HPV Knowledge and Self-Sampling for the Detection of HPV DNA among Inuit women in Nunavik, Quebec

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ABSTRACT

The prevalence of human papillomavirus (HPV), a necessary cause of cervical cancer has been found to be high in Inuit populations. This study examined 1) the level of knowledge about HPV infection and its relation to cervical cancer and 2) the comparability of self-collected cervicovaginal samples to provider-collected cervical samples for the detection of HPV and to assess preference of sampling methods among Inuit women in Nunavik, Quebec. Questionnaires were used to measure HPV knowledge and sampling method preference. To assess comparability of sampling techniques, samples were tested for 36 HPV types with PCR. Previous awareness of HPV was reported by 31% of women. The level of knowledge about HPV was low, but similar to that of other non-Indigenous populations. The agreement in detection of high-risk HPV between paired observations was found to be high. Self-sampling is comparable to provider-sampling and is a promising intervention to increase coverage of cervical cancer screening.

RÉSUMÉ

La prévalence du virus du papillome humain(VPH) est élevée dans la population Inuit du Québec. Nous avons donc 1) documenter le niveau de connaissance concernant le VPH et son lien avec le cancer du col utérin et 2) évaluer le rendement de l'auto prélèvement pour le VPH en comparaison avec le prélèvement fait par l'intervenant de santé et 3) déterminer la préférence des femmes Inuit du Nunavik entre les deux méthodes. Un questionnaire fut utilisé pour évaluer le niveau de connaissance et la préférence entre les modes de prélèvements. La comparabilité entre les modes de prélèvements s'est effectuée sur les résultats du test PCR détectant 36 différents types de VPH. Plus de 31% des femmes Inuit avaient entendues parler du VPH. Le niveau de connaissance général sur le VPH est faible mais semblable à celui rapporté pour des populations non Autochtone. La comparabilité en matière de détection des VPH est élevée entre les deux méthodes. L'auto prélèvement est potentiellement une méthode de prélèvement propice à augmenter le taux de dépistage du cancer du col utérin.

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LIST OF ABBREVIATIONS

AGUS	atypical glandular cells of undetermined significance
ASC-H	squamous cells of undetermined significance, high-grade squamous intraepithelial lesion cannot be excluded as a possibility
ASCUS	atypical squamous cells of undetermined significance
CI	confidence interval
CIN	cervical intraepithelial neoplasia
HC1	hybrid-capture I
HC2	hybrid-capture II
HPV	human papillomavirus
HR	high-risk
HR-HPV	high-risk human papillomavirus
HSIL	high-grade squamous intraepithelial lesion
KAP	Knowledge, Attitudes and Practices
LR	low-risk
LR-HPV	low-risk human papillomavirus
LSIL	low-grade squamous intraepithelial lesion
OC	oral contraceptive
OR	odds ratio
Pap	Papanicolaou
PCR	polymerase chain reaction
RLB	Reverse line blot
SD	standard deviation
SIL	squamous intraepithelial lesion
STI	sexually transmitted infection

1 INTRODUCTION

1.1 BACKGROUND

The human papillomavirus (HPV) has been established as a necessary cause of cervical cancer[1]. This conclusion is supported by the results of an international case series of over 1,000 women with invasive cervical carcinoma, where it was revealed that 99.7% of the cases were HPV-positive[1, 2]. The association between HPV and cervical cancer has a relative risk in the range of 50 to 150, the strongest ever identified in cancer epidemiology[3]. HPV has also been associated with the less common cancers of the anus, penis, vulva and vagina and some mouth and oropharyngeal cancers[4].

At any point in time about 10% of the global female population is positive for HPV in the cervix, making it the most common sexually transmitted infection (STI) world-wide[5]. The prevalence of HPV in Canada has been shown to range from 10 to 29% depending on the population, but the highest prevalence occurs among women soon after the onset of sexual activity[6]. Most sexually active women will acquire an HPV infection during their lifetime[7].

Over 100 HPV genotypes (also known as 'types') have been fully described, of which more than 40 are known to infect the epithelial lining of the anogenital tract and other mucosal membranes[8]. HPV types have been subdivided by their oncogenic potential for cervical cancer as low-risk (LR) or high-risk (HR). These classifications are based on the strength of the association between individual HPV types and cervical cancer found in large molecular epidemiological studies, including pooled analysis of case-control studies with common protocol[9]. Table 1.1.1 displays the latest classification of HPV types by the International Agency for Research on Cancer (IARC)[10], which includes 25 HR types, although all types have not yet been classified with absolute certainty. LR-HPV types are associated with more benign lesions such as genital warts and low-grade squamous intraepithelial lesions of the cervix[3, 11]. Genital warts, which cause substantial psychological morbidity and high healthcare costs, are primarily caused by LR types HPV-6 and -11[11]. HR-HPV types 16 and 18 have been shown to cause approximately 70% of invasive cervical cancers[12].

HPV types have also been classified with phylogenetic criteria, and the phylogenetic groupings have been shown to be highly concordant with the epidemiological classification[8, 9, 13]. All genital HPV types are part of the alpha-papillomavirus genus(α), the largest genus of the *Papillomaviridae* family[8]. HPV types of the alpha-papillomavirus group are further subdivided into 15 species and HPV types within each species share similar biological and pathological properties[8]. HPV types in species α5, α6, α7, α9, and α11 are associated with high-risk mucosal lesions, whereas species α1, α2, α3, α4, α8, α10, α13 and α15 generally contain types that cause low-risk mucosal and cutaneous lesions.

Table 1.1.1: Epidemiologic Classification of HPV types.

Epidemiologic Classification	HPV Types
High-risk	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59
Probable high-risk	68
Possible high-risk	26, 53, 66, 67, 70, 73, 82
Possible high-risk (based on phylogenetic analogy to HR or probable HR types)	30, 34, 69, 85, 97
Low-risk	6, 11, 40, 42, 43, 44, 54, 61, 72, 81, 89
Undetermined risk	34, 57, 83

Note: Adapted from Bouvard et al. 2009[10] and Munoz et al. 2003[9].

HPV is primarily sexually transmitted through direct epithelial (mucosa or skin) contact, and thus condom use does not provide full protection against infection[14]. In accordance with the primary mode of transmission, markers of sexual activity have been consistently shown to be determinants of HPV infection (reporting new partner, number of sexual partners, age at first intercourse and diagnosis of other STIs)[15-20]. Prevalence of HPV declines with age, but a second peak at older ages is commonly found[21-23]. Other risk factors for HPV infection include smoking, oral contraceptive (OC) use, chronic inflammation, immunosuppressive conditions and parity[15, 18-20, 24].

HPV primarily infects the cervix at the transformation zone, the rapidly proliferating junction between the columnar epithelium and squamous epithelium[25]. HPV enters the basal epithelial cells of the basement membrane with the help of micro-abrasions and early genes (E1, E2, E4, E5, E6, and E7) have been implicated in replication and integration[4, 26]. Although HPV infection is common, the majority of HPV infections are asymptomatic and transient, as most are no longer detectable within 1-2 years[3]. HR-HPV infections tend to be more persistent than LR-HPV infections and it has been suggested that viral load is an

important determinant of persistence[3, 27]. Although research suggests that the carcinogenicity of HPV types is not strictly dependent on their persistence, viral persistence of carcinogenic HPV (particularly HPV-16 and -18) has been shown to strongly predict cervical precancer[13, 28, 29].

HPV Vaccine in Canada

Gardasil, the quadrivalent HPV vaccine, which protects against HPV types 6, 11, 16 and 18 (manufactured by Merck Frosst Canada Ltd.), was authorized for marketing by Health Canada in 2006, for females 9 through 26 years of age[30]. All 13 provinces and territories had implemented publicly funded school-based HPV vaccination programs by September 2009[31]. Although, the HPV vaccine has a potential to reduce cervical cancer incidence by 70%, it will still be important for women to continue with regular cervical cancer screening to prevent the remaining 30% of cancers.

Cervical Cancer: Epidemiology and Natural history

Cervical cancer is the second most common cancer affecting women globally[32]. In 2002, there were about 500,000 incident cases of cervical cancer and 275,000 deaths[33]. Over 80% of these cervical cancer cases occur in the developing world, where the 5-year survival rate is less than 50%[34]. In Canada, where the 5-year cervical cancer survival rate is above 70%, it is expected that in 2010 an estimated 1300 women will be diagnosed with cervical cancer and 370 women will die from the disease[35, 36]. Cervical cancer incidence is the highest among women in their 40s and another peak in incidence occurs among women over the age of 70[6].

Although HPV is a common virus, the development of cancer is a rare event. Risk factors for the progression of HPV infection to cervical cancer include genetic, behavioural and lifestyle factors that influence susceptibility and immune function. These include high number of live births[37], long-term use of OCs[38], tobacco smoking[39], failure to attend cervical cancer screening[40, 41], immunosupression[42, 43], human leukocyte antigen (HLA) genes[44] and p53 (tumour suppressor gene) polymorphism[45]. There has been some evidence that dietary factors play a protective role against cervical cancer[46].

In Canada, approximately 70% of cervical cancers arise from squamous cells and 20% arise from glandular cells (adenocarcinoma). The increasing proportion of adenocarcinomas, especially in younger women, is attributed to the Papanicolaou (Pap) test's poor ability to detect these cancers, as they develop further in the endocervical canal[47]. This trend is of concern as these cancers have a poorer prognosis compared to squamous cell carcinomas[48]. The distribution of HR-HPV types associated with these two histological types are different; HPV-16 is more commonly found in squamous cell carcinomas and HPV-18 in adenocarcinomas[12].

The viral oncoproteins produced by HPV (E6 and E7) disturb the cell-cycle of infected cells leading to epithelial abnormalities, known as cervical intraepithelial neoplasia (CIN)[49]. The progression from asymptomatic precancerous lesions to invasive cervical cancer occurs gradually over a period of years or decades. During tumour progression viral DNA can integrate into the host genome[4]. Once a CIN lesion develops it is not necessarily a linear progression to invasive cancer and many of these lesions spontaneously regress, although more severe lesions are less likely to regress[6]. Progression to cancer is thought to be affected by factors such age, viral load, HPV type, persistence and co-infection with multiple types[25, 50].

The latency period from HPV infection to cervical cancer allows for the detection of the disordered cell growth present in precancerous lesions and presymptomatic invasive cancer through cervical cytology. Different classification schemes are used to characterize the severity of cervical abnormalities detected by the Pap test. Although not commonly used in Canada, classification can be based on grades of CIN: CIN1, CIN2, and CIN3, which represent mild dysplasia, moderate dysplasia and severe dysplasia and carcinoma respectively[51]. The Bethesda system of classification was implemented in 1988 to emphasize the tendencies of lesions to develop into cancer[52]. Bethesda classifications include: atypical squamous cells of undetermined significance (ASC-US); atypical glandular cells of undetermined significance (AGUS); atypical squamous cells of undetermined significance in which high-grade squamous intraepithelial lesion cannot be excluded (ASC-H); low-grade squamous intraepithelial lesions (LSIL); and high-grade squamous intraepithelial lesions (HSIL)[52]. Follow-up of an abnormal Pap smear is usually through colposcopic examination of the cervix with a directed collection of biopsies.

1.2 STUDY SETTING

Data was collected for this study in Nunavik, the sub-arctic and arctic region of Northern Quebec (Figure 1.2.1). Nunavik is located above of the 55th parallel, more than 1,900 km north of Montreal. Owing to its vast size of 507,000 km^2, Nunavik has a small population density of only 0.02 inhabitants/km^2 [53]. Nunavik's population of 11,000 is distributed between 14 communities situated on the coasts of Hudson Bay, Hudson Strait and Ungava Bay[54]. Approximately 90% of Nunavik's population self-identify as Inuit. Presently, there are about 2,295 Inuit females between the ages of 20 and 69 in Nunavik[54].

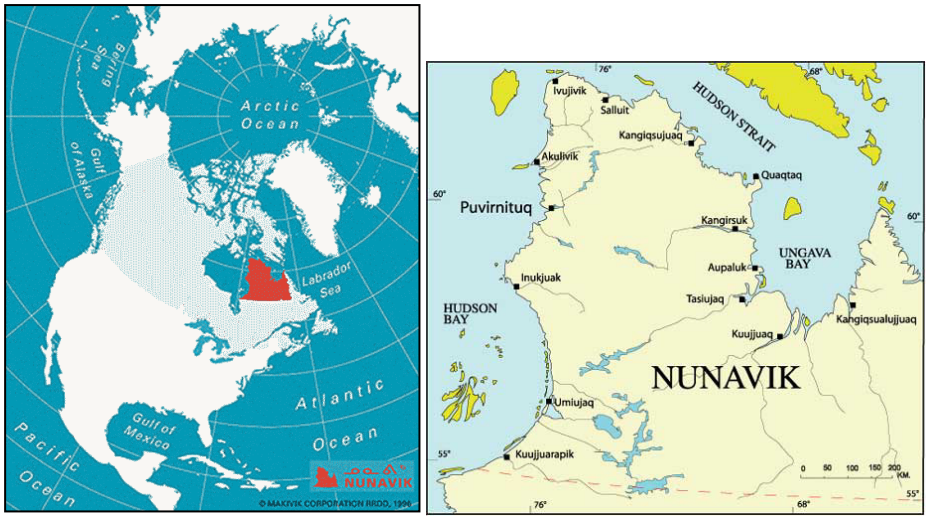

Figure 1.2.1: Map of Nunavik, Quebec[55] (left), and communities of Nunavik[56] (right).

The demographic profile of the province of Quebec is much different than that of Nunavik, which has a young and growing population. The population pyramids of Nunavik and Quebec (Figure 1.2.2) clearly demonstrate the demographic differences between these regions, with over a third of Nunavik's population being 15 years or younger[53]. A comparatively high fertility rate and low life expectancy contribute to Nunavik's distinct age structure. Nunavik's population growth rate between the years 1991 and 2001 was 25.2%, whereas the rate for Quebec was 4.7%[53]. Between the years 2000-2003, the life expectancy at birth of Nunavik's population was about 16 years lower than that of the general population of Quebec[53].

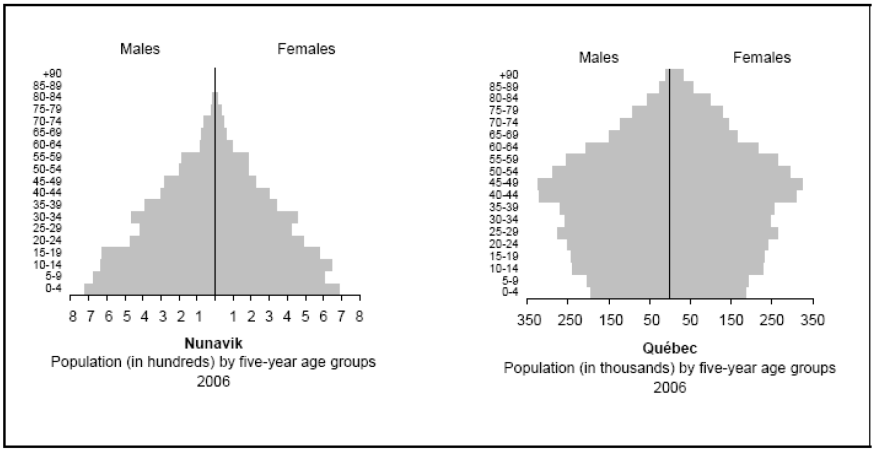

Figure 1.2.2: Population pyramid of Nunavik and Quebec, 2006[53].

Arctic Inuit populations face a 'double burden of disease' worldwide, which is characterized by the high infectious disease rates and rising rates of chronic disease[57]. Tuberculosis is an infection that still remains a major public health problem in Inuit populations despite its very low incidence in the general population of Canada. The Inuit of Nunavik face rates of TB infection approximately 10-fold higher than the rest of Quebec[58]. Likewise, rates of sexually transmitted disease such as chlamydia and gonorrhoea have been shown to be comparatively much higher in Nunavik[59], Nunavut and the Northwest Territories[60] than in other parts of Canada.

Profound social and cultural change experienced by Arctic communities over the past decades has led to many changes to the Inuit lifestyle. Settlement and the shift away from traditional culture have increased the consumption of market foods and led to an increasingly sedentary lifestyle. The Nunavik Inuit Health Survey conducted in 2004 showed that 77% of the population smoke and regularly drink alcohol, and the percentage of the population that is overweight or obese is also high[61]. Rates of cardiovascular disease are expected to increase due to the accumulation of major cardiovascular risk factors (smoking, increasing glucose intolerance, hypertension and obesity)[61, 62]. While, the incidence of cancer has been increasing among the Inuit, the distribution of cancer types has also been changing[63]. Inuit populations continue to be at high risk for traditional cancers such as nasopharyngeal and salivary gland cancers, but 'lifestyle' cancers such as lung, breast and colorectal cancer are increasingly important[63, 64]. Further reactions to these sociocultural changes have also manifested in the

form of social problems such as high rates of suicide[65], physical violence, sexual abuse[61], and substance abuse[61, 66].

In addition to lifestyle changes, the achievement of good health among the Quebec Inuit population is challenged by their socioeconomic environment and geographical isolation. The provision of health care to isolated, fly-in communities has many obstacles. One of these obstacles is high turnover rates of health professionals, which directly affects continuity of care. Due to the small sizes of communities, patients often need to travel between communities or to the south (Montreal) to access highly-specialized care. Health is affected by a variety of other issues relating to the social and geographic environment such as higher rates of non-intentional injury, exposure to environmental contaminants, food insecurity, and household crowding[61, 66].

Cervical Cancer and HPV in Nunavik

The historically high incidence of cervical cancer among the Canadian Inuit population has declined greatly since the 1990s, but they continue to suffer a disproportionate burden of the disease compared to the general population[63]. Among the Canadian Inuit, the age-standardized incidence rate of cervical cancer between 1989 and 2003 was 14.7 per 100,000, which was about three times higher than the Canadian average[63, 67]. This trend is also seen in the Inuit populations of Denmark and the USA[63, 68].

There is limited data on cervical cancer among the Inuit of Nunavik, who represent almost one fifth of Canada's Inuit population because Aboriginal identifiers do not exist in the Quebec Cancer Registry[54, 69]. Using residence codes, one study was able to measure cervical cancer incidence and mortality among the Quebec Aboriginal population living on-reserve and in northern villages, which are predominately populated by the Inuit[69]. The age-standardized incidence rate of cervical cancer among this population was 17.0 per 100,000 (95% CI: 11.9-22.1), whereas in the general population of Quebec it was 6.7 per 100,000 (95% CI: 6.5-6.9). Not only do Aboriginal and Inuit populations face a higher incidence of cervical cancer, but they also have poorer outcomes. The age-standardized mortality rate for cervical cancer was about four times higher in the Quebec Aboriginal population living on-reserve and in northern villages than the general population. Cervical cancer was found to be

the fourth most common cancer, behind lung, breast, and colorectal cancer, representing 6.7% of all cancers.

Consistent with the high risk of cervical cancer in the Inuit populations of Canada, a high prevalence of HPV has been found in Nunavik and in the territory of Nunavut[23, 70]. The overall prevalence of HR-HPV in Nunavut was 26%, and infection seemed to be acquired at a younger age in the Inuit population than the non-Inuit population. The natural history of HPV has been studied in an ongoing cohort of 554 Inuit women from Ungava Bay Nunavik[23, 71, 72]. Before the introduction of the HPV vaccine, the prevalence of any HPV and HR-HPV were 29% and 20% respectively[23]. Of the 32 HPV types detected, the most common types were HPV-16 (5.6%), HPV-31 (3.6%), HPV-61 (3.6%) and HPV-84 (3.1%). Among the women who tested positive for HPV, 40% had multiple HPV type infections. The age-specific rates of any HPV, HR-HPV and LR-HPV followed a U-shape with the highest prevalence detected among women less than 20 years old followed by a decrease with age until a second peak among women age 60 to 69. Determinants of prevalent HR-HPV infection were younger age and having 10 or more lifetime sexual partners[71]. The prevalence rates found in this population were higher than the estimates for the general Canadian population.

Incident HPV infections were measured in this Nunavik cohort with a median follow-up time of 36.3 months[72]. About 40% of the population acquired a new any-type HPV infection at a rate of 14.44 infections per 1000 women-months. Of the 35 HPV types detected in incident infections, the highest incidence rates were among types HPV-31 (1.85%), HPV-61 (1.78%), HPV-16 (1.69%) and HPV-81 (1.39%). Age-specific incidence followed a similar U-shaped curve to that observed with age-specific prevalence rates. Only 36.1% of women cleared their incident infections, which lasted a median of 25.78 months. HR-HPV infections were acquired at a higher rate than LR-HPV infections and had a longer mean duration. Younger age and single marital status were associated with HPV infection acquisition, but no factors were found to predict clearance of HPV infection. Taken together, the results of these studies suggest that Quebec Inuit women are at high risk of HPV infection.

Cervical Cancer Screening and Prevention in Nunavik

In Quebec there is no organized cervical cancer screening program and thus in Nunavik, Pap smear screening is done opportunistically. The Pap test is available in all communities, and is generally preformed by nurse practitioners. Colposcopy is available at the main health centres located in Kuujjuaq and Puvirnituq, so women from the other 12 communities have to fly to these appointments. In the 2004 Nunavik Health Survey, 82% of respondents reported having a Pap smear in the previous two years and 60% in past twelve months. This survey found that not having a Pap test in the previous two years was associated with less education and older age[73]. Unavailability of Pap test at health centre was stated as the reason for not undergoing cervical cancer screening in the previous two years by 40% of these under-screened women.

The HPV vaccination program in Nunavik was implemented in 2008 and was linked with the successful school-based Hepatitis B vaccination program. It was promoted with radio, posters, pamphlets and information sessions provided by health centre nurses at the schools. The vaccine was freely available to girls up to the age of 18 at school and at the health centres. First dose vaccination coverage for girls 9 to 17 years in Ungava Bay was 79.9% and 78.3% for all of Nunavik (Lise Lapierre, personal communication, June 2010).

1.3 STUDY RATIONALE

The discovery that HPV is a necessary cause of cervical cancer has lead to the creation of novel cervical cancer prevention technologies, including vaccinations to prevent HR-HPV infection and screening based on HPV DNA testing. In Canada, the introduction of HPV vaccination and testing has the potential to reduce the burden of cervical cancer disease among the Inuit population. Women's awareness of the viral aetiology of cervical cancer will be crucial to their acceptance and uptake of HPV vaccination and testing.

An understanding of women's level of knowledge about HPV is essential to the design of educational activities on cervical cancer prevention. Currently, there are no published studies on HPV knowledge focusing on the First Nations, Inuit or Métis peoples of Canada. In Chapter 2 we explore the level of knowledge about HPV and predictors of HPV awareness among a sample of Inuit women in Nunavik, Quebec as groundwork for future educational activities.

The uptake of new cervical cancer prevention technologies will only take place in a given setting if they can be practically implemented and are acceptable to the population. Screening with HPV DNA testing on self-collected specimens has been suggested as a way to increase the screening coverage in hard-to-reach populations. To date there have been no published studies on the use and acceptability of HPV testing in Aboriginal women of Canada. In Chapter 3, we aim to provide an understanding of the feasibility of using self-sampling for HPV testing in Inuit women of Nunavik by examining the comparability of self-collected specimens for HPV testing to clinician-collected specimens and women's acceptance of this test.

The results of Chapter 2 and Chapter 3 complement each other, as future implementation of self-sampling as a cervical cancer screening tool in Nunavik will be dependent on women's knowledge of HPV and its relation to cervical cancer.

CHAPTER II: AWARENESS AND KNOWLEDGE ABOUT HUMAN PAPILLOMAVIRUS AMONG INUIT WOMEN IN NUNAVIK, QUEBEC

2.1 LITERATURE REVIEW

2.1.1 HPV AWARENESS

Despite the high prevalence of HPV infection and its potentially serious consequences, many studies have demonstrated a disparity between current biomedical knowledge and general lay awareness of HPV. Table 2.1.1 summarizes studies that reported women's awareness of HPV and their understanding of the causal association between HPV and cervical cancer. This summary shows that although there are numerous publications on HPV awareness, few studies have had a population-based focus. Many of the studies determined awareness among university students and women attending screening or gynaecological appointments. In most studies, less than half of the women report having heard of HPV, but there appears to be a trend of increasing awareness over time. For example, two large nationally-representative studies have measured awareness among women in the USA; one was before the approval of the HPV vaccine (2005) and one after the approval (2007)[74, 75]. Although these studies had different age distributions, the increase in awareness was striking, as the second study found HPV awareness to be twice as high (84%) as what was found in the earlier study (40%).

