in school class (school factor), and use of public swimming pools (public factor). In addition, an exposure sum score in which each of the four environmental risk factors equally contributed (range 0-4) was entered into the model to explore a possible dose-response effect.

RESULTS

Study cohort

The participation rate of 1,134 eligible children at baseline was 97%: 23 children (2%) were absent from school at the time of baseline examinations and 12 children (1%) did not provide parental or child consent (Figure 3.2). Loss to follow-up was 9%: 65 children (6%) left school, 23 children (2%) did not provide parental or child consent at follow-up examination, 9 children (1%) were absent at follow-up examination, and data were missing for 1 child (<1%). Median age of the 1001 children was 7 years ([range 4-12, inter quartile range [IQR] 5-9), 48% was male, 80% had a Caucasian skin type, and 33% had warts at baseline (Table 3.1). At baseline, the parents' response rate to the questionnaires was 77%.

Development of warts

The incidence for developing new warts was 29 per 100 person-years at risk (95%CI 26-32). When stratified for the type of warts, incidence rates were 14 per 100 person-years (95% CI 12-16) for plantar warts, 9 per 100 person-years (95% CI 7-11) for common warts (mostly on hands), and 5 per 100 person-years (95% CI 4-7) for a combination of plantar

Figure 3.2. Flowchart.

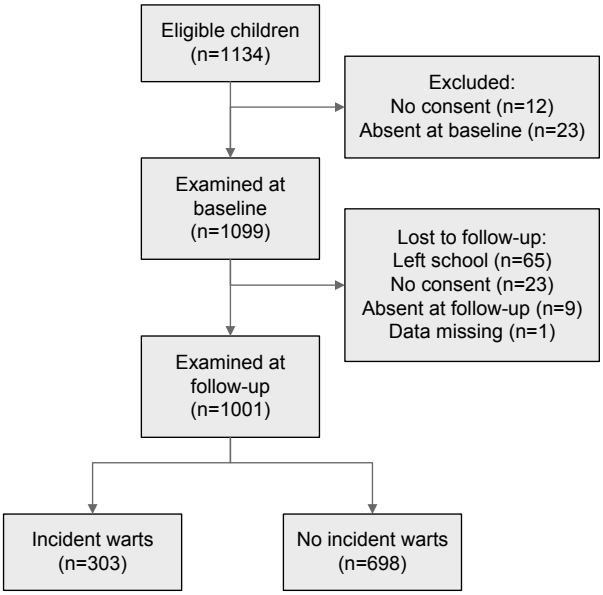


Table 3.1. Baseline characteristics of the primary schoolchildren (n=1001).

Personal	
Median age in years (range)	7 (4-12)
Male sex	485 (48)
Caucasian skin type	799 (80)
Pre-existent warts	333 (33)
Family	
Family member with wart(s)	164 (31)*
Walking barefoot at home	694 (90)*
School	
School	
A (28 classes)	618 (62)
B (8 classes)	110 (11)
C (12 classes)	273 (27)
Wart prevalence in school class ≥ 40%	372 (37)
Close school friends with wart(s)	417 (56)*
Public	
Use of public swimming pools	622 (81)*
Practice sports barefoot	160 (21)*
Use of public showers	103 (14)*

Data are presented as numbers (%), unless stated otherwise

* Total number of children per characteristic is ≤ 1001, because response rates to specific questions on parental questionnaires ranged from 68-100%.

and common warts. The median number of new warts was 1 per child (range 1-10; IQR 1-2). The incident rate in children without warts at baseline was 25 per 100 person-years (95% CI 21-30), and in children with pre-existent warts 37 per 100 person-years (95% CI 21-30) (p<0.001).

Relation with potential risk factors

Univariate analysis showed no relation with sex, but increasing age was related to increased incidence of warts (Table 3.2). There was a high incidence rate in children with a Caucasian skin type; also, several individual, family and school factors were significantly related to the development of warts (Table 3.2). Although the use of public swimming pools almost reached significance level, no significant public factors were identified.
In multivariate analysis, there was no relation with age or sex, but Caucasian skin type was a significant personal factor: HR 2.3, 95% CI 1.3-3.9 (Table 3.3). The degree of exposure, indicated by the presence of family members with warts (HR 2.1, 95% CI 1.5-2.9) and

Table 3.2. Univariate analysis of the association between the degree of HPV exposure and the incidence of warts in primary schoolchildren (n=1001).

