Chapter 7

General discussion and summary
Diskushon general i resúmen
Algemene discussie en samenvatting

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7.
General discussion and summary

7.1 Short summary of the study objective

The research objective described in this thesis was to analyse the best strategy for prevention of cervical cancer on Curaçao. In order to do this correctly we adopted the components needed for the implementation of population screening programmes, as stipulated by the PAHO and WHO (WHO, 2011) (ACCP, 2004) in 2014. The outcomes of this analysis may be useful in developing policies for either primary prevention by vaccination or secondary prevention by screening for cervical cancer on Curaçao.

Experience gained during the set-up of this project were documented, were shared with Fundashon Prevenshon and were helpful for the introduction of a population-based screening programme. All clinical and laboratory steps made during the study came about in close collaboration with the local gynae-oncologist, Analytic Diagnostic Centre (ADC) of Curaçao, Social Security Bank of Curaçao (SVB), and DDL (Delft Diagnostic Laboratories, Rijswijk) and made available through social media sources for care providers and the population.

7.2 Short summary of the study results

Since little or no data were available about HPV prevalence on Curaçao these items were investigated and described in **chapters 4 and 5**. The studies show that HPV type 16 and 18 are most prevalent in cervical cancer, however lower compared to the world data (GLOBOCAN, 2012). The contribution of the

HPV genotypes 31, 45, 51, 52 and 58 is high. Furthermore, we signalled a high HPV prevalence in a population of randomly selected women in four age groups (25-65 years) on Curaçao. HPV prevalence in the total population was 19.7% and in ranking order HPV types 16, 35 and 52 were the most prevalent. Even in women with normal cytology HPV prevalence was high (17.9%) and HPV 35, 18, 52, 16 were the most prevalent. Main risk factor related with HPV infection was young age at first sexual contact.

For implementation of preventive strategies, it is important to get insight in the sexual behaviour on the island and awareness of the need to participate in health programs like screening. Insight in the aforementioned, cultural background and behavioural aspects is the subject of **chapter 2**.

As an example of "lack of awareness" we analysed the proportion of supravaginal hysterectomies over the period 2003-2013 and the knowledge for continuation of screening in case the cervix was left intact (**Chapter 3**). It was shown that the majority of the women (55.3%) were not aware of their cervix status post hysterectomy and discontinued screening for cervical cancer.

The Caribbean region is known as a high-risk region for cervical cancer (Pan American Health Organization, 2017) and on Curaçao the promiscuous lifestyle is common. We therefore studied the HPV prevalence in female sexworkers (FSW) on the island (**Chapter 6**). The results show no significant difference in HPV prevalence between female sexworkers (FSW) (25.0%) and non-female sexworkers (29.4%; p=0.14). Young age was the only risk factor related to HPV prevalence in FSW. A trend for statistical difference was observed in HPV prevalence between FSW from the Dominican Republic (42.1%) and FSW from Colombia (19.2%; p=0.067). Moreover, compared to Non-FSW FSW reported less histories of STD and more often had their previous Pap smear less than 3 years ago (p<0.001). Also during interviews,

they seemed to be more aware about cervical cancer and STD prevention strategies compared to Non-FSW.

In this light it is important to keep track of the male/female sex ratio and erratic development of the population composition, factors that may influence female healthcare. According to the CBS of Curaçao there is a clear skewness in the male-female ratio (ter Bals, 2011). In 2011, this ratio was 46% versus 54% with a greater imbalance in the group above 65 years, respectively 42% men versus 58% women. This imbalance was caused by a surplus of women over men emigrating to Curaçao from regional countries such as the Dominican Republic, Colombia, Haiti and Jamaica (ter Bals, 2011). On top of that, during the last 3 years many people from Venezuela have migrated (fled) to Curaçao, due to political and social-economic instability in the country. Among them was a significant group of women who came as sex workers, the so-called "trago girls". This type of migration can have an impact on changing HPV types on the island and is therefore important to monitor.

Finally, we have assessed the current costs of opportunistic screening, diagnosis and treatment of cervical cancer on Curaçao (Hooi et al, in preparation) based on demographic data from National Statistics bureau (CBS), data from the Sociale Verzekeringsbank Curaçao (SVB) and the department of pathology of Analytic Diagnostic centre Curaçao (ADC). We found the data from 2015 and 2016 to be the most complete and accurate.