Several studies have explored sociodemographic and behavioural predictors of HPV awareness[74-81]. Age[74-76, 79-81], higher education[74-76, 78, 81, 82], previous history of Pap smear[75, 78, 82], higher income[79, 81] , race[74, 75, 79], and history of genital warts[76, 80] have been found to be strongly associated with awareness of HPV. It also seems that some determinants of awareness are specific to certain populations, as a variety of other factors were found to be associated with HPV awareness inconsistently between the studies. These include reproductive health characteristics such as history of Candida[80], history of abnormal Pap smear[80], previous pregnancy[76], former use of OC[76], condom use[76], marital status[76] and being in a monogamous relationship[77]. Health literacy characteristics such as exposure to more health information sources[75], trust in health information[75], and being aware of cervical cancer screening guidelines[75] were also found to be important. Finally, significant associations with awareness were found with smoking status[80], rural residence[78], family history of cancer[78], and knowing someone who had HPV[80].

Table 2.1.1: Summary of published studies on awareness and knowledge about HPV.

Reference (First author, year)	Study Year (s)	Location	Number of participants	Study Population	Age (years)	% that have heard of HPV	% that know HPV is a risk factor for cervical cancer (format)
Vail-Smith, 1992[83]	1989	USA	263	Random sample of female university students enrolled in health courses	Mostly 18-23	13	8 (closed)
Ramirez, 1997[84]	1992	USA	110	Female university students	18-22 Mean: 20	72	44 (closed)
Yacobi, 1999[77]	1996	USA	289	Random sample of female and male university students	Median: 25	38	27 (closed)
Baer, 2000[85]	1996	USA	322	Female and male university students	≥ 18	NA	16 (closed)*
Hasenyager, 1999[86]	1996-1997	USA	154	Female university health centre patients attending an annual gynaecologic examination	18-57 Mean: 23.5	NA	49 (closed)
Buga, 1998[87]	1997	South Africa	260	Female university students	15-40	NA	68 (closed)
Hoover, 2000 [88]	1998	USA	60	Women at beaches	15-28	23	NA
Mays, 2000[89]	1998	USA	40	Women in waiting rooms at health clinics	14-18 and 20-50	18	NA
Lazcano-Ponce, 2001[90]	1998	Mexico	880	Women from a population-based random sample of households	15-49	NA	2 (open)
Dell, 2000[91]	1999	Canada	523	Female and male high school students	≥15	13	NA
Lambert, 2001[92]	NS	USA	60	Female and male college students	≥ 18	NA	53 (closed)
Pitts, 2002[93]	2000	UK	400	Female university employees	19-64 Mean: 40	30	11 (open)
Klug, 2005[94]	2000	Germany	532	Population-based random sample of women	25-75	NA	3 (open)
Philips, 2005[95]	NS	UK	1244	Women eligible for cervical screening	20-64	NA	51 (closed)
Sharpe, 2005[96]	2000-2003	USA	44	Female patients at primary health clinics, diagnosed with high risk HPV positive and abnormal Pap smear	19-63 Median: 36.1	48	80 (closed)
Beatty, 2003[97]	2000	USA	108	Female and male teachers and nurses from middle school and high school	NS	NA	48 (closed)
Gudmundsdottir, 2003[98]	2001	Iceland	163	Population-based random sample of women	18-23 Mean:20.4	NA	34 (closed)
Boardman, 2004[99]	2001	USA	250	Female patients from colposcopy clinic (cancer patients excluded)	13-63	NA	57 (closed)
Holcomb, 2004[100]	2001	USA	289	Female and male patients at a university health service and family practice clinics	≥18	67	39 (closed)

Philips, 2003[101]	NS	UK	222	Female university students	18-23 Mean: 18.9	31	51 (closed)
Waller, 2003[80]	2000-2002	UK	1032	Women attending a well woman clinic	≥16 Mean: 30.2	31	40 (closed)
Anhang, 2004[102]	2002	USA	48	Low-income and minority women	18-81	27	NA
Moreira, 2006[103]	2002	Brazil	204	Women in waiting room of gynaecological clinic	16-23 Mean: 20	NA	10 (unknown)
Waller, 2004[104]	2002	UK	1937 (1091 women)	Females and males from a population-based random sample of households	≥16	NA	1 (open)*
Pruitt, 2005[105]	2002-2003	USA	175	Female patients and community volunteers with abnormal Pap smear	18-79	NA	47 (closed)
Baay, 2004[106]	2003	Belgium	162	Women presenting to general practitioners for a routine check-up, attending lecture on cervical cancer and university students	Mean: 39.6	NA	3 (open)
D'Urso, 2007[107]	2003	USA	351	Female and male university students	≥18	36	NA
Daley, 2008[108]	2003-2005	USA	154	Female patients at health clinics who had abnormal Pap smear and had a positive HPV result	18-45 Mean: 23.4	NA	92 (closed)
Giles, 2006[109]	2004	Australia	1) 30 2) 30 3) 30	Females: 1) attending a dysplasia clinic 2) attending local university health service or, 3) participants in phase 3 vaccine trial	18-30	1) 93 2) 73 3) 100	1) 57 2) 33 3) 73 (closed)
Nohr, 2008[76]	2004-2005	Denmark, Iceland, Norway, and Sweden	68, 998	Population-based random sample of women	18-45	32.6	NA
Li, 2009[78]	2005-2007	China	6024	Population-based sample of women	14-59 Mean: 34.6	16	48 (closed)
Tiro, 2007[75]	2005	USA	3,076	Nationally representative random sample of women (those with history of cervical cancer excluded)	18-75	40	48 (closed)
Benning, 2007[110]	2005	USA	364	Female patients at obstetrics and gynaecology clinics	15-74 Mean: 29	42	27 (closed)
Stark, 2008[111]	NS	USA	328	Women with pathologic diagnosis of in situ cervical cancer between 1996 and 2003	Mean: 39.7	NA	19 (closed)
Cates, 2009[112]	2006	USA	138	Female patients of a public health clinic and an obstetrics and gynaecology clinic, both in a rural location	18-84 Mean: 42	35	NA

Abotchie, 2009[113]	2006	Ghana	140	Female university students	20-35	NA	8 (closed)
Sauvageau, 2007[82]	2006	Canada	471	Female and male patients of outpatient clinics	18-69 Mean: 45	15	NA
Di Giusseppe, 2008[114]	2007	Italy	1341	Females at a random sample of schools (university and high school)	14-24 Mean: 19	30	NA
Dursun, 2009[115]	2007	Turkey	1427	Female patients at gynaecological clinics	17-80 Median: 35.8	45	40 (closed)
Gerend, 2008[116]	2007	USA	124	Female and male university students	18-26 Mean: 19.03	78	92 (closed)
Jain, 2009[74]	2007	USA	1102	Nationally representative sample of women	18-49	84	NA
Marlow, 2007[81]	2006-2007	Britain	1620	Population-based random sample of women	16-75	24	3 (open)
McNair, 2009[117]	2007	Australia	309	Female participants of community festivals and university open house	14-67 Mean: 30.4	68	43 (closed)
Millen, 2009[79]	2007	USA	387	Female and male patients of emergency departments	≥18	63	82 (unknown)
Wong, 2010[118]	2007	Malaysia	650	Female university students	Mean: 21.47	22	NA
Kobetz, 2010[119]	2007-2008	USA	1) 246 2) 470	1) Haitian American women 2) Nationally representative sample of African American women	18-75	1) 22 2) 70	1) 18 2) 75 (closed)
Kietpeerakool, 2009[120]	2008	Thailand	402	Female sex workers	Mean: 27.1	NA	14 (closed)
Sandfort, 2009[121]	2008	USA	1282	Female and male university students	17-45 Mean: 19.4	92	86(closed)*

Note: Adapted from Klug et al. 2008[122]. NA= Not assessed, NS= Not stated, *= females only.
Question format: closed= participants choose from a limited number of responses, open= participants respond any way they choose.

2.1.2 HPV KNOWLEDGE

In numerous populations, women's knowledge about HPV, specifically their understanding of HPV's causal role in cervical cancer, and its transmission, symptoms and prevention has been measured. As noted by Klug et al.[122], the way questions about HPV are asked influence women's responses. Studies have ascertained women's understanding of HPV as a risk factor for cervical cancer using closed questions, where the correct response was listed and with open questions, where women had to name HPV themselves. Knowledge about the cause of cervical cancer was found to be low with both types of questioning (Table 2.1.1), but a much lower knowledge level was found when an open line of questioning was used. For example, when asked to name the cause of cervical cancer, only 2.5% of British women mentioned HPV[81], whereas 48% of American women responded 'yes' when asked if they thought that HPV causes cervical cancer [75]. To further highlight the low public understanding of HPV as a risk factor for cervical cancer, one study found that among women who had a previous diagnosis of cervical cancer, only 19% identified HPV as the primary risk factor[111]. Despite the lack of recognition about the role of HPV, women seem to have a higher understanding about the link between sexual behaviours and cervical cancer [104, 123].

The majority of studies reported HPV knowledge regardless of women's awareness of HPV, but some studies used a stopping pattern when women reported that they had never heard of HPV[75, 78-80, 85, 100, 110, 116]. The comparison of knowledge between different populations is difficult because there is a lack of standardization in the wording and types of questions used. In general, it seems that most women (over 60%) understand that HPV is sexually transmitted, a result even found in population-based studies[75, 79, 80, 100]. In a recent study of female university students, over 70% knew that HPV could be asymptomatic[116]. Even among women who have heard of HPV, several misconceptions about the virus exist such as thinking that the pill protects against it[80], it can be cured with antibiotics[110] and that it causes herpes[100]. Women's understanding of HPV's natural history has not been exhaustively established, but two studies found that very few women knew about the transient nature of HPV infection[75, 116].

Despite the numerous studies on HPV knowledge, there is limited literature on this topic in Aboriginal populations. In a study of 80 Alaska Native parents in 11 focus groups, the

majority of parents knew that the Pap smear was used to screen for cervical cancer and many had heard of HPV, but most were unaware of the link between HPV and cervical cancer[124].

2.1.3 HPV KNOWLEDGE AND THE MEDIA

Health providers are often reported as the main source of information about HPV, but given the attention the HPV vaccine has received in the media lately, the media is emerging as an important distributor of HPV information. This may have significant implications for women's understanding of HPV as several content analyses of print and broadcast media have found that information reported about HPV and the vaccine was often incomplete[125-127]. Information about the complex natural history of HPV (effect of different HPV types, prevention, transmission and transient nature of most infections) and the continued need for cervical cancer screening after vaccination was often missing. Another study found that exposure to more health media was associated with knowing the causal link between HPV and cervical cancer and that knowledge increases followed the increases in media coverage[127].

2.1.4 EFFECT OF HPV AWARENESS AND KNOWLEDGE

Awareness and knowledge about HPV does not necessarily predict future risk and prevention behaviours, but it is a precondition for change[128]. There does not seem be to a strong association between sexual behaviours and HPV knowledge[80, 114, 129], but in two studies HPV knowledge was higher among women who use condoms[76, 100]. Education interventions have been shown to increase knowledge about HPV, but their ability to change sexual behaviours and prevention activities has not been described[92]. Some educational interventions on other STIs were found to be effective at increasing condom use[130, 131].

The causal relationship between HPV and cervical cancer has created new directions for cervical cancer prevention and it is reasonable to assume that women must understand this causal link to understand the benefits of these new technologies. In fact, there is some evidence that HPV vaccination acceptance is associated with higher awareness and understanding of HPV[115, 132].

2.2 METHODOLOGY

2.2.1 OBJECTIVES

The objectives of this study were to:

1) Assess the level of awareness and knowledge held by a sample of Inuit women in Nunavik, Quebec concerning HPV and its relation to cervical cancer.
2) Determine the demographic and health behaviour factors associated with higher levels of awareness.

Based on the literature, it is expected that there will be a low level of awareness and knowledge about HPV and its link to cervical cancer in this population. It is hypothesized that younger and more educated women are more likely to have heard of HPV.

2.2.2 STUDY DESIGN

Overview

A cross-sectional survey design was used to determine the current levels of awareness and knowledge held by a sample of Inuit women in Nunavik, Quebec concerning HPV.

Target Population

The target population of this study was Inuit women aged 18 to 69 years from Nunavik, Quebec. The source population was Inuit women aged 18-69 from two different communities of Ungava Bay, Nunavik. These communities were chosen for their population size and they both previously collaborated and participated in a research study on the natural history of HPV infection.

Eligibility Criteria

Women were eligible for this study if they:

1) Self-identified as Inuit
2) Were between 18 and 69 years of age
3) Were living in Nunavik Quebec

Subject Recruitment

Nurse-practitioners recruited women to this study through convenience sampling between March 1, 2008 and June 31, 2009. Participants were primarily recruited at usual gathering places in the community, such as the CO-OP, Northern Store, and community centre. Women were also recruited from a transit centre in Kuujjuaq, which houses patients and their families who come to the health centre for medical care from other communities in Ungava Bay. Finally, women attending Pap smear appointments at the health centre were asked if they would like to participate in this study. If they were interested, the nurse practitioner determined their eligibility

Ethical Considerations

Ethical approval for this study was obtained from the McGill Institutional Review Board and the Tulattavik Health Centre. Written informed consent was obtained from all study participants with a standardized consent form (Appendix 1).

2.2.3 DATA COLLECTION

Questionnaire

The measurement tool in this study was a questionnaire (Appendix 2), which was initially developed from previous knowledge, attitudes and practices (KAP) surveys designed for sexual health and HPV[80, 93, 109, 133, 134]. The survey contained 59 questions divided into seven sections:

1) Sociodemographics, health and lifestyle characteristics
2) Use of health services
3) Knowledge, attitudes and beliefs about HPV
4) Knowledge, attitudes and beliefs about cervical cancer
5) Knowledge, attitudes and beliefs about the Pap test
6) Sexual behaviour and self perceived risk of STI
7) Knowledge and purpose of HPV vaccines

This study focuses on Section 3, but utilizes information from Sections 1-6. A detailed analysis of the remaining sections will be presented elsewhere.

Questionnaire Validation

In order to validate the survey and ensure its cultural relevance, a Steering Committee was created. The Steering Committee was comprised of Inuit community members and local representatives from the Nunavik Regional Board of Health and Social Services and the Ungava Tulattavik Health Centre. The committee reviewed the questions for comprehensibility and technical aspects such as wording, language level and style. A second purpose of this committee was to ensure that each question accurately reflected the construct that it was intended to measure. After the face validity was verified and cultural adaptations were made, the survey was piloted on 10 Inuit women by a trained survey administrator and the survey was altered based on comments made by both the participants and administrator. Additionally, some changes were made at the start of recruitment to integrate some important comments made by the nurses trained to administer the survey.

Questionnaire Administration

In each community, a nurse-practitioner was responsible for recruitment and questionnaire administration. In one community, two nurses were involved in the study due to staffing turnover at the health centre. The nurses were trained in questionnaire administration and practice sessions with proxy respondents were conducted prior to study commencement.

Once study participants were recruited into the study, they decided on an appropriate time and location to take the survey with the nurse. The survey was most often administered at the site of recruitment, but some were conducted at the participant's house. Although the questionnaire was designed to be administered by a trained nurse in a one-on-one situation with the participant (nurse-administered), it was most often administered among a group of women at one time with the help of a nurse (nurse-assisted). The questionnaire took approximately 20-30 minutes to complete. A compensation fee of $20.00, which was found to be acceptable by the Steering Committee, was offered to all participants after informed consent was obtained and the survey completed. The questionnaire was translated into Inuktitut and French by a professional translator and then translated back into English to ensure validity.

Data Management

A unique identifier was assigned to each study participant at recruitment. In the databank, all identifying information except the unique identifier was excluded to ensure confidentiality of study participants. Access to data collection sheets and consent forms was restricted to research team members.

2.2.4 STATISTICAL ANALYSIS

Statistical significance for all tests and regressions were set at 5%. Statistical analysis was carried out in SAS version 9.2.

Study Variables

Characteristics of Participants

The main sociodemographic and lifestyle characteristics used in this study were age, employment status, household income, educational attainment, marital status, smoking status and alcohol use. The reproductive history and sexual behaviour covariates were number of lifetime deliveries, history of Pap smear, history of abnormal Pap smear, previous STI diagnosis, age at first sexual intercourse, number of sexual partners in previous year and condom use. Other covariates used in the analysis were the number of times in the previous year that participants visited with health providers and if they knew someone who had cervical cancer.

Covariates such as marital status, tobacco use, and alcohol use were dichotomized to make interpretation more comparable to previous literature. Given the Canadian cervical cancer screening guidelines which recommend Pap screening every 3 years in women with previously normal cervixes, history of Pap smear was dichotomized at 3 years[51]. Number of lifetime deliveries was categorized as 'previously given birth' and 'never given birth' based on previous reporting of this variable in the literature[76].

HPV Awareness and Knowledge

Questions in the HPV knowledge, attitudes and beliefs section (section 3 of the KAP survey) were in a closed format in either multiple choice or true/false style. Awareness of HPV was defined by responding "yes" to the question "Have you heard of HPV?". Respondents were

also asked if they knew that HPV was a STI, about its long term effects (causal association to cervical cancer), risk factors, symptoms, and methods of protection. Knowledge about HPV was determined for only the participants who had heard of HPV.

Selection Bias and Coverage of Target Population

To evaluate selection bias, the demographics of the study population were compared to the characteristics of the female population of Nunavik. This method of selection bias evaluation was used because no information was collected about those who refused to participate. Although the collection of some sociodemographic information from women who chose not to participate would have been ideal, it was not feasible in this study.

The coverage of the target and source population was evaluated with the 2006 Aboriginal Population Profile for Nunavik and the participating communities[54]. This data was collected as part of the 2006 Census of Population and provided by Statistics Canada. The overall and age-specific coverage was calculated for the female Aboriginal (predominantly Inuit) population of Nunavik. Coverage was also calculated for the combined female Aboriginal populations of the participating communities. As the 18 and 19 year olds were grouped with 15-17 year olds in the population estimates available for Nunavik, they were not included in the coverage analysis.

Level of Knowledge

Frequencies were calculated for each HPV knowledge item response. The number of correctly answered questions by each respondent was tallied. One question was excluded from the analysis because the correct response was not listed in the multiple choice answers. This question asked about the protection provided by condoms against HPV and although condoms do not provide full protection against HPV the answer choices were in a yes/no format.

Differences in the level of awareness and knowledge between participants who were part of the ongoing cohort and those that were not were assessed using Student's t-tests for continuous variables and Chi-square tests for categorical variables. Fisher-exact tests were used for categorical variables when the cell count was less than 5.

Predictors of HPV Awareness

Univariate Analysis

Unconditional logistic regression analysis was carried out for each covariate to explore their association with the outcome of HPV awareness. Odds ratios (OR) and their associated 95% confidence intervals (95% CI) were calculated. The presence of collinearity was assessed by exploring the relationships between each pair of variables through correlation matrices, scatter plots and cross-tabulations of categorical variables.

Multivariate Analysis

Multivariate analyses were carried out for each variable adjusted for age. Each variable that was found to be significant in the univariate analysis and variables that have been shown to have a potential effect in the current literature were included in a final multivariate analysis. These variables were age[74, 75, 79-81], history of Pap smear[75, 78], and educational attainment[74-76, 78, 81]. Although higher income has been found to be associated with HPV awareness in previous studies, it was not used in this analysis because 40% of women did not know their household income, indicating this covariate was not a reliable predictor of SES[79, 81]. Multivariate unconditional logistic regression analysis was performed using all covariates selected for inclusion in the final model. The presence of interaction was investigated by including interaction terms in the multivariate model and examining the effects on regression estimates and CIs. ORs and their associated 95% CIs were calculated for the relationship between each covariate and the outcome of HPV awareness, adjusted for all other covariates in the final model.

2.3 RESULTS

2.3.1 RECRUITMENT AND ELIGIBILITY

Recruitment lasted for a 12 month period, starting on March 1, 2008 and ending on June 31, 2009. The total number of women recruited at the end of the 12 month period was 182. We were unable to quantify the number of women who refused to participate. Two women were excluded because they were younger than 18 and six were excluded because they had already completed the survey at a previous date. A total of 175 women met the eligibility criteria and were included in the analysis.

2.3.2 COVERAGE OF TARGET AND SOURCE POPULATIONS

The average coverage of the target population was 6.5%. The study captured 8.1% of female 20-29 year olds, 7.7% of female 30-44 year olds, 6.1% of female 45-59 year olds and 4.2% of female 60-69 year olds in Nunavik. Source population coverage was 24.7% and age-specific coverage of females was 35% of 20-29 year olds, 30% of 30-44 year olds, 21% of 45-59 year olds and 13% of 60-69 year olds. The age distribution of the study population was similar to both the target and source population (Figure2.3.1).

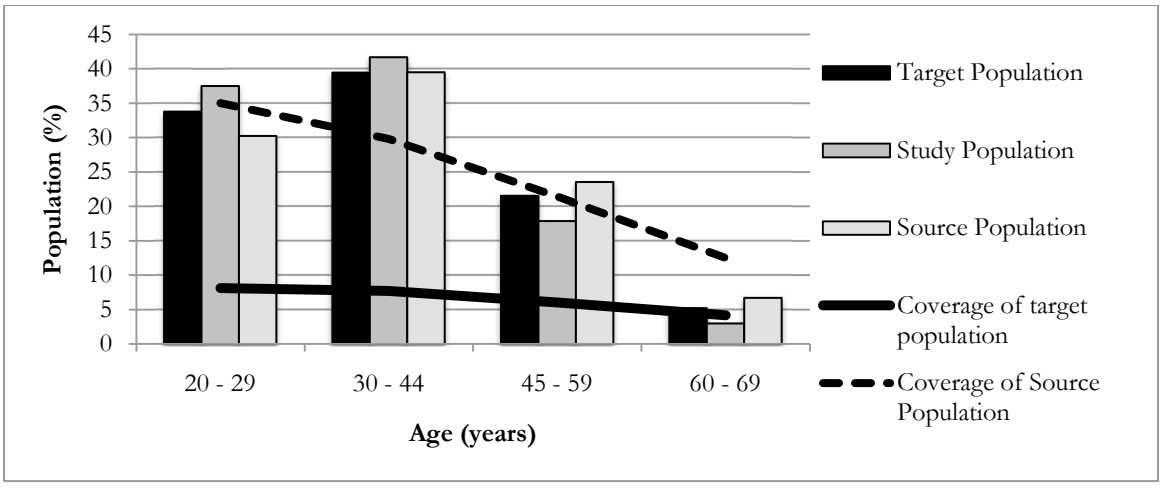

Figure 2.3.1: Age distributions of the target[54], source[54] and study populations and target and source population coverage.

2.3.3 CHARACTERISTICS OF THE STUDY POPULATION

Sociodemographic and Lifestyle Characteristics

Table 2.3.1 presents the sociodemographic characteristics of the study population. The mean age was 34.3 years and age ranged from 18 to 63 years. Ninety-nine women (57%) were also participants in a cohort study on the natural history of HPV in Nunavik, for which cervical specimens were obtained at regularly scheduled Pap smears for HPV DNA testing (between the years 2002 and 2009)[23]. The majority of women were employed (75%), but household income was unknown by almost 40% of participants. Over half of the women were either married, living with a partner or in a common-law relationship and almost 70% of the participants had at least some secondary education (7-12 years). The majority of women were current smokers (82%) and were regular or occasional alcohol drinkers (74%).

Table 2.3.1: Sociodemographic and lifestyle characteristics of the study population (n=175).

Characteristic	n (%)
Age[a]	
18-29	70 (40.00)
30-39	47 (26.86)
≥40	58 (33.14)
Currently employed	
Yes	131 (74.86)
No	44 (25.14)
Household income	
Less than $10,000	20 (11.43)
$10,000 to $29,999	35 (20.00)
$30,000 to $49, 999	38 (21.71)
More than $50,000	13 (7.43)
Unsure	69 (39.43)
Years of education	
6 years or less (at least some primary school)	31 (17.71)
7-12 years (at least some secondary school)	119 (68.00)
13 years or more (at least some post-secondary school)	25 (14.29)
Marital status	
Single/widowed/separated/divorced	76 (43.43)
Married/common-law/living with partner	99 (56.57)
Smoking status	
Current-smoker	148 (82.86)
Ex-smoker/never-smoker	30 (17.14)
Alcohol use	
Regularly/occasionally	129 (73.72)
Ex-drinker	46 (26.29)

[a] Mean (SD): 34.33 (11.72), Range: 18-63

Language

Most women spoke Inuktitut and at least one other language (either English or French) (94%). Nine women reported that their only language was Inuktitut, but only two participants used the Inuktitut version and the rest of the respondents answered the questionnaire in English. The nurse recorded the responses of the remaining seven women who only spoke Inuktitut in English versions of the questionnaire.

Reproductive Health and Sexual Behaviour Characteristics

The mean number of lifetime deliveries in the sample was 3.2 (SD= 2.5) and the average age of first delivery was 18.3 (SD= 2.3) (Table 2.3.2). Thirty women (17%) reported never giving birth. Most women (79%) report having had a Pap smear in the past year. Six women had never had a Pap smear, but only two responded to the question asking why they had not gotten screened. The reasons stated related to a lack of continuity of care and apathy towards Pap smears. Abnormal Pap smear results and previous STI diagnosis was reported by 20% and 66% of the sample, respectively. The mean age at first sexual intercourse was 15.2 (SD= 1.9) and ranged from 7 to 22 years. Almost 70% of women reported having between one and five sexual partners in the previous year, but 15% either refused to answer or were unsure of the number of sexual partners they had been with. Over half of the participants reported that they never or rarely use condoms.