Potential risk factor	No of cases/ person-years†	Incidence rate per 100 person-years	Hazard ratio* (95% CI)	p-value
Personal factors				
Age per year increase			1.08 (1.03-1.14)	0.003
Sex				
Girl	150 / 507	30	1	
Boy	153 / 547	28	1.1 (0.8-1.3)	0.66
Skin type				
Non-Caucasian	38 / 221	17	1	
Caucasian	265 / 832	32	1.9 (1.4-2.7)	<0.001
Degree of exposure to HPV				
Individual factors				
Pre-existent warts				
No	177 / 716	25	1	
Yes	126 / 337	37	1.5 (1.2-1.9)	<0.001
Family factors				
Family member with wart(s)				
No	90 / 396	23	1	
Yes	74 / 155	48	2.1 (1.5-2.9)	<0.001
Walking barefoot at home				
No	23 / 76	30	1	
Yes	216 / 731	30	1.0 (0.7-1.5)	0.97

Table 3.2 (continued)

Potential risk factor	No of cases/ person-years†	Incidence rate per 100 person-years	Hazard ratio* (95% CI)	p-value
School factors				
School				
A	198 / 730	27	1	
B	21 / 92	23	0.7 (0.4-1.0)	0.07
C	86 / 232	37	1.2 (0.9-1.5)	0.23
Prevalence of warts in school class				
< 40%	163 / 668	24	1	
≥ 40%	140 / 386	36	1.5 (1.2-1.9)	<0.001
per 10% increase	-	-	1.2 (1.1-1.3)	<0.001
Close school friends with wart(s)				
No	108 / 335	32	1	
Yes	132 / 440	30	0.9 (0.7-1.2)	0.54
Public factors				
Use of public swimming pools				
No	37 / 162	23	1	
Yes	202 / 645	31	1.4 (1.0-2.0)	0.065
Practice sports barefoot				
No	182 / 634	29	1	
Yes	55 / 163	34	1.1 (0.9-1.6)	0.39
Use of public showers				
No	190 / 651	29	1	
Yes	33 / 111	30	1.0 (0.7-1.5)	0.86

* Generated by univariate Cox proportional-hazards model.
† Sum of person-years per potential risk factor is ≤ 1054 (or 1053 due to rounding off), because response rates to specific questions on parental questionnaires ranged from 68-100%.

the prevalence of warts in the school class (HR 1.2 per 10% increase, 95% CI 1.0-1.4) were independent environmental risk factors for the development of warts. However, pre-existent warts was not an independent risk factor (HR 0.9, 95% CI 0.7-1.3). The use of public swimming pools showed a small non-significant risk (HR 1.17, 95% CI 0.75-1.83). A dose-response effect was present in the exposure sum score of the four environmental risk factors; the risk of warts increased by 3.5 (95% CI 2.9-4.2) per extra positive factor. In the subgroup of children with plantar warts, and the subgroup of children without warts at baseline, similar results were found.

Table 3.3. Association between the degree of exposure to HPV and the risk for developing warts in primary school children.

Factor	Hazard ratio* (95% CI)	p-value
Personal factors		
Age per year increase	1.0 (0.91-1.10)	0.99
Sex	1.2 (0.9-1.6)	0.34
Caucasian skin type	2.3 (1.3-3.9)	0.003
Degree of exposure to HPV		
Pre-existent warts	0.91 (0.7-1.3)	0.58
Family member with warts	2.1 (1.5-2.9)	<0.001
Warts in school class†	1.2 (1.0-1.4)	0.02
Use of public swimming pools	1.2 (0.8-1.8)	0.48
Exposure sum score‡	3.5 (2.9-4.2)	<0.001

* Generated by a multivariate Cox proportional hazards including age, sex, skin type and the four environmental risk factors above representing most important individual, family, school, and public risk factors.
† hazard ratio for prevalence of warts in school class per 10% increase.
‡ hazard ratio per extra positive exposure factor (range 0-4).