Table 7.1
Costs for different interventions based on data from SVB

Phase	Description	Tariffs	
		ANG *1.-	USD * 1.-
Screening			
	HPV/Cytology triage	16	9
Diagnosis			
	False positive referrals	420	235
	Pre-cancerous lesion	420	235
	Cancer	1,920	1,073
Treatment & Follow-up			
	Pre-cancerous lesion		
	CIN 2 and 3	3,722	2,079
	Cancer		
	FIGO I	9,279	5,184
	FIGO II	23,046	12,875
	FIGO III, IV & Palliative	30,961	17,297

We assumed approximate costs of early detection of (pre)cancerous, diagnosis and treatment of cervical cancer as illustrated in table 7.1, based on data from 2015 and 2016. For the suggested screening scenario, we used the data from the present screening programme as depicted in table 1.1 in chapter 1 with referral percentages of women to gynaecologist the figures as derived from the HPV trial as described in chapter 3 and 4 (Table 7.2). Preliminary results show that at present, the costs related to diagnosis and treatment for cervical cancer are higher than the costs of the suggested scenario with 40% coverage and 2.5% referral of women to gynaecologists.

Table 7.2
Current costs versus projected costs

	Current costs		Scenario 1		Difference
	no structured programme		structured screening programme		
Phase	Assumed coverage about 30%		Expected coverage 40%		
	ANG *1,000	USD *1,000	ANG *1,000	USD *1,000	%
Screening	141	79	69	39	-102.93%
Diagnosis	96	54	27	15	-251.06%
Treatment & follow-up	130	73	104	58	-24.37%
Grand Total	**367**	**205**	**201**	**112**	-82.30%
Avg. amount of screening derived for SVB/projected	5,194		4,332		
Average total cost per screening	0.071	0.039	0.046	0.026	-52.02%

Given the high attendance of children to the national vaccination programme (95%) implementation of a vaccination programme is by far the cheapest and very efficient variant (table 7.3). However, the results will only be visible after 15-20 years once the first group that received the vaccine turns 25.

To provide cervical cancer prevention to all women including the children, both now and in the future, we argue for implementation of both strategies, the vaccination and the screening.

With a structured implementation of vaccination and screening, there will be a redistribution of costs, whereby the current costs for opportunistic screening, diagnosis and treatment of cancer will cover the costs of the new vaccination and screening programme. However, for implementation it is important that care providers use uniform guidelines and that information and awareness of HPV and cervical cancer by doctors and patients will be actively stimulated.

The price for a bi-& tetravalent vaccine on the market is about USD32. The vaccine is also available at the discounted price of USD9.80.

Table 7.3
Average yearly vaccine costs

Based on rates without discount	
Costs in ANG1.-	175,993
Costs in USD1.-	98,320
Based on rates with discounts	
Costs in ANG1.-	53,898
Costs in USD1.-	30,111

**: costs are based on the demography of the 9 years old as per 2016, CBS Curaçao*

If the vaccine can be obtained at the discounted price, a cost saving of 227% can be realized on a yearly basis.

7.3 Other remarks

Compared to other Caribbean regions, the incidence and mortality figures related to cervical cancer on Curaçao are not as high (Pan American Health Organization, 2017). However, compared to the Netherlands and other regions with well implemented prevention programs the incidence is high (LEBA, 2016). On Curaçao, cervical cancer is not in the top 3 of medical priorities in the female population. Similar to the rest of the world (Mendis et al., 2014), other chronic non-communicable disease (CNCD) such as cardiovascular diseases and other cancer types are responsible for a low quality of life and high mortality rates and causes high expenses in healthcare (Verstraeten, december 2013 VIC). **(Chapter 2)** Comorbidity like high blood pressure, diabetes mellitus, or both, in women who are being treated for cervical cancer also influence the care costs for cervical cancer. At present cervical cancer is diagnosed in a later stage due to the lack of a screening programme and a low level of awareness in the population. Women on Curaçao are diagnosed at an older age compared to the global data and as a result the survival figures are

lower and the costs for treatment unnecessarily high. Furthermore, the women often have a leading role in family and social life (Ministerie BZK and UNA, 2010). If such a central figure loses her place in the system because of illness or death this will have an important effect on the environment. In terms of public health and financial considerations prevention of cervical cancer is of upmost importance and can be achieved by vaccination and by early detection with screening (Varlack, 2014).