Table 2.3.2: Characteristics of the study population relating to reproductive health and sexual behaviour (n=175).

Characteristic	**n (%) or mean (SD)**
Lifetime deliveries	
Mean number (SD)	3.2 (2.5)[a]
Age at first delivery (N=145)	
Mean age (SD)	18.3 (2.3)[b]
Last Pap smear	
Last year	139 (79.43)
Within the last 3 years	12 (6.86)
More than 3 years	17 (9.71)
Never	6 (3.43)
Did not respond	1 (0.57)
Have you ever had a previous abnormal Pap smear result?	
No	82 (48.52)
Yes	34 (20.12)
Unsure	53 (31.36)
Previous diagnosis of a STI	
No	42 (24.00)
Yes	115 (65.71)
Unsure	18 (10.29)
Age at first sexual intercourse (N=169)	
Mean Age (SD)	15.2 (1.9)[c]
Number of sexual partners in the last year	
0	22 (12.57)
1-5	121 (69.14)
6-10	5 (2.86)
Unsure/refuse to answer	27 (15.43)
Condom use	
Always/often	77 (44.00)
Rarely/never	97 (55.43)
Did not respond	1 (0.57)
Knows someone who had cervical cancer	
No	148 (84.57)
Yes	27 (15.43)

[a] Median: 3 , Range: 0-9, [b] Median: 18 , Range: 14-26 , [c] Median: 15 , Range: 7-22

Use of Health Services

The women in this study were frequent users of the health services available in the community, with 49% consulting a health professional four or more times in the past year (Table 2.3.3). The most common reasons for medical visits in the past year were infections (43%) and injuries (22%). Two of the five women that did not consult with a health professional in the past year responded that they were in good health and did not perceive the need to see a health professional, while the other three did not respond to this question. The majority of women were either 'very satisfied' or 'satisfied' with the health care available in their community (85%). Lack of continuity of care, issues surrounding communication and translation, and wait times were reasons why women in this study were 'not really satisfied' or 'not satisfied at all' with the health services in their communities.

Table 2.3.3: The study population's use of health services (n=175).

Characteristic	**n (%)**
Number of consultations with a health professional in the past year	
4 visits or more	86 (49.14)
1-3 visits	84 (48.00)
None	5 (2.86)
Reason for medical visits in past year*	
Infections	73 (42.94)
Injuries	37 (21.76)
Obstetrics/gynaecological	17 (10.00)
Follow-up/check-up	17 (10.00)
Social support	6 (3.53)
Heart/blood pressure	6 (3.53)
Medication	4 (2.35)
Headache	4 (2.29)
Bones/joints	3 (1.76)
Stomach/GI	2 (1.18)
Substance abuse support	1 (0.59)
Overall satisfaction of health care in community	
Very satisfied	30 (17.14)
Satisfied	118 (67.43)
Not really satisfied	23 (13.14)
Not satisfied at all	4 (2.29)
* Only includes those who have seen a health professional (N=170)	

2.3.4 KNOWLEDGE, ATTITUDES AND BELIEFS ABOUT HPV

HPV Awareness and Knowledge

A total of fifty-five women (31.43%) had heard of HPV prior to their participation in this study. The majority of women who had heard about HPV reported that they heard about it from a health professional/through the health centre (40%) or from the media (20%).

Table 2.3.4 displays responses to the questionnaire items pertaining to knowledge about HPV from only the participants who had previously heard of HPV. The proportion of women answering the HPV knowledge questions correctly ranged from 44% to 67%. Almost 70% of women knew that having multiple sexual partners is a risk factor for HPV, although only half reported that they knew that HPV is a sexually transmitted infection. About half of the women who had heard about HPV knew that there was a causal relationship between HPV and cervical cancer (knew that the long-term effect of persistent HPV was cervical cancer). The possible asymptotic nature of HPV infection was known by 56% of the participants who had heard about HPV. Over 40% of women knew that the contraceptive pill does not offer protection against HPV and 49% knew that HPV was common in sexually active adults. For each HPV knowledge question, there was a fair proportion (20-40%) of women who responded that they were unsure or did not know the answer.

Only 4 (7.3%) women who had heard about HPV knew the correct answer for all six HPV knowledge questions and another 4 (7.3%) women did not respond with the correct answer to any of these questions (Table 2.3.5). Almost half of the women correctly answered 3 or 4 questions.

There were no statistically significant differences in the proportions of women answering the HPV questions correctly or hearing about HPV between women who were participants in the cohort study and those who were not (data not shown).

Table 2.3.4: HPV knowledge among women who have heard about HPV (n=55).

Question	n (%)
Where did you hear about HPV?	
Health professionals/health centre	22 (40.0)
Media	11 (20.0)
Family	2 (3.6)
Friends	3 (5.5)
School	2 (3.6)
Did not respond	15 (27.3)
What do you think HPV is?	
Sexually transmitted infection	28 (50.9)
Respiratory disease	2 (3.6)
Gastrointestinal disease	3 (5.5)
None of the above	10 (18.2)
Do not know	12 (21.8)
Is HPV infection common in sexually active adults?	
Yes	27 (49.1)
No	7 (12.7)
Unsure	21 (38.2)
What is the long-term effect of persistent HPV infection?	
Cervical cancer	29 (52.7)
Disappears and there are no long-term effects	6 (10.9)
Infertility	4 (7.3)
Unsure	16 (29.1)
True or False: The contraceptive pill protects against HPV infection	
False	24 (43.6)
True	16 (29.1)
Unsure	15 (27.3)
What increases the risk of contracting HPV?	
Multiple sexual partners	37 (67.3)
Bad hygiene	5 (9.1)
Sharing underwear or towels	1 (1.8)
Toilet seats	1 (1.8)
Unsure	11 (20.0)
If one is infected by HPV, one will:	
Not necessary feel or know about it	31 (56.4)
Have fever	5 (9.1)
Have a headache	4 (7.3)
Unsure	15 (27.3)

Note: Bolding indicates correct response.

Table 2.3.5: Distribution of the number of HPV knowledge questions answered correctly by study participants who had heard of HPV (n=55).

Number of questions answered correctly	n (%)
0	4 (7.27)
1	5 (9.09)
2	7 (12.73)
3	15 (27.27)
4	12 (21.82)
5	8 (14.55)
6	4 (7.27)

Predictors of HPV Awareness

Univariate Analysis

Univariate analysis of sociodemographic, lifestyle and reproductive health covariates showed two factors to be significantly associated with HPV awareness (Table 2.3.6). HPV awareness was strongly associated with having greater or equal to 13 years of education (OR: 4.31, 95%CI: 1.39-13.41) and knowing someone with cervical cancer (OR: 4.07, 95%CI: 1.74-9.51).

Hearing about HPV was not significantly associated with age, employment, marital status or any of the health and sexual behaviours surveyed. There were positive, although insignificant associations between HPV awareness and current employment, having more sexual partners in the previous year, older age at first intercourse and history of Pap smear in the previous three years. Current smoking status, seeing a health professional four or more times in the previous year, condom use and history of previous abnormal Pap smear had negative associations with HPV awareness, although they were not significant.

Multivariate Analysis

Age-adjusted analysis

The associations between HPV awareness and having greater or equal to 13 years of education and knowing someone with cervical cancer remained significant in the age-adjusted analysis (Table 2.3.6). The age-adjusted estimates for the associations between HPV awareness and each covariate remained similar to the univariate analysis estimates.

Table 2.3.6: Univariate and age-adjusted estimates of associations between awareness of HPV* and sample characteristics (n=175).

Characteristic	Univariate OR (95% CI)	Age-Adjusted OR (95% CI)
Age (per year)	0.998 (0.97-1.03)	--
Current employment		
No	Reference	Reference
Yes	1.30 (0.61-2.78)	1.30 (0.61-2.78)
Years of education		
6 years or less	Reference	Reference
7-12 years	1.06 (0.43-2.60)	1.10 (0.43-2.84)
13 years or more	**4.31 (1.39-13.41)**	**4.51 (1.38-14.74)**
Marital status		
Single/widowed/separated/divorced	Reference	Reference
Married/common-law/living with partner	1.10 (0.58-2.10)	1.10 (0.58-2.11)
Given birth		
No	Reference	Reference
Yes	1.08 (0.46-2.55)	1.12 (0.45-2.80)
Smoking status		
Former/never	Reference	Reference
Current	0.75 (0.33-1.71)	0.74 (0.32-1.71)
Alcohol use		
Former /never	Reference	Reference
Regularly/occasionally	1.06 (0.51-2.21)	1.06 (0.50-2.23)
Number of consultations with a health professional in the last year		
3 or less	Reference	Reference
4 or more	0.81 (0.43-1.53)	0.81 (0.43-1.53)
Number of sexual partners in the last year		
0	Reference	Reference
1-5	1.52 (0.56-4.12)	1.72 (0.59-5.01)
6-10	1.77 (0.24-13.41)	2.10 (0.26-16.83)
Unsure/refuse	0.33 (0.07-1.53)	0.35 (0.08-1.61)
Age at first sexual intercourse (per year)	1.09 (0.92-1.30)	1.10 (0.92-1.30)
Condom use		
Never/rarely	Reference	Reference
Often/always	0.83 (0.60-1.14)	0.81 (0.59-1.13)
Previous diagnosis of a STI		
No	Reference	Reference
Yes	1.06 (0.49-2.27)	1.05 (0.49-2.28)
Don't know	0.86 (0.25-2.91)	0.85 (0.25-2.91)
Knowing someone who had cervical cancer		
No	Reference	Reference
Yes	**4.07 (1.74-9.51)**	**4.10 (1.75-9.61)**
Previous abnormal Pap smear		
No	Reference	Reference
Yes	0.87 (0.37-2.04)	0.87 (0.37-2.05)
Maybe	0.66 (0.31-1.40)	0.65 (0.30-1.41)
History of Pap smear in previous 3 years		
No	Reference	Reference
Yes	1.36 (0.51-3.67)	1.36 (0.50-3.70)

* From the question "Have you ever heard of HPV?"

Multivariate Model

Variables that have been shown consistently to be associated with awareness of HPV in the current literature were selected for inclusion in the final model. These covariates were age, educational attainment, and history of Pap smear in the previous 3 years. Additionally, the covariate of knowing someone with cervical cancer was selected for inclusion into the final model because it was shown to be important in the univariate analysis. One participant was missing information for one of the covariates, and so the multivariate analysis was performed with the information from 174 women. Having 13 years of education or more (OR= 4.38, 95%: 1.28-15.03) and knowing someone with cervical cancer (OR= 3.53, 95%: 1.44-8.68) had strong independent associations with awareness of HPV. Age was not found to have an effect on HPV awareness in this population and history of Pap smear was shown to have a positive association with HPV awareness.

Table 2.3.7: Multivariate estimates of associations between awareness of HPV* and sample characteristics (n=174).

Characteristic	**Univariate OR (95% CI)**	**Multivariate OR (95% CI)**
Age (per year)	0.998 (0.97- 1.03)	1.01 (0.98- 1.04)
Years of education		
6 years or less	Reference	Reference
7-12 years	1.06 (0.43-2.60)	1.28 (0.48-3.43)
13 years or more	**4.31 (1.39-13.41)**	**4.38 (1.28-15.03)**
Knowing someone who had cervical cancer		
No	Reference	Reference
Yes	**4.07 (1.74-9.51)**	**3.53 (1.44-8.68)**
History of Pap smear in previous 3 years		
No	Reference	Reference
Yes	1.36 (0.51-3.67)	1.44 (0.51-4.09)

* From the question "Have you ever heard of HPV?"

2.4 DISCUSSION

The results that have been presented here represent the partial analysis of data collected with a KAP survey, which focused on cervical cancer and HPV knowledge among Inuit women from Nunavik Quebec. The primary results reported were: 1) awareness of HPV; 2) predictors of HPV awareness; and 3) level of knowledge about HPV and its relationship to cervical cancer. By providing an understanding of the current level of knowledge about HPV, these results offer a starting point for future community-based health promotion and prevention programs concerning cervical cancer.

2.4.1 AWARENESS OF HPV

Overall, women in this population had a low level of awareness about HPV, with only 31% reporting that they had previously had heard of HPV. However, the gap between the current biomedical knowledge and public perception of HPV in this population is no larger than that found in other studies surveying knowledge in non-aboriginal populations. Between the years 2004-2007, the general public's awareness of HPV was measured in the USA, UK, China, Denmark, Iceland, Norway and Sweden. In the majority of these studies, the proportion of women who had heard about HPV was low, in the range of 16-41%[75, 76, 78, 81], but the latest nationally representative survey in the USA found a much higher level of awareness (84% in 2007)[74]. In another study, only 15% of respondents had heard of HPV in a sample of a 500 adults from Quebec City[82]. The level of HPV awareness among Inuit women from Nunavik falls in the range found by previous population-based studies, although none measured HPV awareness in the years 2008 or 2009, when our study was conducted.

We hypothesized that HPV awareness would be low in this population, but we expected it to be higher than the level reported for several reasons. Firstly, over 55% of the women in this study were part of a cohort on the natural history of HPV in Nunavik, and were told at recruitment into the cohort study about the link between HPV infection and cervical cancer. Additionally, information about HPV and the importance of regularly attending Pap screening was given in English and Inuktitut on the local radio stations in the two recruitment communities approximately 3 times a year (starting in 2002). The radio is a popular medium in these communities, and is especially popular around lunch hour, which is

when these announcements were made. Finally, our study was conducted during the initiation of a mass vaccination campaign for the HPV vaccine in Nunavik. Although the age group targeted by the vaccination campaign (10-18 year olds) was younger than our participants, informed consent was needed for vaccination from the guardian of these adolescents. Relatively higher proportions of hearing about HPV have been found in studies reporting HPV awareness after the initiation of the HPV vaccination campaign[74, 116, 121].

The discrepancy between the expected and observed level of awareness and knowledge about HPV may be partially explained by the cultural ways of knowing and sharing knowledge in Inuit communities. In a study about Inuit experiences of tuberculosis in Nunavut, a territory of Canada that covers most of Eastern Arctic, it was found that the Inuit are modest concerning their knowledge and will only recount knowledge or experiences about which they are absolutely certain[135]. Based on these findings, it is possible that participants who had heard about HPV would have responded that they had not heard of HPV if they were not absolutely certain they knew about it. By answering that they did not hear about HPV, these women would have avoided the possibility of answering questions inaccurately. This concept may also be reflected in the considerable proportion of women who responded that they were uncertain about each HPV knowledge question, although in another study that provided the 'unsure' option it was also frequently choosen[110].

2.4.2 PREDICTORS OF HPV AWARENESS

In this population of Inuit women, we found education level and knowing someone with cervical cancer to be associated with a higher level of awareness of HPV. Education has been shown to be predictor of HPV awareness[74-76, 78]and knowledge[100, 103, 105, 111] in the previous literature. In one study, it was found that HPV knowledge was correlated with higher academic skills measured from test scores[136]. The cross-sectional nature of our data does not allow us to investigate causality and therefore the mechanism of the effect of education is unknown. It may be that women with more education have better health literacy and are better able to understand news articles and conversations with health professionals about HPV. This may be especially important, given the complexity of HPV infection and the fact that the readability level of articles on the HPV vaccine in Canadians newspapers has been found to be higher than recommended for the general public[137].

One study also found that knowing someone with cervical cancer was a determinant of hearing about HPV and cervical cancer[114]. Women who know someone with cervical cancer may seek more information about its cause, symptoms and risk factors than the general population. In the literature, awareness of HPV has frequently been shown to be associated with history of Pap smear screening[75, 78, 138]. Although not a significant relationship in our study, we found it was positively associated with having heard of HPV. It is unclear if women attend cervical cancer screening because they have heard of HPV or if they hear about HPV when they attend screening. We failed to find a significant association between awareness and age, which has been previously reported[74, 76, 78-81]. The relatively small number of women above the age of 60 may help explain this irregularity.

When interpreting the relationships between HPV awareness and both education level and knowing someone with cervical cancer, it is important to be aware that because HPV awareness is a relatively common outcome in this population (above 30%), the odds ratios derived from the logistic regression analysis likely overestimate the risk ratio[139]. This may explain the large magnitudes of association between HPV awareness and sample characteristics. Further, this study was underpowered to detect many robust associations, evidenced by the wide confidence intervals.

2.4.3 LEVEL OF HPV KNOWLEDGE

Only 53% of the women who had heard about HPV knew that it causes cervical cancer. Studies that have determined this knowledge item with closed-format questions reported similar proportions of understanding[75, 80, 100, 115, 140], although in populations of university students the understanding was much higher[79, 121, 129].

Among women who had heard of HPV, over half knew that HPV infection could be asymptomatic and that having multiple sexual partners increases the risk of acquiring an HPV infection (or that HPV is a STI). This finding is consistent with estimates in previous papers with comparable study design[75, 79, 80, 100, 110, 116]. Some misconceptions about HPV are present among our population as 30% thought that the contraceptive pill protects against HPV infection and some thought that symptoms of HPV infection included headache and

fever. These results suggest that being aware of HPV does not guarantee accurate knowledge about HPV and its relation to cervical cancer.

The majority of women who were aware of HPV heard about it from their health provider or through the media, often the radio. Both these educational interventions are oral, which is the preferred method of learning among the Inuit[135]. However, it was clear that some of the message about HPV was lost or not completely conveyed. Educational interventions using community health workers to increase cervical cancer screening among women in two different American Indian communities were found to be effective at increasing knowledge about cervical cancer prevention[141, 142]. These interventions involved one-on-one visits with female lay health educators from the community. This model of health promotion may be helpful for increasing knowledge about HPV and cervical cancer among Inuit women in Nunavik.

2.4.4 LIMITATIONS

This study has several limitations that must be acknowledged, namely the non-random recruitment strategy and the method of questionnaire administration.

Non-participation and Selection Bias

Women were recruited into this study through convenience sampling and it was not feasible to collect information about the women who chose not to participant in the study. As a result of this, selection bias could only be assessed in a limited way through the comparison of the sociodemographic characteristics of the study and source population. This was accomplished using published statistics from the 2006 Aboriginal Population Profile for Nunavik[54], and the results of the 2004 Nunavik Inuit Health Survey[73, 143-145]. With this method it was not possible to evaluate differences in number of sexual partners, marital status, and household income between our study population and the general population of Nunavik due to the vast differences in the ways these variables were measured.

Among the population of Nunavik that is older than 15 years, 21% have an elementary school education or less, 57% have some secondary school education, and 22% have obtained a secondary school diploma or above[145]. In our study population, 18% had at least

some elementary school education, 68% had at least some secondary school education, and 14% had at least some post-secondary education. These data suggest that the educational attainment of the study population is similar to that of the general Nunavik population, despite differences in categorization.

The age distribution of our study population was similar to the female population of Nunavik and the source population[54]. Health behaviours such as the proportion of non-smokers and alcohol users were also similar between the study population and the population of Nunavik[143, 144]. Some differences between the populations were found though, such as the slightly higher proportion of women who were employed and had previously given birth in our study population[54, 73].

One concern was that our study population seemed to be frequent users of the health services available in the community, with about half reporting that they visited a health professional four or more times in the past year and almost 80% reported that they had a Pap smear test within the same time period. As women who use health services may have more opportunities for health education, it is possible that women who do not use community health services could have a lower level of awareness and knowledge about HPV than what was found in this sample. The average number of health care visits for the population of Nunavik has not been reported, but one case-control study on suicide reported that among population controls the average number of visits to a health provider in the previous year was 3.6[65]. Also, 82% of the female population of Nunavik reported having a Pap test within the previous 2 years and 60% within the last year[73]. These population estimates suggest although our study population were high consumers of health services it should not be viewed as a selection bias, given the health care use in the general population.

Together, these comparisons suggest that despite the sampling method, our study population is fairly representative of the general population of Nunavik and we can be confident that our results reflect the level of awareness and knowledge about HPV that would be reported by the female population of Nunavik.

Questionnaire Administration

The majority of questionnaires were nurse-assisted, where the questionnaire was administered to groups of women at one time. This was not how the questionnaire was designed, however and as a consequence, there remains the possibility that participants misinterpreted questions and were unable to get clarification from the nurse. When the validity of the results was investigated, it was found that having heard of HPV was highly associated with knowing the correct answers for each knowledge item. Although some misclassification was very possible, it appears that those women who answered that they had heard of HPV actually knew more about HPV than those who responded that those that had not heard of HPV.

2.4.5 STRENGTHS

This research strength's must also be recognized, in spite of the above mentioned limitations. Although selection bias could only be assessed in a limited way, it seems that the study population was fairly representative of the target population. Further, as the population of Nunavik is small we had a high coverage of both source (25%) and target populations (7%) compared to other studies. Despite the sensitive nature of the data collected for this study, there was very little missing information and so we were able to perform a complete case multivariate logistic regression with 174 of 175 study participants. We reported HPV knowledge only among women who had heard of HPV to reduce the influence of chance guessing on the estimates.

The most important strength of this research is its novelty and relevance. This is the first study to comprehensively measure knowledge about HPV in a Canadian Inuit population. As this research is done in collaboration with the Nunavik Regional Board of Health, its results will influence the creation culturally relevant cervical cancer education and prevention materials.

2.4.6 CONCLUSIONS

This is the first study to assess the level of awareness and knowledge about HPV among Quebec Inuit women. Accurate knowledge about HPV and its link to cervical cancer is essential for women to understand and make use of cervical cancer prevention and detection opportunities. This study provides a starting point for the creation of educational activities on cervical cancer and HPV that are relevant for this population.

Our results show that awareness of HPV was low, as was knowledge of the causal link between HPV and cervical cancer. Despite this, the majority of women seem to be aware of the importance of sexual behaviours in the transmission of HPV. Educational attainment and knowing someone with cervical cancer were significant predictors of HPV awareness, but age was not found to influence awareness, as has been commonly reported in the literature.

Although the lack of HPV awareness and knowledge found in this study has been consistently observed in other non-Indigenous populations, it is an important finding because of the high prevalence of HPV in this population. Future research should investigate the most effective method of education for this population, which may include interventions that go beyond the provision of information, to include opportunities for women to use discussion-based-learning to process the complex issues surrounding HPV and cervical cancer [141, 142].

CHAPTER III: HPV DETECTION BY SELF-SAMPLING IN NUNAVIK, QUEBEC: COMPARABILITY AND PREFERENCE TO PROVIDER-SAMPLING

3.1 LITERATURE REVIEW

3.1.1 THE ROLE OF HPV TESTING IN CERVICAL CANCER SCREENING

The inclusion of cervical cytology screening into the Canadian health care system has led to a great reduction in cervical cancer incidence and mortality[51], but noncompliance to screening guidelines continues to be a major risk factor for invasive cervical cancer[40, 41]. In 1998, about 20% of Canadian women aged 20-69 reported not having had a Pap test within the 3 previous years and the majority of cervical cancer cases occur among these unscreened or under-screened women[51]. Factors that predict under-utilization of cervical cancer screening in Canada include older age, lower educational attainment, lower socio-economic status, single marital status, birth place outside Canada, being Aboriginal and negative health and lifestyle characteristics[133, 146, 147]. Additionally, women in rural settings have a higher risk of time-inappropriate screening[133]. Pap smear screening among Aboriginal women has been found to be limited by a lack of knowledge about Pap smears and their importance, feelings of embarrassment and a lack of continuity of care due to high turnover of health professionals[148, 149].

Cervical cytology as a screening test has several limitations, which makes frequent testing over the life course necessary to achieve sufficient protection[150]. The Pap smear test has adequate specificity, but its sensitivity for detection of CIN is lower than previously thought, with unbiased estimates found to be as low as 30%[151]. The labour-intensive test is subjective and dependent on well-collected samples[152]. Finally, the infrastructure needed for frequent repeated screenings and follow-up makes cervical cytology screening programs very expensive.

The limitations of cytology and the knowledge that persistent HR-HPV infection is the primary risk factor for the development of cervical carcinoma has created interest in HPV DNA testing contributing to primary cervical cancer screening, triage of ambiguous cytology results, post-colposcopy management and follow-up of women after treatment[1, 153-155]. HPV testing in primary screening has been found to have a 25% higher sensitivity, but 6% lower specificity than conventional cytology for detection of ASCUS or worse and about a 90% sensitivity for high-grade cervical disease[155]. Delaying screening with HPV testing until a later

age, when fewer transient infections are present increases its specificity[154, 156, 157]. HPV testing, which uses an objective molecular test is reproducible and more easily adapted for automated, high-volume testing than cytology[155, 158]. Screening with a combination of HPV testing and cytology offers a higher sensitivity and negative predictive value, which would allow for an increase in the screening interval[158, 159].