DISCUSSION

Summary of main findings

The incidence rate of new cutaneous warts in primary schoolchildren was 29 per 100 person-years. Exposure to HPV in families and school class was associated with the development of warts, whereas no independent associations were found for the presence of warts at baseline and public risk factors.

Strengths and limitations of the study

The development of warts was objectively established by physical inspection of hands and feet. Warts on other parts of the body were potentially missed, but account for only about 4% of all warts [22]. The causal associations between the incidence of warts and environmental risk factors were supported by the biological model of HPV exposure and the dose-response effect in our data. The sufficient numbers of children in this study with a participation rate of 97% and the presence of 20% non-Caucasian skin types (mostly originating from Morocco, Turkey, China, Netherlands Antilles and Surinam), resemble the general Dutch primary school population.[23] Although transmission patterns may differ to

some extent due to local customs, the ways of HPV exposure are probably comparable in Western countries.
A limitation of the study is that some risk factors related to HPV exposure are not considered because they are difficult to measure, for example the sharing of personal items or close contact to children with warts during specific hobbies. Although unlikely, suboptimal inter-observer agreement in assessment of warts or the parental assessment of some risk factors could have diluted associations. For example, parents could have been misinformed about the presence of warts among family members. Lastly, binary analysis of factors did not allow assessment of dose-effect relationships within factors.

Comparison with existing literature

To our knowledge, no other recent studies on incidence rates of warts in the general population are available. Based on entries in general practice registers in the UK and the Netherlands, the annual episode incidence of cutaneous warts for the age group 5-14 years in family practice ranges from 3-5 per 100 children [6;7]. The discrepancy with the much higher incidence rates we observed (29 per 100 person years) is explained by the fact that many warts are unnoticed by children and parents [3], and many warts are treated with over-the-counter medication, or not treated at all.
Studies on environmental risk factors for warts are contradictory and all have a cross-sectional design [3;11-18]. Furthermore, a validated model on the degree of HPV exposure is lacking. This is the first study with a prospective design, which also allows exploring possible causal relations. The risk factors we identified partially confirm the theoretical degree of HPV exposure in the environment: having a family member with warts was a more important risk factor than school class prevalence, which was more important than any public factor (Figure 3.1) [3]. However, pre-existing warts (expected to be the main risk factor according to the individual degree of HPV exposure), was not independently associated with the development of warts. This could be explained by the fact that, besides HPV exposure, immunogenicity and susceptibility of the host to specific HPV type are important to develop warts [10]. In other words, the immune system of the child with warts could already be triggered and might therefore be more effective against the specific HPV type the child exposes itself to. To a lesser extent, genetic aspects of the susceptibility of the child could play a role within families, but identification of school class prevalence as a risk factor confirms that HPV exposure is an important component. Future studies on HPV antibody seroprevalence and HPV typing in families/schools should provide evidence on immunogenicity and the susceptibility to specific HPV types.
Regarding public transmission, exposure to HPV was probably too low to be detected with the risk factors and number of children in this study. A possible explanation could be that some preventive measures had already been effectively carried out. Although there are

informal leaflets from public health institutions with advice on warts in the Netherlands, there are no formal regulations for persons with warts; they are neither actively banned from swimming activities nor recommended to cover their warts with plasters in public places.

Conclusion

This study reveals that the incidence of warts in primary schoolchildren is high and that cutaneous HPV is primarily transmitted via the family and school class. Current preventive recommendations mainly focus on limiting the personal spread of HPV ('Avoid scratching lesions') and reducing the risk of transmission in public places ('Wear flip-flops in communal showers')[19]. Our findings suggest that recommendations should shift towards reducing transmission among families and school classes. For example, covering warts at home potentially prevents transmission more effectively than covering warts in the swimming pool.

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