It should be taken into account that in our studies we did not measure data on the HPV-prevalence in the age group younger than 25 years. Including these data will probably lead to an even higher HPV prevalence outcome since in the age group between 16-25 years the highest HPV prevalence is usually found (Forman et al., 2012).
Furthermore, the trial in FSW refers a lower HPV prevalence in this group, while it's assumed that the prevalence is higher due to important risk factors that this group is exposed to. However, illegal FSW and those working outside the brothel are the majority of FSW on the island. This group may be more at risk because of their low social status and the fact that they may not adhere to routine medical check-ups. This group was not included in our analysis, which may certainly bias the results of this report. **(Chapter 6)**

7.4 Future aspects

Based on the studies described in this thesis the following factors are crucial elements when planning and implementing prevention programmes:

- *Primary prevention.* Vaccinating with a preventive vaccine is safe and cost effective. Considering the increasing numbers of other HPV related cancers vaccinating both genders will also protect against other types of HPV induced

cancers such as anus-, penis-, head and neck cancer and can induce herd immunity. Given the relatively high prevalence of non-HPV-16 and HPV18 in cervical cancers in the present studies it is suggested to opt for the nonavalent vaccine which is guaranteed to protect close to 90% of all HPV associated cervical cancers. However, this vaccine was till June 2017, not available through the PAHO Revolving Fund and the price was in excess of USD100 per dose which at present is not affordable. This leaves the option open for the vaccines mentioned in our budget impact analysis, for which the costs are lower. It is recommended to start vaccinating at 9 years old for both genders. This can be easily implemented because the island has a well functioning Youth Health Department and an efficient vaccination programme, which is already included in primary school healthcare routines.

- *Secondary prevention.* All care providers concerned with screening should preferably switch jointly to screening by means of the same clinically validated HPV assay with cytology triage with exception of the age group between 25-29 years. Since the high prevalence of HPV in this age group of which the large majority will be transient and will not lead to cervical lesions, screening by cytology is recommended here. During our trials, the population showed little interest in the self-test device. The reason for this should be investigated, because in other regions the introduction of the self-test device resulted in a higher screening response. Possibilities for improvement have been discussed in **Chapter 2.**

- *Awareness.* As found out in our studies women should be well informed about the importance of prevention for cervical cancer (WHO Comprehensive cervical cancer control, 2014). It is important to avoid unnecessary anxiety. At the same time neglect due to misinformation must be prevented. This can be achieved if the medical advice given, reaches the population properly with help of experts in the field of communication. **(Chapter 2)**

- *Quality and Monitoring.* Quality control, programme monitoring, synchronisation of information and communication between the laboratory and health centres are important factors for a successful implementation. An independent programme coordinator could be appointed with mandate, expertise, authority, and resources to direct, audit and monitor the programme. Coverage of the vaccinated and screened population in correlation with costs and data registration are important data for this purpose. For quality control, epidemiological monitoring and financial reasons it is more efficient if all data are registered by the national pathology lab.

- *Role of care providers including family practitioners.* It is important that all healthcare professionals are committed to uniformed practice and follow the prevention guidelines. Development of a training plan for care providers is advised and the usage to instruct professionals about interpreting and following these guidelines. Hereby also the role of family practitioners is essential as they are the main actors to realize secondary prevention of cervical cancer on the island. Also, this may facilitate data registration and programme monitoring.

7.5 Final arguments

In this study we researched scientific background for best ways to implement preventive programmes for cervical cancer and HPV on Curaçao. From this research we got a clear picture of the medical facts and specific occurrence of HPV in relation to cervical cancer on Curaçao. The findings of the study led to suggestions and recommendations for effective and viable prevention strategy and its implementation. We expect that this will lead to prevention of cervical cancer cases and its precursors and reduction of costs in the curative healthcare sector. Most importantly, lives will be saved.

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