Various screening algorithms, which incorporate HPV testing have been investigated for accuracy and cost efficiency. An algorithm that uses HPV testing as a primary screening tool with cytology for triage of positive tests has been recommended, as it would reduce the referral and over-treatment of women who are likely to have transient infections[154, 155]. In a large RCT, when compared with conventional cytology alone, this screening algorithm was more sensitive in detecting cervical cancer and pre-cancerous lesions and in the case of women above the age of 35, it is more specific[160, 161]. Further, a recent modeling study suggests that HPV testing with cytology triage of positive tests beginning at the age of 25, at intervals of three years in Canada would reduce cervical cancer incidence at a lower cost than the current program[162]

The current American guidelines on the use of HPV DNA testing, state that HR-HPV testing is appropriate for co-testing of women older than 30, triage management of ASCUS in women 21 years and older, triage management of LSIL in postmenopausal women, post-colposcopy management and post-treatment surveillance[163]. Screening can occur at intervals of 3 years in women who are cytology and HPV negative[163]. In Canada, consensus guidelines only recommend HPV-testing in the triage of ASCUS Pap smear results[164].

3.1.2 SELF-SAMPLING

Another advantage of HPV testing is that it can be conducted on vaginal specimens collected by the patients themselves. By avoiding speculum examination, self-sampling has the potential to increase the number of women screened. As self-sampling is a less invasive test, it may be appealing to women who avoid clinician sampling because of previous abuse[165], feelings of embarrassment[149], perceived inconvenience[166], and cultural and religious reasons[167, 168]. A screening program that includes self-sampling could be less costly and thus it would

also have applications in developing countries, where infrastructure costs are prohibitive to the creation and maintenance of extensive cervical cancer screening programs[169].

The practicality of self-sampling has been established, as women have been able to adequately collect high quality samples in situations with only written instructions[170], with verbal and written instructions[171], and in supervised[172] and unsupervised settings[173, 174]. The use of self-collected vaginal specimens for HPV testing is possible because HPV DNA is present in cells that are shed from the surface epithelia of the cervix and vagina of infected women[150]. The feasibility to screen traditionally hard-to-reach women with self-sampling and contact them with their results was demonstrated in a population of previously unscreened homeless and housing-unstable women in Vancouver[175]. In a study where Swedish women who had not attended cervical cancer screening for over 6 years were mailed self-sampling kits, 58% collected specimens and returned them to the laboratory by mail showing that self-sampling at home is technically feasible[176]. In an ethnically diverse group of women from the UK, few reported that self-sampling goes against their cultural or religious beliefs[177]. Self-sampling has also proved to be an acceptable and reliable method for the detection of sexually transmitted diseases in a geographically isolated population[178], further emphasising the potential for self-sampling to increase screening coverage in hard-to-reach populations.

Comparability of Self-Sampling to Clinician-Sampling

The accuracy of self-collected specimens to detect HPV has been investigated with collection devices such as tampons[179], swabs[180], brushes[181], pads[182], cervicovaginal lavages[183], and urine specimens[184]. The Dacron swab is particularly useful as a self-sampling device as it is easy to manipulate[185], does not require any other devices for collection[186] and can be easily processed in the same manner as clinician-obtained samples[185]. It has been suggested that compared to swabs, tampons produce a larger cellular pellet that can be used for further testing, but this comes at the cost of increased processing time[187]. Table 3.1.1 contains a summary of studies that compare the accuracy and agreement of self-collected samples to provider-collected samples where the self-collection device is the swab. In these studies HPV DNA was detected by PCR, most often with PGMY09/11 consensus primers, the second generation Hybrid Capture system (HC2) and RNA-DNA dot blot. Among these 21 studies, 11 used

swabs for both self- and provider-collection, nine used cervical brushes for clinician-collection and one study did not clearly state what collection device was used by the clinician.

The majority of the studies that evaluated the accuracy of an HPV positive sample to detect high grade cervical disease found that the sensitivity of self-collected samples was high, but somewhat lower than clinician-collected samples[169, 173, 184, 188-193]. The specificity, positive predictive value and negative predictive value of self-collected samples for the detection of HSIL were also found to be comparable to clinician-collected samples. It is important to note that many of these studies suffer from verification bias[157, 188, 190, 191], as only women with abnormal Pap smears or positive HPV tests were referred to colposcopy (the gold standard for cervical lesion detection). When verification bias was avoided or corrected, the sensitivity of self-collected samples generally remained high and comparable to the sensitivity of provider-collected samples[173, 189, 193, 194], except in one study were an undesirable sensitivity was found[195]. In one study, 5% of the women who tested negative with cytology and HPV testing were randomly chosen for colposcopy with biopsy to correct for verification bias[173]. The sensitivity to predict CIN2/3 or cancer was 81% for self-collected samples and 100% in provider-collected samples. Sellors et al.[184] compared self-samples obtained by vaginal swab, vulvar swab and urine to clinician-collected cervical swabs for accuracy in the detection of high grade cervical lesions or invasive cancer in the absence verification bias. This study revealed that the sensitivity to detect HSIL was highest for clinician-collected specimens and that the sensitivity of self-collected samples decreased as they were obtained further from the cervix, although specificity increased. Finally, self-sampling has been shown to be as sensitive as [173] or more sensitive[157, 169, 188, 190] than the Pap smear, although less specific[157, 173, 188].

Self-sampling has been shown to be comparable to clinician-sampling for the detection of virological endpoints. In a recent meta-analysis, which included studies with all types of self-sampling devices, the overall agreement between sampling methods for the detection of any HPV (kappa (κ):0.66 , 95% CI: 0.56-0.76) and HR-HPV (κ: 0.66, 95% CI: 0.50-0.82) was good[196]. In studies that used swabs for self-collection the percent agreement for the detection of HPV DNA was high, ranging from 77% to 96% (κ range: 0.48-0.84) for the detection of any HPV and 74% to 99% (κ range: 0.37-0.96) for the detection of HR-HPV[157, 169, 171, 174, 180, 184-188, 191-195, 197]. The agreement for the detection of HR-HPV was similar in studies that used

brushes for clinician-collection and those that used swabs for clinician-collection. One study compared sampling method agreement for the detection of HR-HPV between HC2 and PCR diagnostic methods and found the agreement was slightly higher for PCR methods[169]. Similarly, the range of agreement estimates for the detection of HR-HPV was higher for studies that used PCR (κ range: 0.60-0.84)[169, 174, 180, 185, 187, 192, 193, 195] than those that used HC2 (κ range: 0.37-0.96)[157, 173, 184, 188, 191, 194, 197]. Several studies that measured low-risk and high-risk HPV types did not separately report the agreement of sampling methods to detect HR-HPV[171, 186, 191]. In the two studies that reported the agreement results for LR-HPV types, the agreement between sampling methods for the detection of HR-HPV was higher than the agreement for LR-HPV[180, 185].

Self-sampling has been shown to be comparable to provider-directed sampling for the detection of virological[196], and pre-cancer and cancer outcomes[173, 184, 193], although self-sampling has a somewhat lower sensitivity to detect cervical disease than clinician-sampling. However, the potential gains in screening coverage provided by self-sampling would compensate for its lower screening accuracy.

Acceptability of Self-Collected Samples for HPV Testing

Women must view self-sampling as an acceptable screening method if it is going to play a role in increasing screening coverage and reducing cervical cancer mortality. To determine if women would adopt self-sampling as a screening method, the construct of 'acceptance' has been measured in a variety of ways. Acceptability, when measured with indices created with items such as discomfort, embarrassment, pain, privacy, anxiety, trust in test results, unpleasantness, and confidence in ability collect sample has been found to be high[170, 198, 199]. Several studies used proxies for acceptance such as women's willingness to provide a self-sample for the study or in the future[172, 177, 187, 200], although women were not always provided with a chance to try self-sampling[177]. In these studies there was a large proportion of women willing to provide self-samples[172] or get tested in the future[177, 187]. Satisfaction with the self-sampling experience was used as a measure of acceptance in one study, which found that among a sample of Hispanic American women, the majority reported 'excellent' or 'very good' satisfaction with the convenience and ease of use of the test, understanding the results and their overall experience [201].

Although women generally reported a high acceptance of self-sampling, their sampling method preferences were found to be more variable. Preference towards self-sampling with either swabs or brushes was high in previously screened Mexican (68%)[199], American (80%)[202], Haitian immigrant (87%)[167], and German (94%)[203] women. Additionally, when asked to rank sampling methods Canadian colposcopy patients consistently put self-sampling methods (urine, vulvar and vaginal sampling) before provider-sampling of the cervix[184]. Preference for self-sampling was lower in populations of minority women (32%)[204] adolescents (27%)[198], internal medicine patients (63% had no preference)[181] and women attending cervical cancer screening (54% preferred provider-sampling)[194].

In general, women reported that self-sampling was easy to do[167, 170, 181, 204] and some of the reasons it was appealing were that it was less embarrassing[30,61,65], uncomfortable[170, 199], unpleasant[170] and anxiety inducing[170] and more private[199] than a clinician examination. Among a small group of women from Ontario, self-sampling was perceived to be an attractive test because it would provide faster and more definitive results compared to the Pap test[205]. However, even among populations with a strong preference for self-sampling, women have expressed concern about their ability to collect adequate specimens and generally had more confidence in the test when conducted by a clinician[170, 177, 199, 204]. Most women reported that self-sampling was less painful than speculum examination, but some women did experience pain when collecting their sample[167, 199, 204].

Ten studies have explored the factors affecting women's preference and acceptance to self-sampling. Ethnicity has been established as a factor associated with sampling method preference[204], acceptability scores for self-sampling[170, 198], willingness to provide a self-sample for a study[202] and overall satisfaction with self-sampling experience[201], although one study found that intention to use self-sampling in the future was not associated with ethnicity[177]. Younger age was shown to be associated with higher self-sampling acceptability scores among a sample of Mexican women[199] and satisfaction with self-sampling in a sample of Hispanic American women[201]. Education also seems to be an important indicator of women's feelings towards self-sampling, as higher educational attainment was associated with preference[204] and satisfaction[201] with self-sampling in populations from the USA. Further,

one study that looked at the acceptability of self-sampling in rural China found that women with more education were more comfortable with performing the test[206]. Other characteristics found to influence self-sampling preference and acceptability were higher income[199], study recruitment site[204], marital status[170], but these characteristics were found inconsistently across populations[194, 201, 202].

Given the effect of ethnicity on women's attitudes towards self-sampling and their ability to collect adequate samples, it is important that the comparability and acceptability of self-sampling be assessed in a population before it is integrated into their cervical cancer screening program[167, 170, 198, 201, 202, 204, 206]. Despite numerous reports on self-sampling, there are currently no published studies on its feasibility, comparability or acceptability in the Canadian Inuit population.

Table 3.1.1: Summary of published studies comparing the accuracy and agreement of self-collected samples to provider-collected samples for the detection of HPV DNA in women, where swabs were used as the self-collection device.

Reference (First author, year)	Location/Setting/ Population/Number analyzed	Clinician Collection Device /Diagnostic Method	Accuracy to Predict Cervical Disease and HPV Prevalence		Agreement in the detection of HPV	
			Self-sampling results	Provider-sampling results	% agree-ment	Kappa
Moscicki, 1993[186]	• USA • Study participants previously tested HPV+ • N=114	Swab, RNA-DNA dot-blot	To predict abnormal cytology: Sens: 80* Spec:76* PPV:33* NPV :96*	To predict abnormal cytology: Sens: 73* Spec:75* PPV:31* NPV:95*	Any: 91	Any: 0.84*
Sellors, 2000[184]	• Canada • Colposcopy clinic • Mean age:31.5 • N=200	Brush, HCII and PCR	To predict HSIL/CC: Sens: 86 Spec:54 PPV:43 NPV:91 HR-HPV += 58%	To predict HSIL/CC: Sens: 98 Spec:52 PPV:46 NPV:99 HR-HPV += 62.5 %	NR	HR: 0.76
Wright, 2000[188]	• South Africa • Community • Previously unscreened 35-65 years (median 39) • N=1365	Brush, HCII	To predict HSIL/CC: Sens: 66 Spec: 81* PPV:13* NPV:98* HR-HPV +=21.3%	To predict HSIL/CC: Sens: 84 Spec:83* PPV:17* NPV:99* HR-HPV +=21.5%	HR: 82	HR: 0.45
Belinson, 2001[189]	• China • Community-based • N=1997	Plastic spatula and brush, HCII	To predict HSIL/CC: Sens: 83 Spec: 86 PPV:21 NPV:99 HR-HPV +=17%	To predict HSIL/CC: Sens: 95 Spec: 85 PPV:23 NPV: 100 HR-HPV +=18%	NR	NR
Gravitt, 2001[185]	• USA • Study participants • 268	Swab, PCR with PGMY09/11/ HMB01 primers and reverse line blot (RLB)	Any HPV+=34.3%	Any HPV+= 32.8%	Any: 88.1 HR: 73.6 LR: 52.9	Any: 0.73 HR: 0.78 LR: 0.66
Rompalo, 2001[171]	• USA • Clinic at army medical centre • 18-59 • N=319	Swab, PCR with PGMY09/11/ HMB01 primers	To predict abnormal cytology: Sens:54* Spec: 68* PPV: 28* NPV:86* Any HPV+=33.2%	To predict abnormal cytology: Sens:58* Spec: 68* PPV: 30* NPV:88* Any HPV+=35.1%	Any: 76.8	Any: 0.48
Chang, 2002[157]	• Taiwan • Community-based • Median age: 51.3 years • N=1194	Brush or spatula, HCII	To predict HSIL/CC: Sens: 96 Spec:92 PPV:35 NPV:99* HR-HPV +=12.1%	HR-HPV+= 13%	HR: 99.1	HR: 0.96

Harper, 2002[187]	• USA • Colposcopy clinic • N=103	Swab, PCR with PGMY09/11 and HMB01 primers and RLB	HR-HPV+=31%	HR-HPV+=35%	HR: 88	HR: 0.74+
Lorenzato, 2002[195]	• Brazil • Screening program participants • 16-88 years (mean 38.1) • N=253	Brush and spatula, PCR with PGMY09/11 primers, genotyped with restricted fragment length polymorphism	To predict HSIL/CC: Sens: 50* Spec:86* PPV:53* NPV:82* Any HPV+=23% HR-HPV+=17%	To predict HSIL/CC: Sens: 75* Spec:88* PPV:69* NPV:91* Any HPV+=29% HR-HPV+=26%	NR	Any: 0.62 HR: 0.60
Salmeron, 2003[190]	• Mexico • Patients of cervical cancer screening services • 15-85 years (mean: 42.5) • N=7732	Brush, HCII	To predict HSIL/CC: Sens: 71 Spec:89 PPV:9 NPV: 100 HRHPV +=11.6%	To predict HSIL/CC: Sens: 93 Spec:92 PPV:14 NPV: 100 HRHPV +=9.3%	NR	NR
Kahn, 2004[192]	• USA • Teen health centre • Age 14-21 • N=99	Swab, PCR with PGMY09/11 primers and RLB	To predict LSIL/HSIL/CC: Sens: 63 Spec:56 Any HPV+= 45% HR-HPV += 38%	To predict LSIL/HSIL/CC: Sens:63 Spec: 60 Any HPV+= 42% HR-HPV+= 35%	Any: 85	Any: 0.72
Lack, 2005[172]	• Gambia • Study participants • N=210	Brush, PCR with gp5+/6+, ELISA	Any HPV+= 16.3%	Any HPV+= 15.3%	NR	NR
Petignat, 2005[180]	• Canada • HIV-positive women from cohort study • 10-70 years • N=146	Swab, PCR with PGMY09/11 primers and RLB	Any HPV += 65.1% HR-HPV += 50.75% LR-HPV += 46.6%	Any HPV += 53.4% HR-HPV += 42.5% LR-HPV += 33.6%	Any: 87.0 HR: 91.8 LR: 85.6	Any: 0.73 HR: 0.84 LR: 0.71
Karwalajtys, 2006[194]	• Canada • At annual cervical screening a) 15-49 years, N=307 b) 50 years and older, N=152	Swab, HCII	a) HRHPV +=20.8 % b) HR-HPV += 9.9%	a) HR-HPV +=17.6 % b) HR-HPV += 8.6%	HR: a) 85.7 b) 89.5	HR: a) 0.54 b) 0.37
Seo, 2006[193]	• South Korea • Women with abnormal Pap smears • 17-64 years (mean 46.2 years) • N=118	Swab, PCR with HPVDNAchip™ oligonucelotide probes	To predict CIN3/CC: Sens: 91 Spec: 29 PPV: 41 NPV:85 HR-HPV+= 78%	To predict CIN3/CC: Sens:88 Spec: 33 PPV: 42 NPV: 83 HR-HPV+= 75%	HR: 93.2	HR: 0.81
Jones, 2007[191]	• South Africa • Community health centre	Brush a) HCII b) PCR with	To predict HSIL/CC: a) Sens: 88+ Spec: 61+	To predict HSIL/CC: a) Sens: 100+ Spec: 65+	a) HR:81.5 b) Any: 85.6	a) HR: 0.61 b) Any: 0.71

	• 18+ • N= a) 222 b) 90(of 222)	RLB	PPV: 8+ NPV: 99+ b) NR a) HR-HPV+= 41% b) Any HPV+= 42.2%	PPV: 10+ NPV: 100+ b) NR a) HR-HPV+= 37.8% b) Any HPV+= 43.3%		
Safaeian, 2007[197]	• Uganda • Cohort study participants • 15-49 years • N=606	Swab, HCII and PCR	HR-HPV+= 19%	HR-HPV+= 19%	HR: 92	HR: 0.75
Szarewski, 2007[173]	• UK • Attending for routine Pap smear • N=920	Brush, HCII	To predict HSIL/CC: Sens: 81 Spec:82 PPV:10 NPV:99	To predict HSIL/CC: Sens: 100 Spec:85 PPV:13 NPV:100	NR	NR
Winer, 2007[174]	• USA • Cohort study participants a) 23-32 years (mean 27.9), N=296 b) 18-25 years (mean 20.7), N= 211 • * Patients collected more than 1 samples	Swab, PCR with PGMY09/11 primers and RLB	a) HR-HPV+=21.2% Any HPV+=27.6% b) HR-HPV+= 12.9% Any HPV+=16.7%	a) HR-HPV+= 16.9% Any HPV+=23.3% b) HR-HPV+=12.8 % Any HPV+=15.5%	Any: a) 86.5 b) 95.7	Any: a) 0.65 b) 0.84
De Alba, 2008[201]	• USA • Community-based • 18 years and older • N=386	NR , HCII	To predict LSIL/HSIL/CC: Sens: 55 Spec:79 PPV:6 NPV:99 HR-HPV += 18.1%	To predict LSIL/HSIL/CC: Sens:50 Spec: 94 PPV: 15 NPV:99 HR-HPV+= 7%	HR: 87.8	NR
Sowjanya, 2009[169]	• India • Community based • 25 years and older (median 32) • N=432	Swab a) HCII b) PCR with PGMY09/11 primers and RLB	To predict HSIL/CC: a) Sens: 82+ Spec:88+ PPV:15+ NPV:100+ b) Sens: 91+ Spec: 86+ PPV: 14+ NPV: 100+ a) HR-HPV +=14.1% b) Any HPV += 25.9% HR-HPV +=16.4%	To predict HSIL/CC: a) Sens: 91+ Spec:82+ PPV:12+ NPV:100+ a) b) Sens: 100+ Spec: 82+ PPV: 12+ NPV: 100+ a) HR-HPV +=20.2% b) Any HPV +=27.1% HR-HPV +=20.6%	a) HR: 90.8 b) Any:89.6 HR: 92.6	a) HR: 0.7 b) Any: 0.7 HR: 0.8

Note: Adapted from Stewart et al., 2007[207].* = Calculated by Stewart et al., 2007[207], + =Calculated by author, NR= Not reported, Any= Any HPV type, HR= any HR-HPV type, LR= any LR-HPV, Sens= Sensitivity (%), Spec= Specificity (%), PPV=Positive Predictive Value (%), NPV=Negative Predictive Value (%).

3.2 METHODOLOGY

3.2.1 OBJECTIVES

The objectives of this study were to:

1) Assess the comparability of self-collected cervicovaginal samples and provider-collected cervical samples for detection of HPV DNA among Inuit women participating in an ongoing cohort study in Nunavik, Quebec.
2) Determine the demographic and behavioural predictors of preference for self-collection of cervicovaginal specimens in this population.

Based on the current literature, it was hypothesized that self-sampling will be highly comparable with provider-sampling. It was expected that a majority of women will prefer self-sampling to provider-sampling and determinants of preference towards self-sampling will include higher education level and younger age.

3.2.2 STUDY DESIGN

Overview

A measurement study with a cross-sectional design was used to investigate the above listed objectives. This study utilized HPV DNA test results from paired specimens collected from the genital tract by study participant and health provider. Information from a baseline questionnaire administered at cohort entry (Appendix 3) and a sampling-method preference questionnaire (Appendix 4) were also used.

Target Population

The target population of this study was Inuit women aged 18 to 69 years in Nunavik, Quebec. The source population was a cohort, formed between 2002 and 2010 that was comprised of 554 Inuit women between the ages of 15 and 69 living in Nunavik, Quebec. Women were invited to participate in the cohort study by nurse-practitioners as they presented for regularly scheduled Pap smears at clinics serviced by the Ungava Tulattavik Health Centre in four different communities (Kuujjuaq, Kangiqsualujjuaq, Kangiqsujuaq and Kangirsuk). Additionally, some women were recruited to the cohort through a mobile mammography screening program in communities along the coast of Hudson Bay and

Ungava Bay between August and October 2004. The prevalence and age distribution of HPV infection in this cohort has been previously described[23].

Eligibility Criteria

Women were eligible for this self-sampling sub-study if they:

1) Self-identified as Inuit
2) Were between 18 and 69 years of age
3) Were born in Nunavik, Quebec
4) Had an intact uterus and had no current referral for hysterectomy
5) Did not report use of vaginal medication in the last 2 days
6) Did not report treatment for cervical disease in the last 6 months
7) Were no more than 12 weeks pregnant

Subject Recruitment

Recruitment for the self-sampling sub-study occurred between December 2007 and June 2010 in two communities of Ungava Bay, Nunavik, which were chosen for their size. Recruitment was done by nurse practitioners who systematically asked all non-enrolled cohort participants if they would like to participate in the study as they came to the clinic for regularly scheduled Pap tests. If they were interested, the nurse practitioner determined their eligibility.

Ethical Considerations

Written informed consent was obtained from all study participants with a standardized consent form at study entry (Appendix 4). Ethical approval for this study was obtained from the McGill Institutional Review Board.

3.2.3 DATA COLLECTION

Baseline Questionnaire and Medical Chart Review

At cohort entry, a baseline questionnaire (Appendix 3) was administered by a nurse practitioner to collect baseline information on sociodemographic characteristics, medical history, lifestyle factors, and reproductive and sexual history. The questionnaire was adapted from a previously validated questionnaire developed by Dr. Eduardo Franco for use in HPV

community-based surveys. This research instrument was validated for this population by a steering committee comprised of members from the Nunavik community, the Tulattavik Health centre and the Nunavik Regional Board of Health and Social Services. Pilot testing was conducted in a group of ten Inuit women to ensure comprehensibility and ease of use. The questionnaire was provided in English, French and Inuktitut and to ensure accuracy of translation the Inuktitut version was back-translated into English.

Medical chart reviews were performed with a standardized form to extract additional information on the medical history of study subjects, including reproductive history, cervical cancer screening history, results from previous Pap smears, and diagnoses of STIs.

Biologic Samples

After the eligibility was determined and the consent form completed, the nurse practitioner explained the procedure for self-collection of vaginal samples and study participants were provided with a diagram outlining the procedure (Appendix 5). Consenting women were asked to collect a self-sample, unsupervised in the examination room just before the nurse practitioner conducted a pelvic examination with direct cervical cell sampling. The Dacron swab was used as the method of collection by both study participant and nurse-practitioner.

Women were asked to squat or put one foot up on chair and insert a sterile 15 cm Dacron swab into the vagina up to the vault and to rotate the swab 3 times in the vaginal vault. To preserve the integrity of the epithelial cells, the swab was then placed in a dry tube and kept at 4°C until they were transported on wet ice to Dr. François Coutlée's laboratory in Montreal for HPV typing.

The nurse practitioner then collected ectocervical and endocervical cells through direct cervical sampling with a Dacron swab. Specimens collected by the clinician were preserved in a tube that contained 1.5mL of a methanol-based liquid, PreservCyt (Cytyc Corporation, Boxborough, MA). Cell suspensions were kept at 4°C until they are transported. This method has been used on this cohort since 2002 and has been proven successful.

Cervical smear slides were created with the sampled ectocervical and endocervical cells and sent to Quebec City to be read blindly by an experienced cytopathologist. Cytopathology reports were based on the Bethesda classification systems for cytological diagnoses[52]. The results were sent back the treating physician and were added to the medical file.

Laboratory Analysis

Cervical cell suspensions were centrifuged at 1300 x g for 15 minutes at 22ºC. The supernatant was discarded, the cell pellet was left to dry and it was resuspended in 300 µl of 20mM Tris buffer, pH 8.3. DNA was purified with Master Pure (Epicentre, Madison, WI)[208]. The quality of the DNA samples was assessed by amplifications of a 268-bp region of the human β-globin gene using GH20 and PC04 primers. Subjects with a negative β-globin result were not considered to have a baseline HPV result of acceptable quality.

HPV DNA was detected by PCR amplification using PGMY09-PGMY11 consensus primers and quality controlled Line Blot assay (Roche Diagnostics), as previously described[209]. Specimens were coded and given to laboratory personnel who were blinded to any information about the subjects from which the samples were obtained. Standard precautions were taken to prevent contamination. This method is widely used and has been validated. HPV genotyping was accomplished with oligonucleotide probes to identify 36 genital HPV types: 6, 11, 16, 18, 26, 31, 33, 34, 35, 39, 40, 42, 44, 45, 51, 52, 53, 54, 56, 58, 59, 61, 62, 66, 67, 68, 69, 70, 71, 72, 73, 81, 82, 83, 84, and 89.

Preference Questionnaire

To assess women's preferences for sample collection method, a short standardized questionnaire (Appendix 4) was administered to study participants after both methods of specimen collection were completed. Women were asked with an open ended question about which sampling method they preferred (self-collection or provider-collection) and why.

Data Management

A unique identifier was assigned to each study participant at recruitment to link questionnaire, medical chart review and laboratory results. In the databank, all identifying information except the unique identifier was excluded to ensure confidentiality of study

participants. Access to data collection sheets and consent forms was restricted to research team members.

3.2.4 STATISTICAL ANALYSIS

Study Variables

HPV Status

Samples were considered HPV positive if they were positive for any of the 36 HPV types and also positive for β-globin. Samples were considered HPV negative if they were negative for all HPV types.

HPV types were classified as either high risk (HR) or low risk (LR) based on their oncogenic potential. Probable and possible HR types were grouped with HR types that have more established evidence for oncogenic potential 16, 18, 26, 31, 33, 34, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 67, 68, 69, 70, 73, and 82[10]. Unclassified types were grouped with low risk types: 6, 11, 40, 42, 54, 55, 61, 62, 71, 72, 81, 83, 84, and 89. HPV types were also classified into papillomavirus species groupings (α1, α3, α5, α6, α7, α8, α9, α10, α11, α13 and α15) to examine species-specific agreement measures[13]. Finally, species were grouped based on their preference for specific niches in the genital tract; α3 and α15 grouped as vaginal species and α5, α6, α7, α9, and α11 grouped as cervical species[210].

Method of Collection Preference

Women's preference for self-sampling or provider-sampling was classified from the preference questionnaire.

Characteristics of Participants

Sociodemographic, lifestyle, reproductive, and sexual history information were collected from the questionnaire administered at cohort entry and baseline medical chart review. The covariates used in this study were age, marital status, employment status, and education level, smoking status, alcohol use, number of lifetime deliveries, use of any birth control, history of Pap smear in previous 3 years, self-reported history of STI, age at first sexual intercourse, and number of lifetime sexual partners.

Education was originally categorized on the baseline questionnaire as less than Grade 9, some high school or graduated high school. Few women (n=9) reported that they had graduated high school, so they were grouped with those who had at least a Grade 9 education. Although the baseline survey collected information about number of sexual partners in the participant's lifetime, past year and past month, the number of lifetime sexual partners was chosen for this analysis. The survey was administered as long as 8 years ago for some participants, so it was felt that lifetime sexual partners categorized as more or less than 10 partners would best capture the participant's general level of sexual activity. The number of births was categorized *a priori* into "given birth" vs. "not given birth", as it was thought that once a woman give birth her relationship with health providers and screening preferences would change.

Coverage of Target Population and Selection Bias

The coverage of the target population was evaluated with the 2006 Aboriginal Population Profile for Nunavik[54]. This data was collected as part of the 2006 Census of Population and provided by Statistics Canada. As the eighteen and nineteen year olds were grouped with 15-17 year olds in the available population estimates available for Nunavik, they were not included in the coverage analysis. The overall and age-specific coverage was calculated for the female Aboriginal (predominantly Inuit) population of Nunavik. Coverage of the source population was also determined using the population profile of the original cohort from which women in this study were recruited.

To evaluate selection bias the characteristics of the study population were compared to the characteristics of the women who declined to participate in the study, as there was information collected at cohort entry for both groups of women. Differences in the distribution of demographic characteristics and health behaviours between these groups were assessed using Student's t-tests for continuous variables and Chi-square tests for categorical variables. Fisher-exact tests were used for categorical variables when the cell count was less than 5.

Comparison of Sampling Techniques

The prevalence of HPV infection was calculated for any HPV infection, and type-, species-, and risk-specific HPV infection. Exact binomial 95% confidence intervals were calculated for prevalence estimates. Concordance between self- and provider-collected specimens for the detection of any HPV DNA was calculated to assess the percentage of test results that were in agreement. The concordance between the two sampling strategies was also determined for the detection of HPV-16 or HPV-18, type-, species-, and risk-specific HPV DNA.

Unweighted kappa statistics (κ) were calculated to determine the percent agreement between the two collection methods above that expected by chance. Kappa statistics were calculated for the detection of any HPV DNA, HR-HPV DNA, LR-HPV DNA, HPV-16 or HPV-18, type- and species-specific HPV DNA. The associated 95% confidence intervals were calculated. Arbitrary categorizations of kappa values are often used to describe the agreement beyond chance. Values of kappa were categorized based on the amount of agreement they suggest as follows: $\kappa > 0.75$ represents excellent agreement; $0.40 < \kappa < 0.75$ represents fair to good agreement; and $\kappa < 0.40$ represents poor agreement[211].

McNemar's test was used to assess the split of discordant pairs. It tested whether the proportion of samples classified as positive by self-collection and negative by provider-collection were unequal to the proportion of samples classified as negative by self-collection and positive by provider-collection. This was of interest, as self-sampling would be less useful in a clinical setting if the self-collection method classified a sample as negative when it was found to be positive by provider-collection more often than when the self-collection method classified a sample as positive when it was found to be negative by provider-collection.

The non-parametric Wilcoxon's signed rank test was used to compare the median number of types of HPV found by self- versus provider-collected specimens, classified as any HPV DNA, HR-HPV DNA and LR-HPV DNA. All comparability analyses were conducted in SAS version 9.2 and statistical significance for all tests was set at 5%.

Predictors of Preference for Self-Sampling Collection Method

Missing Data

The proportion of missing data for each covariate of interest for the logistic regression analysis for preference of self-sampling ranged from 0% (age) to 16.5% (number of sexual partners). Due to this small amount of missing data for the majority of variables, the dataset that contained only those participants with complete data for all variables of interest (n=63) was substantially smaller than the whole study population (n=85), given the already small number of study participants. Thus all univariate and multivariate analyses were carried out on both a complete dataset and imputed datasets. All logistic regression analyses were conducted in the statistical computing program R version 2.11.1 and statistical significance for regressions was set at 5%.

Univariate Analysis

Unconditional univariate logistic regression was performed for each covariate to explore their association with the outcome of preference for self-collection. Odds ratios (OR) and their associated 95% confidence intervals (95% CI) were calculated. The presence of collinearity was assessed by exploring the relationships between each pair of variables through correlation matrices, scatter plots and cross-tabulations of categorical variables.

Multivariate Analysis

Multivariate analyses were carried out for each variable adjusted for age. Each variable that was found to be significant after adjusting for age, as well as other variables that have been shown to have an effect on preference in previous studies were included in a final multivariate analysis such as age[199, 201], education[201, 204, 206], and marital status[170] . History of Pap smear in previous 3 years was also included because it was found to be potentially important in one study[204] and has been shown to be associated with acceptance of HPV testing[200]. A multivariate unconditional logistic regression was performed using all variables selected for inclusion in the final model. The presence of effect measure modification was investigated by including interaction terms in the multivariable model and examining the effects on regression estimates and CIs. ORs and their associated 95% CIs were calculated for the relationship between each covariate and the outcome of preference for self-sampling, adjusted for all other covariates in the final model.

Multiple Imputation

Multiple imputation and subsequent analysis with the multiple imputed datasets were conducted in R version 2.11.1 with the MICE package[212]. The function *mice* executes the imputation algorithm based on a prediction matrix, which can be supplied by the user. Twenty imputed data sets were created using a prediction matrix that allowed information from all covariates included in the complete case analysis to predict the missing values for each missing variable. Logistic regression on each of the twenty imputed dataset was performed with the function *glm.mids* and then regression estimates were averaged over the repeated analyses with the function *pool*.

Reasons for Preference Sample Collection Method

Reasons for preference towards self-sampling and reasons for preference towards provider-sampling were grouped into various dimensions based on response theme. Common themes for preference towards self-sampling were convenience, privacy, comfort, and ease of test. Confidence in ability to self-sample, convenience and ease of provider-administered test and lack of comfort with self-sampling were themes for preference towards provider-sampling. The first response listed by study participants was taken as the main reason for preference when grouping the responses. For each sampling method, the proportion of women in each preference reason response category was calculated.

3.3 RESULTS

3.3.1 RECRUITMENT AND ELIGIBILITY

A total of 107 women were approached to participate in this study and their flow through the recruitment and data collection phases of the study is shown in Figure 3.3.1. Fourteen women (13.08%) refused to participate and one woman approached did not meet study eligibility criteria as she was younger than 18 years and was therefore excluded. Of the 106 women who were eligible to participate in this study, 92 women (86.79%) accepted to participate. When the demographic, health and lifestyle information was compared between those who refused to participate in this study and those who consented, it was found that the only significant difference between these populations was that women who took part in the study had a lower age of first sexual intercourse (P< 0.001) (Table 6.1 in Appendix 6) .

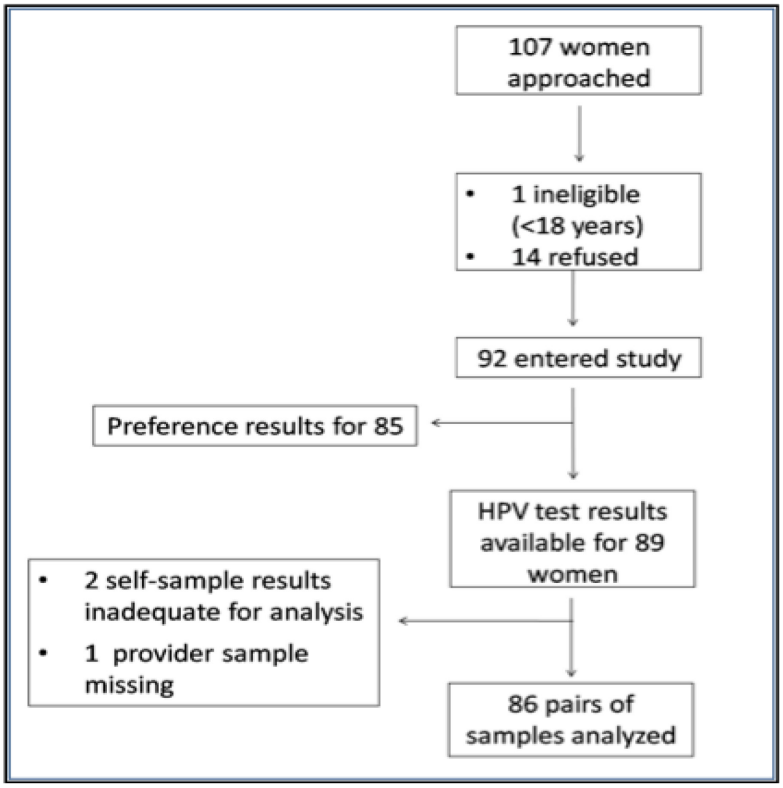

Figure 3.3.1: Flow chart of recruitment and data collection.

HPV DNA laboratory results were available for 89 of the participants. One sample did not have a matching provider-collected sample and thus was excluded from analysis. Two samples, both obtained through self-sampling were found to be inadequate for HPV analysis as they lacked β-globin amplification. Inadequate samples were also excluded, leaving 86 pairs of lab results to be analyzed. The sampling-method preference questionnaire was completed by 85 of the 92 study participants (92.4%).

3.3.2 COVERAGE OF TARGET AND SOURCE POPULATIONS

The average coverage of the target population was 3.5%. The study captured 4.00% of female 20-29 year olds, 3.78% of female 30-39 year olds, 3.62% of female 40-49 year olds and 1.93% of female 50-69 year olds. Source population coverage was 16.9% and age-specific coverage of females was 19.02% for 20-29 year olds, 19.35% for 30-44 year olds, 25.37% for 40-49 year olds and 6.61% for 50-69 year olds. As seen in Figure 3.3.2 the distribution of age in the study population was similar to both the target and source population, but the oldest age group (50-69) was largely underrepresented in the study population.

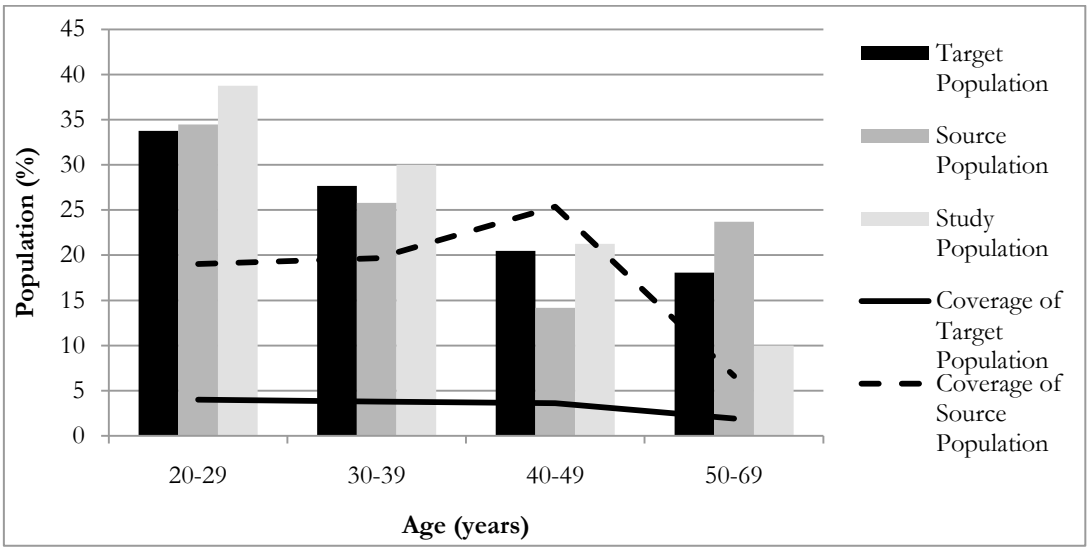

Figure 3.3.2: Age distributions of the target[54] , source[213] and study populations and target and source population coverage.

3.3.3 CHARACTERISTICS OF THE STUDY POPULATION

Table 3.3.1 presents the sociodemographic, lifestyle, reproductive and sexual history characteristics of study participants. The mean age of participants entering the self-sampling sub-study was 33.2 years (SD=11.1), and age ranged from 18 to 61 years. Women had been participants of the cohort study for up to 8.2 years, but were in the cohort an average of 4.9 years (SD=1.7) prior to study entry. In this time women returned an average of 3.5 times (range: 0-8) before entering the self-sampling study. About half (51.1%) of the study population were married or living with a partner at cohort entry. Most women at baseline had a Grade 9 education or higher (68.5%), were smokers (75.0%) and used alcohol (64.1%). Twenty-three women (25.0%) reported never having given birth and among women who had given birth the mean number of deliveries at baseline was 2.1 (SD=1.9). Over half (54.4%) of the women reported at baseline that they were not using any form of birth control. A history of Pap smear in the previous three years before cohort entry was reported by 64.1% of the study population and previous history of STI was reported by 66.3%. The mean age of first sexual intercourse was 14.6 (SD=1.8) years and ranged from 11 to 20 years. About 30% of women reported having ten or more lifetime sexual partners at baseline. At the time of cohort entry, all but one participant (1.1%), whose information was missing, reported that they previously had sexual intercourse. There were no systematic differences between women who had complete data and those who had some missing covariates.

Cytology results corresponding to the date of self-sampling study entry were available for 88% of the women in the study. The majority of women had a normal result (79.4%), but eight women (8.7%) had an abnormal cytology result and they were classified as either ASCUS (7.6%) or LGSIL (1.1%).

Table 3.3.1: Study participant characteristics at baseline (n=92).

Characteristic	n (%) or mean (SD)
Age (mean (SD))*	33.17 (11.12)[a]
Marital status	
Single/divorced	41 (44.57)
Married/living with partner	47 (51.09)
Missing	4 (4.35)
Education	
Less than Grade 9	23 (25.00)
Grade 9 or higher	63 (68.48)
Missing	6 (6.52)
Employment status	
No	23 (25.00)
Yes	63 (68.48)
Missing	6 (6.52)
Smoker	
No	19 (20.65)
Yes	69 (75.00)
Missing	4 (4.35)
Alcohol use	
No	29 (31.52)
Yes	59 (64.13)
Missing	4 (4.35)
Lifetime deliveries (mean (SD))	2.06 (1.92)[b]
Use of any birth control	
No	50 (54.35)
Yes	37 (40.22)
Missing	5 (5.43)
History of Pap smear in previous 3 years	
No	31 (33.70)
Yes	59 (64.13)
Missing	2 (2.17)
Cytology Result*	
Normal	73 (79.35)
ASCUS	7 (7.61)
LGSIL	1 (1.09)
Missing	11 (11.95)
Self-reported history of STI	
No	27 (29.35)
Yes	61 (66.30)
Missing	4 (4.35)
Age at 1st sexual intercourse (mean (SD))	14.58 (1.77)[c]
Lifetime number of sexual partners	
Less than 10	50 (54.35)
10 or more	27 (29.35)
Missing	15 (16.30)

[a] Median: 31.41 , Range: 18-61
[b] Median: 2 , Range: 0-8
[c] Median: 14, Range: 11-20, N=82
*At time of self-sampling study entry

3.3.4 COMPARISON OF SELF-SAMPLING TO PROVIDER-SAMPLING

HPV DNA Prevalence and HPV Types Detected

Figure 3.3.3 displays the overall prevalence of HPV infection and the HPV prevalence when HPV is grouped by risk, HPV-16 and HPV-18, and papillomavirus species. The overall prevalence and the prevalence of each papillomavirus species was higher in self-collected samples than provider-collected samples, but the overlapping 95% confidence intervals of prevalence indicate that these estimates are not statistically different from one another.

The presence of any HPV DNA was detected in either single or multiple infections in 56.98% of the self-collected samples and 39.37% of the provider-collected samples. Of the 36 distinct HPV types that were analyzed, 30 were detected by self-sampling and 29 were detected by provider-sampling. Species α3, whose HPV types have a preference for the vaginal epithelium, was the most prevalent species detected in the cervicovaginal samples collected by study participants (27.9%). The next most frequent papillomavirus species detected in self-collected samples were α7 (22.1%), α9 (15.1%) and α6 (12.8%), which all contain HR-HPV types and have a preference for cervical epithelium. The most prevalent species detected in the cervical samples collected by clinicians were the same as those detected by self-sampling (α3 (15.1%), α7 (14.0%), α9 (14.0%) and α6 (7.0%)). HPV types in species α1 were not detected by provider-sampling and HPV types in species α15 were not detected by either sampling method.

The prevalence of HR-HPV DNA was 38.4% in self-collection samples and 27.9% in provider-collected samples. Of the 22 distinct HR-HPV types that were analyzed, 18 types were detected in the self-collected samples and 19 types were detected in the provider-collected samples. Figure 3.3.4 displays the type-specific prevalence of each HR type detected by self-collection and provider-collection (see Table 6.2 in Appendix 6 for type-specific prevalence estimates detected by self-sampling and provider-sampling grouped by papillomavirus species). Self-sampling had a higher rate of detection for the following HR-HPV types: 18, 39, 51, 53, 56, 58, 59, 66, 67, 70 and 73. Provider-sampling had a higher rate of detection for four HR-HPV types: 16, 31, 33 and 45. Self-sampling and provider-sampling had equal rates of detection for HR-HPV 26, 52, and 68. Types 35, 69 and 82 were not

found by either sampling method. The most common HR-HPV types detected in single or multiple infections by self-collection were 58 (8.1%), 59 (8.1%), and 70 (8.1%), whereas 58 (7.00%), 16 (5.8%) and 70 (5.8%) were the most common HR-HPV types detected by provider-sampling. The presence of HPV 16 or HPV 18 was detected in 8.14% of study participants by both sampling methods.

The prevalence of LR-HPV DNA was 34.9% in self-collection samples and 17.4% in provider-collected samples. Of the 14 LR-HPV types that were analyzed, 12 were detected in the self-collected samples and 11 were detected in the nurse-collected samples. Figure 3.3.5 displays the type-specific prevalence of each LR type detected by self-collection and provider-collection. Self-sampling had a higher rate of detection rate than provider-sampling for all LR-HPV types, except HPV types 55 and 83 which had equal rates of detection between the sampling methods. LR-HPV types 11 and 71 were not found by either sampling method. The most common LR-HPV type detected in single or multiple infections by self-collection and provider-collection was HPV-62 (12.8% and 5.8% respectively).

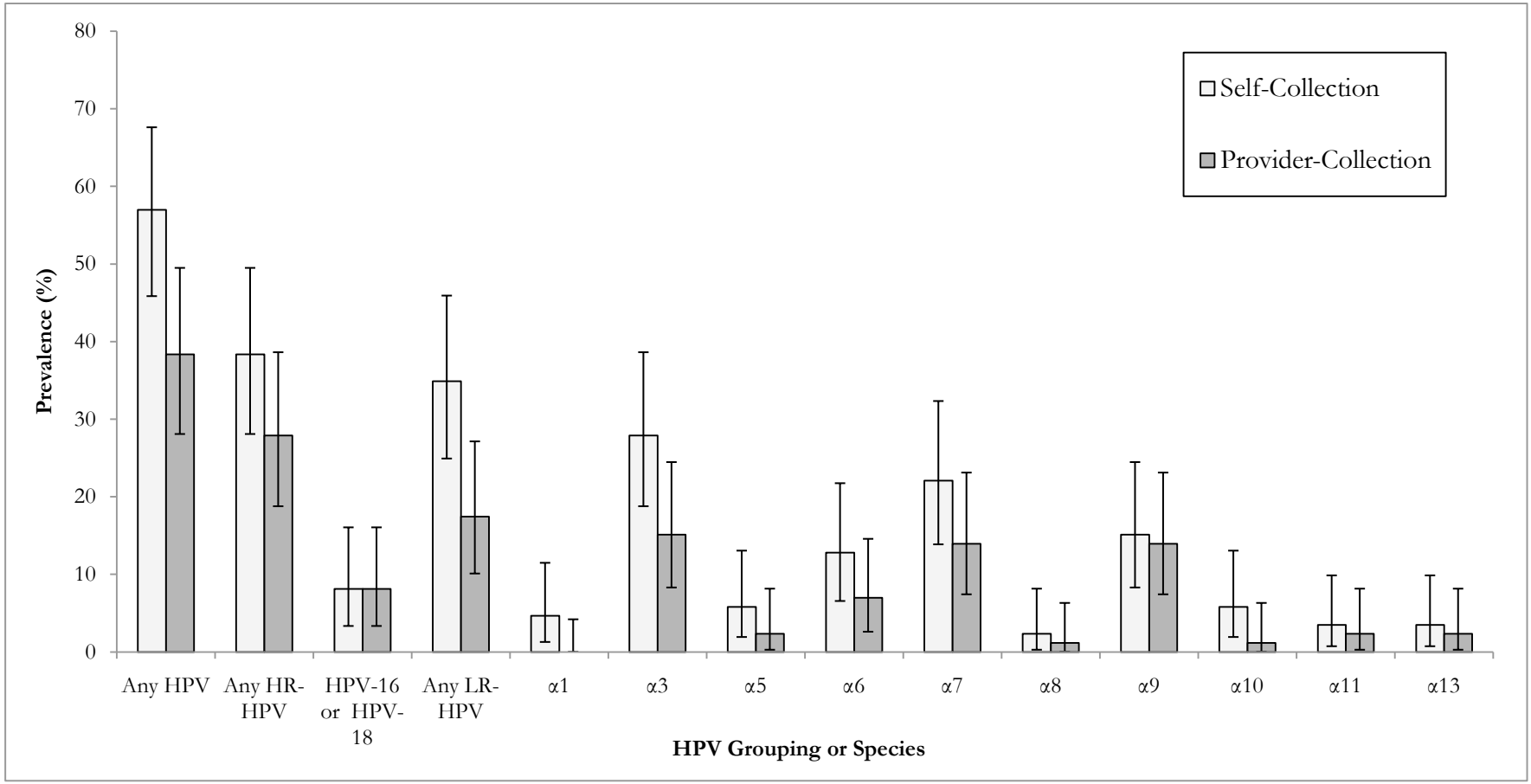

Figure 3.3.3: Prevalence estimates and associated 95% CI for HPV species and type groupings by self-collection and provider-collection (n=86).

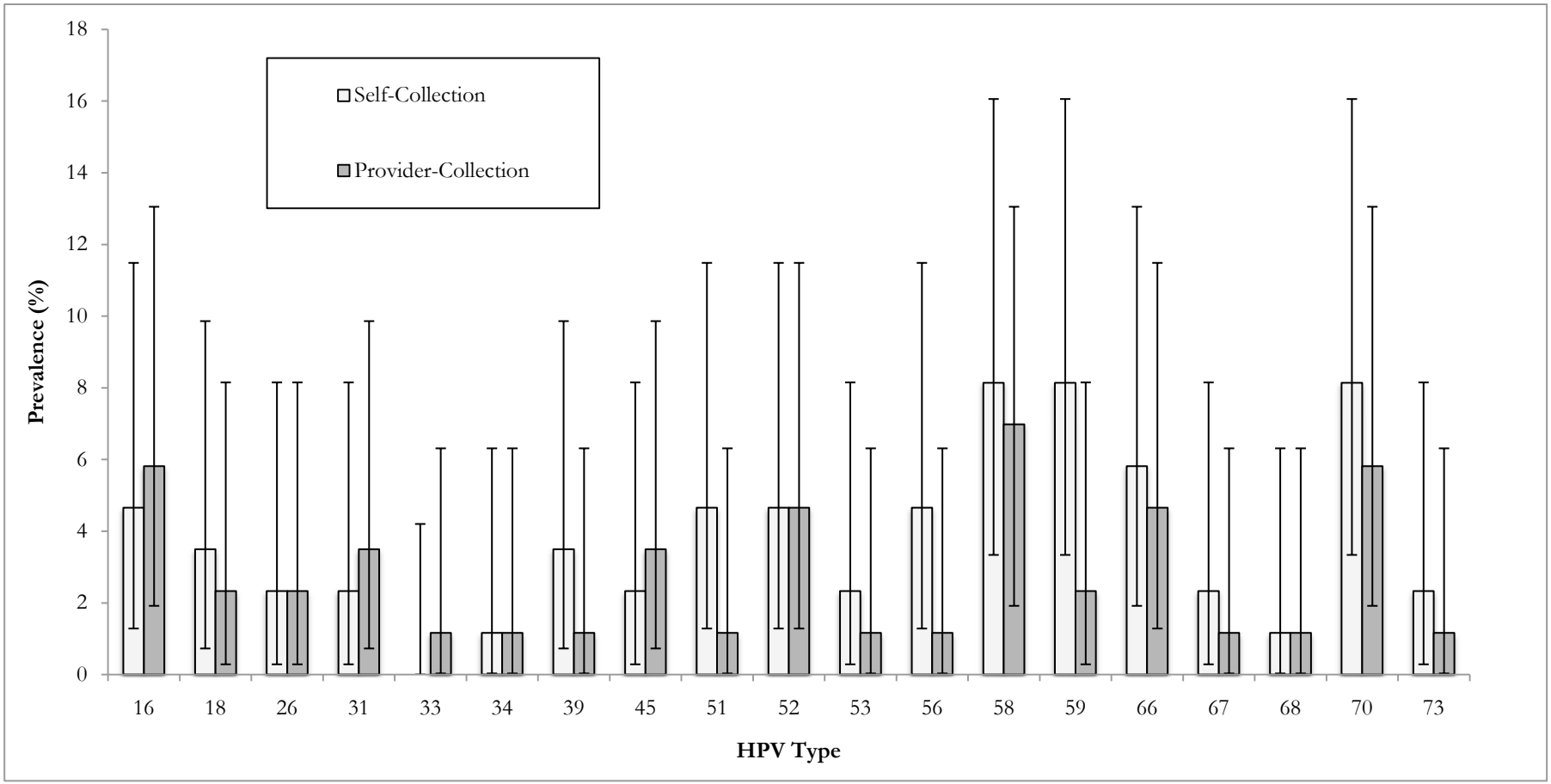

Figure 3.3.4: Prevalence estimates and associated 95% CI for HR-HPV types detected by self-collection and provider-collection (n=86).

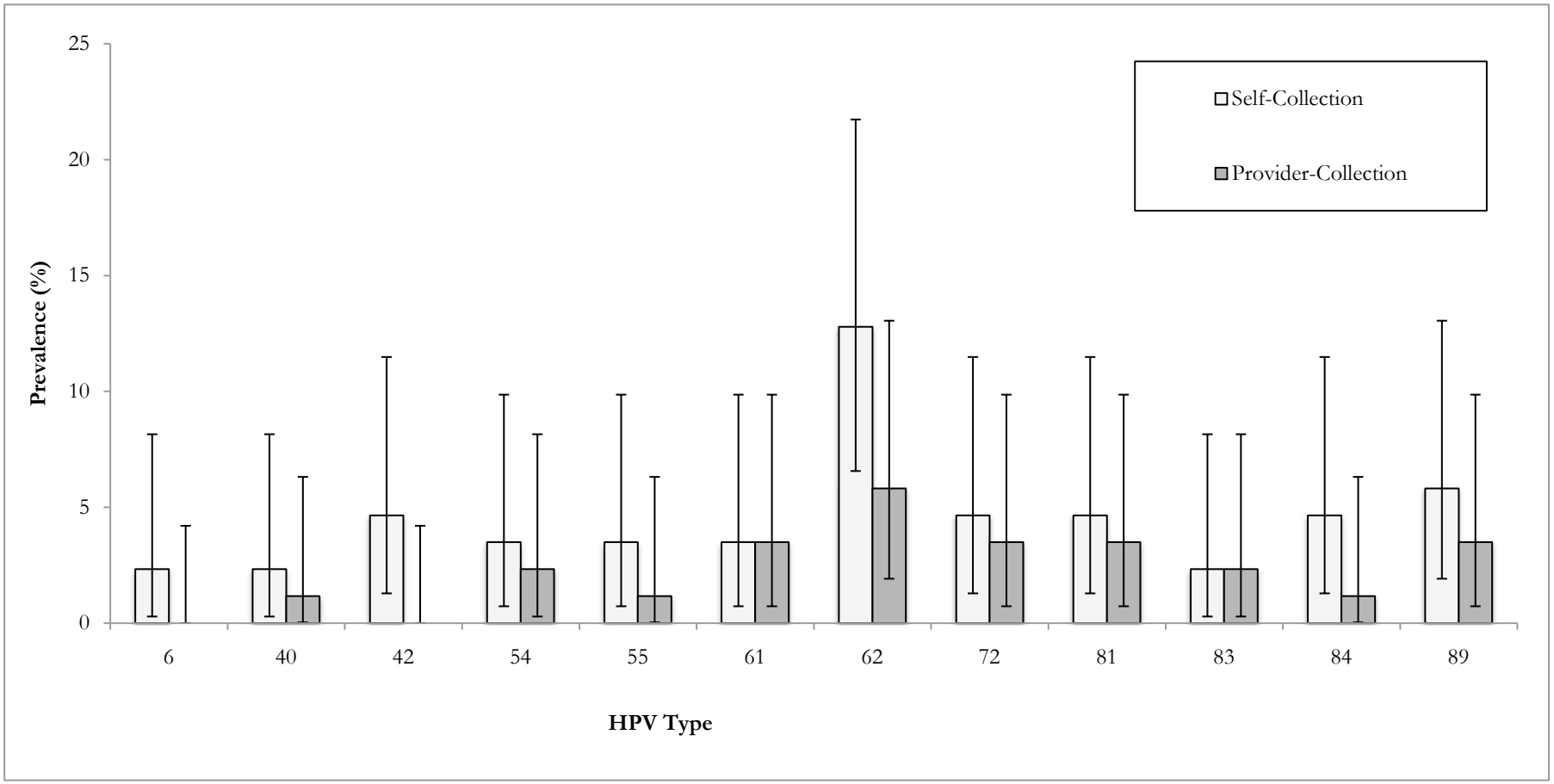

Figure 3.3.5: Prevalence estimates and associated 95% CI for LR-HPV types detected by self-collection and provider-collection (n=86).

Agreement between Sampling Methods

As expected, the agreement between sampling methods for the detection of any HPV DNA was good, with a concordance of 76.8% (66 of 86 pairs) and an unweighted kappa statistic of 0.55 (95% CI: 0.39-0.71) (Table 3.3.2). The agreement of sampling methods for detection of HR-HPV DNA (84.9% agreement, κ (95%CI): 0.66 (0.50-0.83)) and HPV16/18 (95.4% agreement, κ (95%CI): 0.69 (0.40-0.98)) was higher than for the detection of LR-HPV DNA (80.23% agreement, κ (95%CI): 0.51 (0.32-0.71)). Among the discordant results for any HPV, HR-HPV DNA and LR-HPV DNA detection, the self-collected samples were more likely to be positive than the provider-collected samples (McNemar's P-value <0.05). The sampling methods were not found to be significantly different in the classification of samples as positive for HPV16/18 (McNemar's P-value=1.00).

Table 3.3.2: Agreement between self- and provider-collected samples for the detection of any HPV, any HR-HPV, any LR-HPV, HPV-16 or HPV-18, and HPV by species (n=86).

	Number of samples positive for HPV DNA			Concordance	Kappa (95% CI)	McNemar's Test P-Value
	Self - collection only	Provider-collection only	Self-collection and provider collection			
Any HPV type	18	2	31	76.75	0.55 (0.39-0.71)	0.0004
Any HR-HPV	11	2	22	84.88	0.66 (0.50-0.83)	0.02
Any LR-HPV	16	1	14	80.23	0.51 (0.32-0.70)	0.0003
HPV-16 /HPV-18	2	2	5	95.35	0.69 (0.40-0.98)	1.00
HPV species						
α 1	4	0	0	95.35	-	0.13
α 3	12	1	12	84.88	0.56 (0.36-0.76)	0.003
α 5	3	0	2	96.51	0.56 (0.12-1.00)	0.25
α 6	6	1	5	91.86	0.55 (0.26-0.84)	0.13
α 7	9	2	10	87.21	0.57 (0.35-0.80)	0.07
α 8	1	0	1	98.84	0.66 (0.04-1.00)	1.00
α 9	2	1	11	96.51	0.86 (0.70-1.00)	1.00
α 10	4	0	1	95.35	0.32 (-0.16-0.80)	0.13
α 11	1	0	2	98.84	0.79 (0.40-1.00)	1.00
α 13	1	0	2	98.84	0.79 (0.40-1.00)	1.00
α 15	0	0	0	100	-	-

Species α9, which contains HPV-16, was detected with excellent agreement between sampling methods with a κ of 0.86 (95% CI: 0.70-1.00) and a concordance of 96.5%. The concordance between sampling methods for species α7, which contains HPV-18 and is more

likely to be found in the endocervical canal, was 87.2% (κ (95%CI): 0.57 (0.35-0.80)). Species α3, a vaginal species containing low-risk types was detected by the sampling methods with 85% concordance and a kappa of 0.56 (95%CI: 0.36-0.76). Concordance between sampling methods for the other papillomavirus species were between 92% and 100% with the unweighted kappa statistics ranging from poor to excellent (0.32-0.79).

McNemar's test showed a significant difference in the detection of HPV between self-collected samples and provider-collected samples for species α3 and therefore vaginal species, as α15 was not detected (P=0.003). This difference is again attributable to the higher proportion of self-collected samples found to be positive for HPV types in species α3 than in samples collected by the provider. For all other papillomavirus species, the discordance in detection of HPV by sampling method is due to the higher proportion of self-collected samples found to be positive compared to provider-collected samples, but these differences did not reach statistical significance due a lack of power given the small sample size and small prevalence estimates detected.

Type-specific agreement is presented in Table 3.3.3, where it can be seen that type-specific concordance is high, ranging from 93% to 100%. The kappas comparing the detection of HPV-16 and HPV-18 between self-and provider-collection were 0.65 (95% CI: 0.28-1.00) and 0.79 (95% CI: 0.40-1.00), respectively. The majority of type-specific unweighted kappa statistics comparing sampling methods were 0.5 or higher, except in the detection of the following HPV types: 39, 51, 55, 56, 59, 68, 84, and 89.

Multiple type HPV infections were detected in 25 of the 29 (51%) and in 16 of 33 (48.5%) women found to be positive for any HPV type by self-collection and provider-collection, respectively. The number of HPV types was concordant in 50 (58.1%) specimen pairs (35 had no HPV types, 10 had 1 type, 3 had 2 types, and 2 had 3 types). Only one specimen pair that was concordant by number of HPV types was not concordant by HPV type. Of the 35 specimen pairs that were discordant for the number of HPV types, an additional type was found in the self-sample for 18 pairs and in the provider-sample for 4 pairs.

Table 3.3.3: Agreement between self- and provider-collected samples for the detection of type-specific HPV (n=86).

	Number of samples positive for HPV DNA					
	Self - collection only	Provider-collection only	Self-collection and provider collection	Concordance	Kappa (95% CI)	McNemar's Test P-Value
HR types						
16	1	2	3	96.51	0.65 (0.28-1.00)	1.00
18	1	0	2	98.84	0.79 (0.40-1.00)	1.00
26	0	0	2	100	1.00 (1.00-1.00)	-
31	0	1	2	98.84	0.79 (0.40-1.00)	1.00
33	0	1	0	98.84	-	1.00
34	0	0	1	100	1.00 (1.00-1.00)	-
35	0	0	0	100	-	-
39	2	0	1	97.67	0.49 (-0.11-1.00)	0.50
45	0	1	2	98.84	0.79 (0.40-1.00)	1.00
51	3	0	1	96.51	0.39(-0.15-0.93)	0.25
52	0	0	4	100	1.00 (1.00-1.00)	-
53	1	0	1	98.84	0.66 (0.04-1.00)	1.00
56	3	0	1	96.51	0.39 (-0.15-0.93)	0.25
58	1	0	6	98.84	0.92 (0.76-1.00)	1.00
59	5	0	2	94.19	0.42 (0.02-0.82)	0.06
66	2	1	3	96.51	0.65 (0.28-1.00)	1.00
67	1	0	1	98.84	0.66 (0.04-1.00)	1.00
68	1	1	0	97.67	-0.01 (-0.03-0.01)	1.00
69	0	0	0	100	-	-
70	3	1	4	95.35	0.64 (0.32-0.97)	0.63
73	1	0	1	98.84	0.66 (0.04-1.00)	1.00
82	0	0	0	100	-	-
LR types						
6	2	0	0	97.67	-	0.50
11	0	0	0	100	-	-
40	1	0	1	98.84	066 (0.04-1.00)	1.00
42	4	0	0	95.35	-	0.13
54	1	0	2	98.84	0.79 (0.41-1.00)	1.00
61	0	0	3	100	1.00 (1.00-1.00)	-
72	1	0	3	98.84	0.85 (0.56-1.00)	1.00
81	2	1	2	96.51	0.55 (0.10-1.00)	1.00
89	3	1	2	95.35	0.48 (0.04-0.91)	0.63
55	2	0	1	97.67	0.49 (-0.11-1.00)	0.50
62	6	0	5	93.02	0.59 (0.31-0.88)	0.03
71	0	0	0	100	-	-
83	0	0	2	100	1.00 (1.00-1.00)	-
84	3	0	1	96.51	0.39 (-0.15-0.93)	0.25

The number of types detected by self-sampling and provider-sampling is displayed in Table 3.3.4. The number of types detected by self-sampling was greater than the number found by provider-sampling for any HPV and when HPV types were categorized as HR-HPV, LR-HPV and vaginal HPV. Overall, the median number of HPV types detected was 1 (mean (SD): 1.27 (1.67) types/sample) in self-collected samples and 0 (mean (SD): 0.80 (1.52) types/sample) in provider-collected samples (P<0.0001). The median number of HR-HPV (cervical) types detected was 0 in both self-collected samples (mean (SD): 0.72 (1.11) types/sample) and provider-collected samples (mean (SD): 0.52 (1.09) types/sample) (P=0.008). More LR-HPV types (P<0.0001) and vaginal HPV types (P =0.002) were detected by self-sampling than provider-sampling, although the median LR-HPV and vaginal HPV types was 0 in both samples (LR-HPV types: mean (SD): 0.55 (0.89) types/self-collected sample and mean (SD): 0.28 (0.70) types/provider-collected sample; vaginal HPV types: mean (SD): 0.38 (0.69) types/self-collected sample and mean (SD): 0.23 (0.61) types/provider-collected sample).

Table 3.3.4: Number of HPV types detected in self-collected and provider-collected samples (n=86).

	No. (%) of samples positive for HPV	
No. of types detected	**Self-Collected**	**Provider-Collected**
0	37 (43.02)	53 (61.63)
1	24 (27.91)	17 (19.77)
2	10 (11.63)	7 (8.14)
3	5 (5.81)	6 (6.98)
4	6 (6.98)	1 (1.16)
5	1 (1.16)	0 (0)
6	0 (0)	1 (1.16)
7	3 (3.49)	0 (0)
8	0 (0)	0 (0)
9	0 (0)	0 (0)
10	0 (0)	1 (1.16)

3.3.5 COLLECTION METHOD PREFERENCE

The preference questionnaire was filled out by 85 (92.4%) of the 92 women in this study. Self-sampling was preferred by 48 (56.5%) of these respondents and the other 37 (43.5%) women preferred provider-collection. The demographic characteristics of the study participants by sampling method preference are displayed in Table 3.3.5. The most striking difference between the group of women who preferred self-sampling and the group of women who preferred provider-sampling was their educational attainment. There was a higher proportion of women who had at least a grade 9 education among women who preferred provider-sampling (81%) compared to the women who preferred self-sampling (54%). Smaller differences were also observed between the groups with regards to their marital status, smoking status, and history of childbirth and Pap smear. The mean age, mean age at first sexual intercourse and the proportions of women who were employed, used alcohol, used birth control, had 10 more lifetime sexual partners and had a self-reported history of STI at baseline were very similar between the two groups of women.

Predictors of preference for self-sampling

As there were no substantial differences between the complete case analysis and the multiple imputation analysis, only the results from the univariate and multivariate multiple imputation analysis will be presented here.

Univariate Analysis

Univariate analysis of sociodemographic and lifestyle variables showed one characteristic to be significantly associated with preference for self-sampling (Table 3.3.6). As expected from the descriptive statistics comparing the two groups of women, education was significantly associated with preference. Women who had at least a Grade 9 education had a lower odds of preferring self-sampling than women who had less than a Grade 9 education at baseline (OR: 0.33, 95%CI: 0.11-0.97). Preference for self-sampling was positively associated with history a Pap smear in the previous 3 years and having had given birth, and negatively associated with smoking and being single or divorced at baseline, although these associations were not significant.

Table 3.3.5: Characteristics of study participants by sampling method preference (n=85).

Characteristic	Sampling Method Preference	
	Self-sampling (n = 48) n (%) or mean (SD)	**Provider-sampling (n = 37) n (%) or mean (SD)**
Age (mean (SD)	33.78 (12.24)	33.86 (10.40)
Marital Status		
Single/divorced	17 (35.4)	17 (45.9)
Married/living with partner	28 (58.3)	19 (51.4)
Missing	3 (6.3)	1 (2.7)
Education		
Less than Grade 9	17 (35.4)	6 (16.2)
Grade 9 or higher	26 (54.2)	30 (81.1)
Missing	5 (10.4)	1 (2.7)
Employed		
No	12 (25.0)	9 (24.3)
Yes	31 (64.6)	27 (73.0)
Missing	5 (10.4)	1 (2.7)
Smoker		
No	13 (27.1)	5 (13.5)
Yes	32 (66.7)	31 (83.8)
Missing	3 (6.3)	1 (2.7)
Use alcohol		
No	16 (33.3)	12 (32.4)
Yes	29 (60.4)	24 (64.9)
Missing	3 (6.3)	1 (2.7)
Previously given birth		
No	9 (18.8)	11 (29.7)
Yes	37 (77.1)	25 (67.6)
Missing	2 (4.2)	1 (2.7)
Current use of birth control		
No	25 (52.1)	20 (54.1)
Yes	19 (39.6)	16 (43.2)
Missing	4 (8.3)	1 (2.7)
History of Pap smear in previous 3 years		
No	13 (27.1)	15 (40.5)
Yes	33 (68.8)	22 (59.5)
Missing	2 (4.2)	0 (0.0)
Self-reported history of STI		
No	14 (29.2)	10 (27.0)
Yes	31 (64.6)	26 (70.3)
Missing	3 (6.3)	1 (2.7)
Age at 1st sexual intercourse	14.73 (1.75)	14.57 (1.88)
Lifetime number of sexual partners		
Less than 10	28 (58.3)	19 (51.4)
10 or more	13 (27.1)	11 (29.7)
Missing	7 (14.6)	7 (18.9)

Table 3.3.6: Univariate and age-adjusted estimates of the association between preference for self-sampling and sample characteristics (n=85).

Characteristic	Univariate	Age-Adjusted
	OR (95% CI)	**OR (95% CI)**
Age (per 10 years)	1.07 (0.73-1.58)	-
Marital status at baseline		
Married/living with partner	Reference	Reference
Single/divorced	0.68 (0.27-1.67)	0.68 (0.25-1.83)
Educational attainment at baseline		
< Grade 9	Reference	Reference
≥ Grade 9	**0.33 (0.11-0.97)**	**0.32 (0.11-0.99)**
Baseline Employed		
No	Reference	Reference
Yes	0.86 (0.30-2.42)	0.86 (0.30-2.42)
Current smoker at baseline		
No	Reference	Reference
Yes	0.38 (0.12-1.21)	0.38 (0.12-1.22)
Alcohol use at baseline		
No	Reference	Reference
Yes	0.81 (0.32-2.07)	0.79 (0.31-2.04)
Self reported history of STI		
No	Reference	Reference
Yes	0.81 (0.31-2.12)	0.75 (0.27-2.06)
Age at 1st sexual intercourse (per year)	1.05 (0.81-1.36)	1.03 (0.76-1.39)
Lifetime # of sexual partners		
< 10 partners	Reference	Reference
≥ 10 partners	0.87 (0.32-2.34)	0.81 (0.29-2.30)
Previously given birth		
No	Reference	Reference
Yes	1.67 (0.62-4.51)	1.82 (0.54-6.20)
Current use of any birth control		
No	Reference	Reference
Yes	0.97 (0.40-2.37)	1.00 (0.40, 2.44)
History of Pap test in previous 3 years		
No	Reference	Reference
Yes	1.70 (0.68-4.31)	1.74 (0.63-4.75)

Multivariate Analysis

Age-adjusted analysis

Education, which was the only covariate that was associated with preference for self-sampling in the univariate analysis, remained significantly associated with preference after adjustment for age (OR: 0.32, 95%CI: 0.11-0.99) (Table 3.3.6). The age-adjusted estimates for the association between preference for self-sampling and the other covariates remained similar to the univariate estimates.

Multivariate Model

Variables that have been shown to be associated with preference or acceptance of self-sampling in the current literature were selected for inclusion in the final model. These covariates were age, educational attainment, marital status and history of Pap smear in the previous 3 years. Interaction between educational attainment and history of Pap smear was investigated, but it was not found to be significantly associated with preference.

In the final multivariate model, educational attainment showed a sustained association with preference (OR: 0.25, 95% CI: 0.08-0.82) (Table 3.3.7). The respective associations between preference and age, marital status, and history of Pap smear were strengthened slightly in this model, but all associations remained insignificant. In the univariate analysis, age had a small positive association with preference, and in the fully adjusted model, age was found to have an insignificant, but strong negative association with preference.

Table 3.3.7: Multivariate model estimates of the association between preference for self-sampling and sample characteristics (n=85).

Characteristic	Univariate	Multivariate
	OR (95% CI)	**OR (95% CI)**
Age (per 10 years)	1.07 (0.73-1.58)	0.77 (0.47-1.27)
Marital status at baseline		
Married/living with partner	Reference	Reference
Single/divorced	0.68 (0.27-1.67)	0.55 (0.19-1.59)
Educational attainment at baseline		
< Grade 9	Reference	Reference
≥ Grade 9	**0.33 (0.11-0.97)**	**0.25 (0.08-0.82)**
History of Pap test in previous 3 years		
No	Reference	Reference
Yes	1.70 (0.68-4.31)	1.94 (0.66-5.73)

Reasons for preferences

Women were asked why they preferred one sampling method over the other and these responses were grouped into various themes. Reasons for preference towards self-collection grouped into response themes are shown in Table 3.3.8. The most common reason for preference towards self-sampling was that it was faster and more convenient than provider-sampling (25%). Grouped into this dimension of 'convenience' were three responses by women who noted the convenience of performing the self-sampling at home. The privacy aspect of self-sampling was the most important reason for preference towards self-collection for 11 (23%) women. The dimension of 'more comfortable' was the primary reason for preference towards self-sampling for nine women (18.8%), and it included the responses of self-sampling being 'less embarrassing' and 'less painful' then provider-sampling. Seven women (14.6%) preferred self-sampling because it was easy to do. Nine women (18.8%) did not give a reason for their preference towards self-sampling.

Table 3.3.8: Reasons for preference of self-collection grouped by response theme (n= 48).

Response theme	n (%)
Self-sampling was faster and more convenient	12 (25.0)
Self-sampling was more private	11 (22.9)
Self-sampling was more comfortable	9 (18.8)
Self-sampling was easy to do	7 (14.6)
Did not respond	9 (18.8)

Table 3.3.9 displays the reasons for women's preference towards provider-collection. The most common reason for preferring provider-sampling was the fear of obtaining a sample incorrectly or the belief that a provider does it more accurately (32.4%). Eight women (21.6%) stated that their reason for preferring provider-sampling was that it was easier to have a provider to do the sample. Five women (13.5%) had responses that fit into the dimension of 'uncomfortable with self-sampling' as their reason for preference to provider-collection. This dimension included responses like "it feels weird doing it", "don't like to do it" and "afraid to hurt myself". Two women (5.4%) preferred provider-sampling because it was more convenient as they would have to come into the clinic anyways and thus preferred to have all tests at the same time. A large proportion (27%) did not give a reason for their preference to provider-collection.

Table 3.3.9: Reasons for preference of provider-collection grouped by response theme (n= 37).

Response theme	n (%)
Worried about ability to do self-sample	12 (32.4)
Provider-collection is easier to do	8 (21.6)
Uncomfortable with self-sample method	5 (13.5)
More convenient	2 (5.4)
Did not respond	10 (27.0)

To understand the effect of education on sampling method preference, reasons for preference were stratified by level of education (Table 3.3.10). The most common reason for more educated women to prefer provider-sampling (n=30) was that they worried about their ability to do the self-sample correctly, whereas the top reason for more educated women to prefer self-sampling (n=26) was that it was faster and more convenient. Women who were less educated stated that their main reason for preference towards provider-sampling (n=6) was that they were uncomfortable with the self-sampling method, but the less educated women who preferred self-sampling (n=17) did so because it was more private than provider-sampling.

Table 3.3. 10: Reasons for sampling method preference stratified by education level (n=79).

		Sampling Method Preference	
		Self- Sampling	**Provider- Sampling**
Education Level	**Less than Grade 9**	• More private (35.3%) • More comfortable (23.5%) • Faster and more convenient (17.6%) • Easy to do (11.8%) • Did not respond (11.8%) (n=17)	• Uncomfortable with self-sample method (50%) • Worried about ability to do self-sample (16.6%) • Did not respond (33.3%) (n=6)
	More than Grade 9	• Faster and more convenient (26.9%) • Easy to do (19.2%) • More private (15.4%) • More comfortable (15.4%) • Did not respond (23.1%) (n=26)	• Worried about ability to do self-sample (36.7%) • Easier to do (23.3%) • Uncomfortable with self-sample method (6.7%) • More convenient (6.7%) • Did not respond (26.7%) (n=30)

3.4 DISCUSSION

The data presented in Chapter 3 of this thesis represents the cross-sectional analysis of data collected from a sample of women in an ongoing cohort study of HPV infection among Inuit women residing Nunavik, Quebec. The main results reported in this study were: 1) the comparability of self-collected cervicovaginal samples to provider-collected cervical samples for detection of HPV DNA and 2) sociodemographic predictors of preference for self-sampling. As far as the author knows, this is the first published report on self-collection of samples for the detection of HPV in an Aboriginal population of Canada. These results provide valuable insight into the use of self-sampling for cervical cancer screening in this population and for its potential use in future public health programs at the health centres of Nunavik.

3.4.1 COMPARISON OF SAMPLING TECHNIQUES

Both the overall prevalence of HPV and the prevalence of HR-HPV were found to be higher in the provider-collected specimens than the baseline prevalence reported for the entire cohort (29% and 20%, respectively)[23]. Although the overall distribution of HPV types in this study was quite similar to that found in the cohort at baseline, some notable departures were observed. For example, we found type-specific prevalence in our population to be at least twice as high compared to the baseline estimates for HPV-18, HPV-52, HPV-66, HPV-45, HPV-62 and HPV-70. These differences likely reflect a shift in the current distribution of HPV types and the higher HPV prevalence may indicate that this population is a higher risk subset of the original cohort due to non-random sampling.

Overall, the HR-HPV and LR-HPV prevalence detected in self-collected specimens was higher than in the provider-collected specimens. We also observed higher species-specific prevalence in the self-collected specimens. Despite these findings we did not find a significant difference in the HPV point prevalences found by self- and provider-sampling. This higher HPV prevalence found in self-collected specimens was consistent with those found in previous studies for any-HPV[174, 180, 185, 191], HR-HPV types [174, 180, 190-192, 194] and LR-HPV[180].

The agreement in detection for any-HPV and HR-HPV between self-collected and provider-collected samples were comparable to those found in the literature, but we observed slightly lower kappas for detection of any HPV[169, 174, 185, 192] and HR-HPV[169, 180, 185, 187, 197] compared to studies with similar sampling techniques and laboratory protocol. Petigniat et al.[180] note that differences in agreement may exist between studies because women were given different instructions for sample collection, as there is no standardized approach to self-sampling. These differences may also be explained by the increased detection of HPV in self-collected samples. In our study McNemar's test detected a systematic over-identification of HPV and HR-HPV by self-sampling among the discordant specimen pairs. Although, this increased detection with self-sampling has been shown with any-HPV type[180] and HR-HPV[169, 180] before, the majority of the previous studies found discordances to be equally distributed between sampling methods for the presence of any-HPV[169, 185, 193] and HR-HPV [157, 187, 192, 197].

The lower agreement found for the detection of LR-types (κ: 0.51) compared to HR-types (κ: 0.66), which was found in this study and others, was due to a higher detection of LR-HPV types in the self-collected samples[180, 185, 191]. Species α3 and α15, which contain low-risk types, have been shown to preferentially infect the keratinized tissue found in the vagina, whereas high-risk types have been shown to infect the whole genital tract equally[210]. Our results agree with this research, as types in species α3 were less likely to be detected in the cervical samples. The prevalence of species α3 in self-samples (28%) was almost double the prevalence found in the provider-samples (15%). In our study, the lowest species-specific concordance was for α3 and it was the only species that was significantly different between the discordant pairs.

Castle et al.[210] suggest that self-collected specimens contain both vaginal and cervical cells in an unknown ratio, which is affected by the sample collector and tool. Vaginal contamination is also possible during speculum examination, as evidenced by the high prevalence of species α3 detected in provider-samples. Women were told to insert the Dacron swab as far as it could go, so it is probable that the self-collected samples also contain cervical cells.

In a study that followed a cohort of female university students at four month intervals, the presence of vulvovaginal HPV infection was associated with reporting a new partner within the past four months, but the presence of cervical HPV infection was only associated with having a new partner after at least 5 months[214]. These associations are evidence that HPV DNA may be detected in vulvovaginal sites before it is detected in the cervix and thus may help explain the high detection rate of both LR- and HR-HPV types in vaginal samples.

Self-collected specimens were always collected before provider-collected specimens, as in the current literature[169, 171, 173, 174, 180, 191, 193, 197]. Although there may be less exfoliated cells to be recovered by provider-sampling with this procedure, a randomized trial of sampling methods found that the detection of HR-HPV was not dependent on the order of sample collection[187]. Further, more frequent sampling has not been shown to influence detection rates of HPV[215].

Multiple infections were common in the study population, as generally found in young populations[216]. We also found a high level of type-specific concordance that was similar to what has been observed in the literature[169, 174, 180, 185, 187, 192, 193]. Consistent with the higher systematic detection of HPV in self-collected samples, a marginally higher number of HPV types were detected in these samples. Two studies have assessed the difference in number of HPV types between the sampling methods and report conflicting results. One study found that the number of HR-HPV types was not different between the sampling methods[197], and the other found that more HR-types were detected in self-collected samples than provider-collected samples[180].

The majority of self-samples were adequate for analysis, a finding also reported in previous studies[169, 173, 174, 180, 180, 185, 185, 197], implying that self-sampling is reliable and reproducible. Compared to other studies, we found a larger difference in the detection of HPV between sampling methods, which was driven by the higher recovery of HPV from self-sampling. The surfaces of both the vagina and cervix are able to support infection by HPV, but only those that infect the transformation zone of the cervix will lead to cervical cancer. It is possible that many of the HR-HPV infections detected in self-sampling are vaginal and may never infect the cervix, thereby reducing the specificity of self-sampling. However, given that the

type-specific agreement between methods was generally high and samples were highly concordant by type, it seems that self-sampling is detecting a pattern of infection that resembles the one in the cervix. Additionally, self-sampling is as good as provider-sampling in the detection of HPV-16, HPV-18, species α7 and species α9. As self-sampling has a high recovery of HR-HPV and is comparable to provider-sampling, we can conclude that self-sampling would have benefits in cervical cancer screening in this population.

3.4.2 PREFERENCE OF SELF-SAMPLING

HPV testing on self-collected specimens, if incorporated into cervical cancer screening programs has the potential increase screening coverage as it could encourage women who are uncomfortable with speculum examination to be screened. We found that among a sample of Inuit women from Nunavik, self-sampling was preferred to provider-sampling by 57% of the population. Women were recruited into this study as they came into the health centres for regularly scheduled Pap smears, but they had to be participants of an ongoing HPV cohort study to be eligible. Women were also recruited into the original cohort study when they came for regularly scheduled Pap tests. Thus, our study population is comprised of women who are generally very dedicated to cervical cancer screening. The previous research on sampling method preference has also focused on populations of women who have a history of cervical cancer screening. These studies have found preferences towards self-sampling to range from 23% to 94% and our study's level of preference fell within this range. Differences in these study's protocols, target populations and reporting of sample characteristics makes them hard to compare with the results of this study.

Low preference towards self-sampling was found in three studies[181, 194, 204]. Dannecker et al.[181] found in their study of German women recruited from outpatient clinics that only 23% had a clear preference for self-sampling, while 63% had no preference. Despite this, it seems that self-sampling was generally very acceptable to women as almost all women would be willing to do the test at home and 60% were willing to pay for the test. Another study that sampled American women who were regular cervical cancer screeners gave them a short education session about HPV and cervical cancer before samples were taken[204]. This study found that only 32% of women preferred self-sampling, but almost 60% of women reported that there was nothing they didn't like about self-sampling. Finally, one study that recruited Canadian

women who were attending cervical cancer screening and measured preference with a Likert scale found that 46% of women either preferred self-sampling or had no preference, although the proportion of women with a clear preference for self-sampling was not reported[194]. The authors of this study suggest that provider-sampling was preferred because this well-screened population was accustomed to their routine speculum examination. This reasoning could be extended to our study population, as they have had samples collected for HPV testing by their provider an average of 3.5 times for the cohort study and women who may have originally preferred self-sampling could have become sensitized to the provider-sampling process. Despite their experiences with screening during the cohort study, 56% of the population did prefer self-sampling, suggesting that some women are never fully comfortable with clinician sampling and would still want to perform the test themselves.

Women's reasons for their sampling method preference helped to delineate why self-sampling preference was not higher. Women's lack of confidence in their ability to collect their own sample was found to be an important reason for women's preference towards provider-sampling in this population, as almost a third of the women who preferred provider-sampling felt this way. Despite this fear, over 97% of participants collected adequate specimens and detection of HPV in self-samples was high, suggesting that this population can accurately collect their own samples. Women's fear that self-collected samples will not adequately detect the risk of cancer has been consistently observed in a variety of populations[167, 170, 177, 198, 199, 204], and in one study it was one reason women gave for refusing to provide a self-sample altogether[176]. Women in our study also felt that it was easier to have a clinician perform the test (22%) and it was more convenient to go to the clinic to deal with all health issues at once (5%). This indicates that although these women do not necessarily prefer self-sampling, they might not object to performing self-sampling if necessary because they seem to have no problem with the testing procedure itself. This is not the case for all women, as 14% of women preferred provider-sampling because they were uncomfortable with the self-sampling method.

Women in this study reported that they preferred to collect their own specimens because it was more convenient (25%), private (23%), and comfortable (19%) than when sampling was performed by a clinician. These sentiments towards self-sampling have been consistently

found in the current literature[198, 199, 201, 204]. Women also reported that they preferred self-sampling because it was easy to do (15%), which was also reported by the majority of women in previous studies[167, 170, 181, 198, 201, 204].

Difficulties with the self-sampling device and protocol were reported in some studies, although we did not come across these problems[187, 206]. In one study in rural China, problems such as contamination of sampling brush, transport liquid spills, and anatomical unawareness were encountered during self-sampling among a group of women who had not been screened in over 10 years[206]. In another study that used Dacron swabs, women felt pain when a couple of swabs broke during sampling[187].

The only demographic or lifestyle characteristic found to be a significant predictor of preference for self-sampling in this population was educational attainment. Having at least a Grade 9 education was associated with a lower preference for self-sampling compared to having less than a Grade 9 education. In a previous study, education was shown to be associated with preference for self-sampling, but this study found that women with more education were more likely to prefer self-sampling than those with less education[204]. Further, higher education was found to be associated with overall satisfaction with self-sampling experience[201] and comfort while performing self-sampling[206]. To understand our unexpected results, reasons for preference were stratified by education level. It seems that among more educated women, there is a stronger concern that self-sampling isn't as accurate as clinician-sampling, whereas among less educated women comfort during specimen collection was the driving force behind their preferences. A sensitivity analysis was performed for the relationship between preference and education to confirm that the categorizations made to education were valid. The association between preference and education was similar for those who graduated high school (OR: 0.28, 95%CI: 0.06-1.41) and those that had at least some high school education (OR: 0.31, 95%CI: 0.10-0.93), but because so few women in our study graduated high school, this association was not significant and so the binary categorization was reported. Additionally given the common outcome of preference towards self-sampling, the ORs derived from the logistic regression analysis may exaggerate the risk associations and therefore the ORs should not be interpreted as approximations of the risk ratios[139].

We failed to replicate previous findings suggesting that marital status[170] and age[199, 201] are associated with preference for self-sampling, but these associations have not been found consistently in the literature[194, 201, 202, 204]. Although not a significant association, it seemed that women who had a history of Pap smear within 3 years preferred self-sampling over provider-sampling. This trend, although also not significant was also found in a population of American women who had a history of cervical cancer screening[204]. As it seems that there was a higher preference towards self-sampling among women who regularly participate in cervical cancer screening in this population, it is possible that if self-sampling was instituted in Nunavik, the women who were already regular attendees of cervical cancer screening would be most the likely to switch to self-sampling. In this situation, the opportunity for health education by the clinician would be lost. In fact, this concern has been predicted by women themselves in a study of American women where although 94% of women were willing to accept self-sampling for their yearly screen, they would continue with speculum examination if self-sampling meant that they wouldn't have access to a physician[187].

An issue that has not been fully developed in the literature is how tampon use affects women's acceptability of self-sampling. One study which assessed previous tampon use found that it was positively correlated with higher acceptability scores for self-sampling in the dimension of comfort of testing[198]. We were unable to measure tampon use in this study, but we have anecdotal evidence from the nurses that tampon use is not high among women in Nunavik. Women who are accustomed to inserting tampons would likely be more comfortable with self-sampling, and thus, the low levels of tampon use may help explain the lower preference for self-sampling found in this study.

In this population, there was not an overwhelming preference towards self-sampling, suggesting that if it was implemented into the screening program in Nunavik not everyone would want to use self-sampling. There are, however, certain situations where the use of self-sampling would be appropriate. For example, women in Nunavik usually will not engage in Pap smear screening if it is done by a male clinician and circumstances can arise where the only clinician in a community is male. In these situations, self-sampling may be a beneficial way to increase screening coverage. Further, even though only 56% preferred self-sampling,

87% of women agreed to collect a sample and enter the study, indicating that more women would accept to obtain a sample if needed.

Although we were unable to measure the opinions of women who traditionally avoid screening, one study of under-screened women reported that some refused to give self-samples because they did not believe that the test was necessary and they wanted an opportunity to discuss issues with their provider[176]. In a population of Canadian Aboriginal women, it was found that lack of awareness about the Pap smear and its importance was a barrier to screening[149]. It is very likely that in Nunavik, women's use of screening services is also affected by these barriers. This possibility and the knowledge that many participants felt that sampling was more accurately done by a provider, suggests that implementation of self-sampling in these communities should be concurrent with an education campaign.

3.4.3 LIMITATIONS

When considering the results of this study and their implications, it is necessary to recognize the study's limitations, which include non-random study subject recruitment, use of baseline questionnaire data, small sample size and missing data.

Subject Recruitment and Selection Bias

Women who were part of the main cohort study were recruited into the self-sampling sub-study as they came into the clinic for a Pap smear and 13% of the women approached refused to participate. The characteristics of non-participants and participants were compared and it was found that those who refused had a significantly older age of first sexual intercourse than those who participated. This difference in sexual behaviour suggests that some non-participation bias is present in this study.

Women had to be cervical cancer screening attendees to enter into the HPV cohort study and self-sampling study. Research has shown that women who participate cervical cancer screening are different than those who do not[133, 147]. To investigate the selection bias from the non-random sample of women attending cervical cancer screening the characteristics of study participants were compared to that of the female population of Nunavik using published statistics from the 2006 Aboriginal Population Profile for Nunavik[54, 147], and the

results of the 2004 Nunavik Inuit Health Survey[73, 143, 144]. Study participants were fairly similar to the general population in terms of smoking status[143], marital status, employment[54] and proportion of women who have given birth[73].

Alcohol use in the previous year was not stratified by gender in the 2004 Nunavik Inuit Health Survey, but it appears that alcohol use may be lower in the study population than in the general population (77% of the male and female population of Nunavik used alcohol in previous year vs. 64% among the study participants)[144]. The age distribution of the study population and female population of Nunavik was similar, but women over the age of 50 years were underrepresented in the study population[54]. This may be because fewer women in this age category were attending cervical cancer screening[73]. The educational attainment level of the study population was similar to the population of Nunavik in terms of the proportion who have less than a Grade 9 education and the proportion who have more than Grade 9 education, but the proportion of our study population that had completed secondary school (9.8%) was smaller than the proportion in the general population of Nunavik (22.2%)[145]. In the 2004 Nunavik Inuit Health Survey, 51.8% of women 15 and older reported having one partner in the year before the survey, 18.5% reported having two or more partners and 30.3% reported having no sexual partners[73]. The authors of this report disclose that the notion of sexual partner was misunderstood by some participants, in that they generally did not include their spouse in their definition of partner. In our study population of women 18-69 years, 60% reported having one partner, 35% reported having two or more partners and 5% reported having no sexual partner in the year before cohort entry. It seems that our study population may be more sexually active than the population of Nunavik, but these estimates are hard to compare due to the measurement error in Nunavik Inuit Health Survey and the age difference between the populations.

These comparisons suggest that the study population may be different than the general population of Quebec Inuit on some important characteristics such as age, alcohol use, education, number of sexual partners and history of cervical cancer screening but that they are generally representative of the residents of Nunavik on variables such as smoking status, marital status, employment and the proportion of women who had given birth. These differences would not affect the comparability of sampling methods to detect HPV, but they

could have biased the preference analysis as the women who consented to collect sample for the study may find self-testing to more be acceptable than women who did not participate.

Questionnaire Data

Sociodemographic characteristics, reproductive and sexual history, medical history and lifestyle factors for participants were obtained from a questionnaire administered at cohort entry. Women had been in the cohort for an average of 4.86 years, but some were part of the cohort for 8 years before entry into self-sampling study. Many of these covariates would have changed over this period, but as it was not considered feasible to re-survey study participants when they entered this study, only baseline information was used. With this in mind, the associations between baseline characteristics and preference for self-sampling should be interpreted with caution as measurement error is likely present. But baseline education level should be fairly stable throughout the study period, as women were eligible for cohort entry if they were between 15 and 69, which is past the standard age for entry into Grade 9 and education was classified in this study as less than grade 9 or grade 9 and higher. As such, the estimate for the association between education and preference may still be slightly affected by misclassification, but we can infer that there is a true association between these variables.

As women in our cohort were dedicated cervical cancer screeners and were followed in the cohort for an average of 3.5 visits for cytology and HPV tests, almost all women had a Pap smear in the previous 3 years from entry into the self-sampling study. Thus we used Pap smear in the previous 3 years from cohort entry to get a measure of women's historical use of screening services, although it is not necessarily representative of their current screening behaviours.

Missing data

The covariates of STI history and number of lifetime deliveries were collected from medical chart reviews and self-reported questions on the baseline questionnaire, but because of a significant amount of missing data for these covariates on the medical chart review the self-reported data was used. The proportion of missing data for individual covariates ranged from 0% to 16.5%. As complete data was available for only 63 of the 92 study participants, it was necessary to use multiple imputation to generate a set of values for the missing data. Multiple

imputation is widely used and is considered a valid method for handling missing data when used appropriately, so missing data was not viewed as a serious limitations in this study[217, 218]. The results of the multiple imputation analysis were very similar to the complete case analysis, confirming the robustness of our results.

Study Sample Size

The total number of women recruited into this study was 92, but laboratory analysis and preference information was only available for 86 and 85 women respectively. This is a small sample size to detect differences between sampling methods and predictors of preference for self-sampling. For example, to detect, at 80% power, a significant difference of 17.61% in the prevalence of any HPV between the sampling methods, as was found in this study, a sample size of 129 would be needed. The large confidence intervals around the estimates for the association between preference for self-sampling and individual covariates also confirms that this study is underpowered to detect significant predictors of preference to self-sampling. Consequently, as we cannot rule out an association between preference for self-sampling and other covariates, such as history of Pap smear, but these associations will be helpful in generating hypothesis for future studies. Additionally, few cytological abnormalities were found in this small sample, so we were unable to compare the sensitivity and specificity of self-collected samples to detect precancer and cancer. Using disease endpoints would have been ideal, but as the sensitivity and specificity of HPV positive self-collected specimens to detect high-grade disease has been well documented, it was felt the use of virological endpoints alone could demonstrate that self-sampling is feasible and practical for the detection of HPV DNA in this population.

Sampling and Laboratory Protocol

In this study, the self-collected samples and the provider-collected samples were stored and transported in different types of containers, so the laboratory personnel could not blinded to which samples were collected by clinicians and which samples were collected by study participants. The linear array used for the detection of HPV DNA is an automated objective molecular test, so lack of blinding should be not considered a serious limitation.

The sampling and laboratory protocol for clinician collected samples has been used since the beginning of the cohort study and has been shown to be valid. The protocol was slightly different for self-collected samples, which were kept in a dry tube instead of being placed in a liquid transport medium. In a recent study, the use of dry swab samples was investigated and the authors conclude that although the viral load in dry samples was slightly lower, it is comparable to wet samples for the detection HPV DNA[219].

3.4.4 STRENGTHS

The strengths of this study must be recognized in spite of the above limitations. We used preference to measure women's acceptability towards self-sampling, which may give a better idea of the potential uptake of self-sampling than satisfaction, willingness to give a sample and scores based on acceptability scales. We measured women's preferences after they had experienced both sampling methods, whereas some studies did not give women the opportunity to attempt self-sampling.

A protocol with PCR was used for HPV detection, so we were able to describe type-specific and species-specific prevalence and agreement. This is one of the few studies to report agreement on LR-HPV, which may be less important for cervical cancer screening, but good detection of LR-HPV is vital to studies on the natural history and transmission of HPV. In our protocol Dacron swabs were used for both self-collection and provider-collection, making the results from each collection site more comparable. Often studies compared self-collection with Dacron swabs to provider-collection with cervical brushes. Further, to ensure that differences in detection rates were not due to transient infections we collected both samples on the same day, unlike some studies[157, 174, 185].

Although, self-sampling has been studied in a variety of other populations, this study is the first to look at the comparability and acceptability of self-sampling in Inuit women. Given that this population is at high risk for HPV and cervical cancer, research on novel screening methods is highly relevant.

3.4.5 CONCLUSIONS

This study is the first to report on the comparability and acceptability of self-sampling in Inuit women. These data suggest that self-sampling could be beneficial in increasing screening coverage in this population that is at high risk for cervical cancer. Our results show that self-sampling is highly comparable to provider-sampling in the detection of any HPV, HR-HPV and LR-HPV. Results of the preference analysis suggest that although only 57% of the study population had a clear preference for self-sampling, education on the accuracy to self-collected samples to detect HR-HPV may increase the proportion of the population willing to use self-sampling in situations where they would traditionally avoid speculum examination. Self-sampling can also be beneficial for epidemiological studies of HPV infection and surveillance of vaccine efficacy. Self-sampling may reduce the costs of HPV testing, while increasing compliance and reducing loss to follow-up.

It is important to highlight that acceptance and preference for self-sampling does not automatically correspond to future screening behaviour. Further, there is no guarantee that women who have a positive HPV test result will follow-up accordingly with their health providers, which has traditionally been a problem with cytology based programs. Future studies should focus on the effect of self-sampling on cervical cancer mortality, cervical cancer incidence, screening participation rates and quality of life.

4 OVERVIEW

The objectives of this research were 1) to assess the level of knowledge about HPV and its relation to cervical cancer and 2) to determine the comparability and acceptability of self-sampling to clinician-sampling for HPV testing among Inuit women in Nunavik, Quebec. In Chapter 2, we showed that awareness of HPV was low, as was knowledge of the causal link between HPV and cervical cancer. We found higher educational attainment and knowing someone with cervical cancer to be significant predictors of HPV awareness. In Chapter 3, we demonstrated that self-sampling was highly comparable to provider-sampling for the detection of HPV. Self-sampling was preferred to clinician-sampling by 57% of women and preference for self-sampling was associated with lower educational attainment. As far as we know, this thesis is the first to report on HPV knowledge and the use of self-sampling among Inuit women in Nunavik.

These results suggest that in Nunavik, education about HPV and its relation to cervical cancer is needed and that self-sampling may be useful for increasing screening coverage. Given that the relationship between HPV and cervical cancer was not well known in this population and that some women perceived self-sampling to have a lower accuracy for HPV detection, educational activities about HPV will be especially important in the process of introducing self-sampling as a screening option. Communication about HPV and cervical cancer will continue to be important even after any implementation of self-sampling, as the diagnosis of being HPV positive can be stressful and confusing, especially given the transient nature of many HPV infections[102, 108, 220].

In Chapter 2, we propose that the community health worker model may be helpful in increasing HPV knowledge and screening coverage. This model can also play a role in the implementation of self-sampling, as community health workers may be able to better access women in the community who have traditionally avoided speculum examination, while taking the time to explain the implications of positive HPV test[167].

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APPENDIX 1: KAP STUDY CONSENT FORM

McGill University Health Center
Division of Clinical Epidemiology of the Royal Victoria Hospital

Human papillomavirus and cervical cancer among Inuit Women in Nunavik

Information Document – Women's understanding
November 2007

Researchers: **Dr Paul Brassard**, Department of Medicine, McGill University, **Dr Eduardo L. Franco**, Department of Oncology, McGill University, **Dr Mary Ellen Macdonald,** Dept of Nursing, McGill University.

A) Context and purpose

We have been conducting a project in Nunavik on the human papillomavirus (HPV) during the last 5 years. We know that Inuit women are generally more at risk of developing cervical cancer and that HPV is the main cause of cervical cancer. We now want to understand how much you know and how you feel about cervical cancer, HPV, the Pap test, and the vaccine against cervical cancer.

B) Procedure

If you agree to participate, you will be asked to answer a short questionnaire with the help of the interviewer. It should not take more than 20 minutes to go through the questionnaire. You will be able to determine which time and location is best to answer the questions. You may be also asked to participate in a group discussion on the best ways of working with the communities to increase overall knowledge and awareness of HPV and cervical cancer.

C) Participation

Your participation in this study is **of your own free will**. If you feel uncomfortable with any section of the questionnaire you can refuse to take part in the project. If you stop participating in any part of the project or at any time it will not affect your health care in any way. You will get a copy of this consent form and you have the right to ask the interviewer any questions you want about the study before accepting to participate.

D) Compensation

You will be given $20 after answering the questionnaire and/or participating in the group discussion to compensate you for your time.

E) Risks and Benefits

We will not ask questions on sexual behavior or on your lifestyle. But, if you still feel uncomfortable with any question, tell the interviewer and he or she will move on to the next question. There is no additional risk related to this study as answering the questionnaire or participating in the group discussion is safe. Your participation will help developing information and educational programs on cervical cancer.

F) Confidentiality

In order to ensure your privacy and confidentiality, your name will not appear on any study record or results presented by the research team. Instead, an identification number will be assigned to you and will appear in all your records. Only the interviewer and the researchers in Montreal will have access to the study number. All information about you will be treated in the same confidential manner as other medical records and you will not be identified in any reporting of results.

G) Questions?

If you have any specific questions about this study, now or at any time, please do not hesitate to contact Dr René Leclerc, the Director of Professional Services of the Ungava Tulattavik Health Center, at (819) 964 2905 *or* make a collect call to the chief investigator, Dr Paul Brassard at (514) 843 1564.

McGill University Health Care Center
Division of Clinical Epidemiology of the Royal Victoria Hospital

Human papillomavirus and cervical cancer among Inuit Women in Nunavik

Voluntary consent – Women's Understanding
November 2007

By signing this form, I acknowledge having received and read a copy of the information paper concerning this study. I have had the opportunity to ask any questions I may have about this study, and they have been answered to my satisfaction. I agree to participate in this study and I may withdraw this agreement at any time. My decision whether or not to participate will not change any health care I might receive or my legal rights. All information will be kept strictly confidential. My file will be coded and kept in a place where only the research team will have access.

☐ **I agree to answer questions on HPV and cervical cancer with the help of the Interviewer**

☐ **I accept to attend a group discussion on HPV and cervical cancer**

Write your name in block letters: _____

Signature: _____

Date: _____

Community: _____

Interviewer section
I recognize having offered to the participant a copy of this consent form and a copy of the information document.

Participant ID number: _____

Signature of the interviewer: _____

Date: _____

APPENDIX 2: KAP STUDY QUESTIONNAIRE

Kuujjuaq, 12 mars 2008

HPV SURVEY

59 questions

7 sections:

I. Sociodemographics, health and lifestyle characteristics
II. Use of health services
III. Knowledge, attitudes and beliefs about HPV
IV. Knowledge, attitudes and beliefs about cervical cancer
V. Knowledge, beliefs and intentions about Pap test
VI. Sexual behaviour and self perceived risk of STBI
VII. Knowledge and purpose of HPV vaccine

Acronyms:

HPV:	Human papillomavirus
Pap test:	Papanicolaou test
STBI:	Sexually transmitted and blood-borne infection

I. SOCIODEMOGRAPHICS, HEALTH AND LIFESTYLE CHARACTERISTICS

1. In which age group are you?
   a. 18-29
   b. 30-44
   c. 45-59
   d. 60-69

2. Do you currently have a paid work?
   a. Yes
   b. No

3. Are you on social welfare?
   a. Yes
   b. No

* Read if necessary: *Income is important in analyzing the health information we collect. For example, this information helps us to learn whether persons in one income group use certain types of medical care services or have certain conditions more or less often than those in another group.*

4. Last year, what was your household income (see annex 1 for ranges)?
    a. Card A, letter _____
    b. Card B, letter _____

5. How many years of education do you have?
    a. 6 years or less (some years of elementary school)
    b. 7-12 years (elementary school and some years of high school)
    c. 13 years or more (high school completed and college, university)

6. What language(s) do you speak?
    a. Inuktitut only
    b. English only
    c. Inuktitut and English
    d. Inuktitut, English and French
    e. Other (specify): _____

7. What is your marital status?
    a. Single (not living with partner)
    b. Married or common-law or living with partner
    c. Widowed or separated or divorced

8. How many times have you given birth?
    Answer: _____ times

9. How old were you when you first gave birth?
    Answer: _____ year old

10. How frequently do you do physical activity, exercise:
    a. Regular / occasional (once or more per week)
    b. Infrequent (less than once per week)
    c. Never

11. What is your emotional well-being?
    a. Happy/interested in life
    b. Somewhat happy
    c. Somewhat/very unhappy

12. About smoking habits, are you:
    a. Current-smoker
    b. Ex-smoker
    c. Never-smoker

13. About alcohol drinking habits, do you drink:
    a. Regularly (daily, weekly)
    b. Occasionally (monthly)
    c. Ex-drinker
    d. Never drank alcohol

II. USE OF HEALTH SERVICES

14. How many visits with a medical doctor/nurse practitioner have you done last year:
    a. None
    b. 1-3 visits
    c. 4 visits or more
        i. If "*none*", what would be the statement closest to your reality:
            1. Scheduling problems
            2. Fear of what doctor/nurse might find
            3. Experienced disrespectful treatments in the past
            4. Other reason, specify _____

15. What category corresponds the most to the reasons of your visits?
    a. Infections
    b. Injuries
    c. Social support
    d. Substance abuse support
    e. Diet counselling
    f. Other, specify: _____

16. When was your last blood pressure check?
    a. 2 years or less
    b. Never or more than 2 years

17. What is your overall satisfaction of the health care in your community?
    a. Very satisfied
    b. Satisfied
    c. Not really satisfied (please, specify why: _____)
    d. Not satisfied at all (please, specify why: _____)

III. KNOWLEDGE, ATTITUDES AND BELIEFS ABOUT HPV

18. Have you ever heard of the human papillomavirus (HPV) infection?
    a. Yes
    b. No
        i. If "yes", how did you hear about it? Please, specify: _____

19. Do you think HPV is a: (STBI)
    a. Sexually transmitted and blood-borne infection (STBI)
    b. Respiratory disease
    c. Gastrointestinal disease
    d. None of the above
    e. Don't know

20. Do you think HPV infection is common in sexually active adults? (yes)
    a. Yes
    b. No
    c. Not sure

21. What is the long-term effect of a persistent HPV infection? (cervical cancer)
    a. Disappears and there are no long-term effects
    b. Cervical cancer
    c. Infertility
    d. Don't know

22. True or False: The pill protects against HPV infection: (false)
    a. True
    b. False
    c. Not sure

23. Condoms protect about STBI's (ex. Chlamydia, HIV, ghonnorhea). Do condoms protect also against HPV?: (No)
    a. Yes
    b. No
    c. Not sure

24. Which of the following increase the risk of contracting HPV? (multiple sexual partners)
    a. Sharing underwear or towels
    b. Multiple sexual partners
    c. Toilet seats
    d. Bad hygiene
    e. Don't know

25. If one is infected by HPV, one will: (not necessary feel or know it)
    a. Have fever
    b. Not necessary feel or know it
    c. Have a headache
    d. Don't know

IV. KNOWLEDGE, ATTITUDES AND BELIEFS ABOUT CERVICAL CANCER

26. Have you ever heard of cervical cancer?
    a. Yes
    b. No

27. Do you know anybody who had cervical cancer?
    a. Yes
    b. No

28. Which of the followings might increase the risk of cervical cancer? (high number of sexual partners)
    a. Failure to use condoms
    b. Diet
    c. Smoking
    d. Taking the contraceptive pill
    e. High number of sexual partners
    f. Don't know

29. Personally, what do you think your chance is of developing cervical cancer? – or how likely do you think you are to develop
    a. Very low
    b. Low
    c. Average
    d. High

30. Do you think that when cervical cancer is detected early in its course, it: (increases the chance for cure)
    a. Does not make any difference
    b. Increases the chance for cure
    c. Don't know

V. KNOWLEDGE, BELIEFS AND INTENTIONS ABOUT PAP TEST

31. What is a Pap test: (scraping to look for abnormal cervical cells)
    a. Scraping to look for abnormal cervical cells
    b. Treatment for cancer
    c. Test for a sexually and blood-borne transmitted infection
    d. A test necessary to get birth control pills prescribed
    e. Don't know

32. How frequently should a Pap test be performed? (yearly)
    a. Every 6 months
    b. Yearly
    c. Every 2-3 years
    d. Every 5 years
    e. Every 10 years
    f. Don't know

33. When should a woman have her first Pap test? (when her sexual activity begins)
    a. When she has her first pregnancy
    b. When she wants to start oral contraception
    c. When her sexual activity begins
    d. Don't know

34. What do you think an abnormal Pap test result might mean? (abnormal, precancerous cervical cells)
    a. Abnormal, precancerous cervical cells
    b. Pregnancy
    c. Infection
    d. Don't know
    e. Other, specify: _____

35. When was the last time you had a Pap test?
    a. Last year
    b. Within the last 3 years
    c. More than 3 years
    d. Never
        i. If "*never*", why?
            1. Never heard about it
            2. Embarrassment
            3. Fear of pain
            4. Cannot get an appointment
            5. Do not bother
            6. Other, specify: _____

36. Do you feel embarrassed or awkward when undergoing a Pap test?
    a. Yes
    b. No

37. Do you prefer if the nurse/doctor explains each step of the examination during the Pap test?
    a. Yes
    b. No
    c. Does not matter

38. Do you feel more comfortable undergoing a Pap test if the nurse/doctor is:
    a. A female
    b. A male
    c. A doctor/nurse you already know
    d. Does not matter

39. In the case where the doctor/nurse administering your Pap test is a man, would you:
    a. Refuse having the test
    b. Feel embarrass/awkward, but still get tested
    c. Don't care male of female doctor/nurse

40. Do you feel pain when undergoing a Pap test?
    a. Yes
    b. No
    c. Sometimes

41. Do you have any intention of going for a Pap test in the next year?
    a. Yes
    b. Maybe
    c. No

42. Have you ever had a previous abnormal Pap test result?
    a. Yes
    b. No
    c. Don't know

VI. SEXUAL BEHAVIOR AND SELF PERCEIVED RISK OF STBI

43. What is your *lifetime* number of different sexual partner(s)?
    a. 0
    b. 1-5
    c. 6-10
    d. 10 or more
    e. Unsure/refused

44. What is your number of different sexual partner(s) *in the last year*?
    a. 0
    b. 1-5
    c. 6-10
    d. 10 or more
    e. Unsure/refused

45. What is your number of different sexual partner(s) *before* age 20?
    a. 0
    b. 1-5
    c. 6-10
    d. 10 or more
    e. Unsure/refused

46. How old were you when you first had sex? (*if asked, the interviewer can precise that sex means having a vaginal penetration)
    a. _____ year old

47. When you have sex, how often do you use condom?
    a. Never
    b. Rarely
    c. Often
    d. Always

48. Have you ever had a STBI?
    a. Yes
    b. No
    c. Don't know

49. What do you personally think your chance is of catching an STBI?
    a. None
    b. Low
    c. Moderate
    d. High

VII. KNOWLEDGE AND PURPOSE OF HPV VACCINE

50. Have you heard of a vaccine against HPV?
    a. Yes
    b. No

51. What are the potential benefits of the HPV vaccine? (protection against cervical cancer)
    a. Protection against cervical cancer
    b. Treatment of current cervical cancer
    c. Don't know

52. If one gets the HPV vaccine, will one still need to go for Pap tests? (yes)
    a. Yes
    b. No
    c. Don't know

53. If a new HPV vaccine was available, would you:
    a. Find out more information
    b. Get the vaccine as soon as possible
    c. Wait for other people to have it first
    d. Don't know

54. Do you believe that HPV vaccine is safe?
    a. Yes
    b. No
    c. Don't know

55. If HPV vaccine may *help you staying healthy*, do you see any need for it?
    a. Yes
    b. No
    c. Don't know

56. If you would like to know more about HPV or HPV vaccines, what would be your main source of information? (chose only one answer)
    a. Family
    b. Friends
    c. Doctor/nurse
    d. School
    e. Other health professional
    f. Other, please specify: _____

57. Who could influence your choice of getting HPV vaccination (or not)?
    a. Doctor/Nurse
    b. Teacher/school principal
    c. Friends and family
    d. Nobody

58. Do you think that HPV vaccine should be given to teenagers before the onset of sexual activity?
    a. Yes
    b. No
    c. Don't know

59. As a parent, would you be interested in having your child/children vaccinated for HPV?
    a. Yes
    b. No
    c. Don't know

Annex 1

Card A

INCOME:

U	$20,000 - $24,999
V	$25,000 - $29,999
W	$30,000 - $34,999
X	$35,000 - $39,999
Y	$40,000 - $44,999
Z	$45,000 - $49,999
ZZ	$50,000 and over

Card B

INCOME:

A	Less than $1,000 (including loss)
B	$1,000 - $1,999
C	$2,000 - $2,999
D	$3,000 - $3,999
E	$4,000 - $4,999
F	$5,000 - $5,999
G	$6,000 - $6,999
H	$7,000 - $7,999
I	$8,000 - $8,999
J	$9,000 - $9,999
K	$10,000 - $10,999
L	$11,000- $11,999
M	$12,000 - $12,999
N	$13,000 - $13,999
O	$14,000 - $14,999
P	$15,000 - $15,999
Q	$16,000 - $16,999
R	$17,000 - $17,999
S	$18,000 - $18,999
T	$19,000 - $19,999

APPENDIX 3: BASELINE QUESTIONNAIRE

HPV-INUIT

Research Coordinator Section

Date _____ dd/mm/yyyy Chart number _____ Date of birth _____ dd/mm/yyyy

A. Participant Identification

2- What is your current marital status ?

☐ Single (Not married and not living with partner) ☐ Married ☐ Divorced/Separated ☐ Widowed ☐ Living with partner

B. Socio economic status

3- Are you employed ? ☐ Yes ☐ No

4- What is your highest level of schooling ? ☐ Less than grade 9 ☐ Grade 9 to 13 ☐ More than grade 13

5- What is the current employement status of your husband or living partner ? ☐ Employed ☐ Unemployed

If employed, what type of work does he do ? _____

C. Life habits

6- Are you a current smoker ? ☐ Yes ☐ No

If yes, a) how many cigarettes do you smoke a day ? : _____

b) how long (in years) have you been smoking ? : _____

If no, a) have you ever smoked ? : ☐ Yes ☐ No

If yes, how long (in years) has it been since you stopped smoking ? : _____

7- Do you drink alcohol ? ☐ Yes ☐ No

If yes, a) how long (in years) have you been drinking ? : _____

b) how often do you drink :

Beer :	Never	Occasionally	Once a week	More than once a week	Every day
Wine :	Never	Occasionally	Once a week	More than once a week	Every day
Wisky/Gin/Vodka or any hard liquor	Never	Occasionally	Once a week	More than once a week	Every day

8- Are you currently using any birth control method ? Yes No

	For how long in years	Birth control methods
If yes, a) what kind of method do you currently use ? (you can put down more than one)		Birth control pills
		Latex safe (condom)
		Spermicides (gel)
		I.U.D (coil)
		Diaphragm
		Depo-Provera (injections)
		Rythm, calendar, natural meth od
		Other :

D. Sexual behavior

9- Have you ever had sex? Yes No **If no,** go to question 17.

10- How old were you when you first had sex ? :

11- Throughout your life, what is the number of partners with whom you have had sex ? (appr oximately)

0-4 5-9 10 and more

12- How many sexual partners have you had in the last year ?

13- How many sexual partners have you had in the last month ?

14- Does your partner(s) have other sexual partner(s) cur rently ? Yes No Unknown

If yes, how many partners does he currently have (approximat ely) ?

E. Gynecological and obstetric events

15- Are you pregnant ? ☐ Yes ☐ No

16- Up to now :

How many times did you deliver a living baby ? ☐

How many times did you have an abortion ? ☐

How many times did you have a miscariage ? ☐

17- Have you ever had a gynecological exam in the past (excluding the current one) ? ☐ Yes ☐ No ☐ Unknown

Year

If yes, what year did you have the first one (approximately) : ☐

what year did you have the last one (approximately) : ☐

18- Have you ever experienced sexually transmitted disease
(STD's or infection with herpes, chlamydia, gonorrhea, syphillis) in the past ? ☐ Yes ☐ No ☐ Unknown

If yes, ☐ Once ☐ 2-4 times ☐ 5 times or more

F. Health conditions

19- Are you experiencing one or more of the following health problems ?

☐ HIV infection

☐ Had an organ transplant

☐ Use of cortisone (injection or pills) for more than 1 month

☐ Other health problems: ☐

G. Comments (please, write down any comment you want about a specific item or about the study in general) :

☐

APPENDIX 4: SELF-SAMPLING STUDY CONSENT FORM AND QUESTIONNAIRE

McGill University Health Center
Division of Clinical Epidemiology of the Royal Victoria Hospital

Human papillomavirus and cervical cancer among Inuit Women in Nunavik

Information Document - Self sampling
November 2007

Researchers: **Dr Paul Brassard**, Division of Clinical Epidemiology, Royal Victoria Hospital, **Dr Eduardo L. Franco**, Department of Oncology, McGill University, **Dr François Coutlée** and **Dr Michel Roger**, Department of Microbiology, Notre-Dame Hospital, University of Montreal Hospital Center.

A) Context and purpose

You have previously given consent to be part of the study on human papillomavirus (HPV) infection among Inuit women in Nunavik. In short, we use samples from your Pap test to check for HPV infection. We now want to explore another method of collecting samples from the vagina and the cervix without having to insert a speculum (spoons) into your vagina.

B) Procedure

If you agree to participate, you will be asked to squat and insert a swab (Q-tip) into your vagina (all the way to the end of your vagina) and turn the swab 3 times. You can look at the picture provided by the nurse to help you understand what is expected from you. You will then give the swab to the nurse and get your usual Pap test. At the same time as she performs the Pap test, the nurse will also collect a sample. After the exam, you will be asked to tell us which method of sampling you preferred and why. The nurse will accompany you in the process. This procedure will be done only once.

C) Participation

Your participation in this study is **of your own free will**. If you feel uncomfortable with anything you can refuse to participate in this part of the project. You can also stop participating in any part of the project at any time and this will not affect your health care or treatment in any way. You will get a copy of this consent form and you have the right to ask the nurse any questions you want about the study before accepting to participate.

D) Risks and Benefits

There is no additional risk related to this study as the self sampling and Pap smear are safe procedures. You will not have more visits to the clinic; you will only spend a little more time to do the self sampling. Your participation will help in deciding which is the best way to test for HPV infection.

E) Confidentiality

In order to ensure your privacy and confidentiality, your name will not appear on any study record or results presented by the research team. Instead, a patient identification number will be assigned to you and will appear in all your records. Only the nurse and the researchers in Montreal will have access to the study number. All information about you will be treated in the same confidential manner as other medical records and you will not be identified in any reporting of results.

F) Questions?

If you have any specific questions about this study, now or at any time, please do not hesitate to contact Dr René Leclerc, the Director of Professional Services of the Ungava Tulattavik Health Center, at (819) 964 2905 *or* make a collect call to the chief investigator, Dr Paul Brassard at (514) 934 1934 ext 36910.

McGill University Health Care Center
Division of Clinical Epidemiology of the Royal Victoria Hospital

Human papillomavirus and cervical cancer among Inuit Women in Nunavik

Voluntary consent - Self sampling
November 2007

By signing this form, I acknowledge having received and read a copy of the information paper concerning this study. I have had the opportunity to ask any questions I may have about this study, and they have been answered to my satisfaction. I agree to participate in this study and I may withdraw this agreement at any time. My decision whether or not to participate will not change any health care I might receive or my legal rights. All information will be kept strictly confidential. My file will be coded and kept in a place where only the research team will have access. This procedure will only occur once.

☐ **I agree to perform the self sampling procedure and answer a few questions on how I felt about it.**

☐ **I refuse to perform the self sampling**

Signature: _____

Date: _____

Community: _____

Nurse section
I recognize having offered to the participant a copy of this consent form and a copy of the information document.

Participant ID number: IN- _____

Signature of the nurse: _____

Date: _____

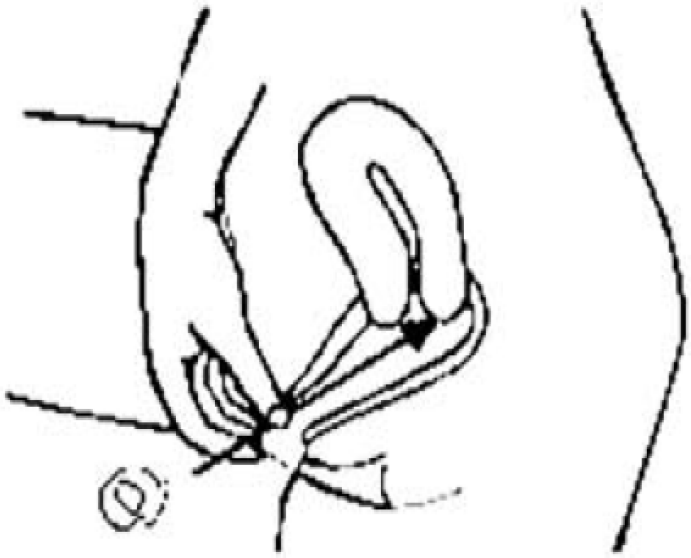
Which method was preferred? ☐ **Self Sampling** ☐ **Nurse Sample**

Why? _____

APPENDIX 5: SELF-SAMPLING INSTRUCTIONS

Instructions for self-collection of vaginal swab

1. **Remove clothes from the waist down.**
2. **Remove the swab from the wrapping, being very careful not to touch anything with it.**
3. **Choose a comfortable position (either standing with one foot on a chair, or standing with legs apart and knees slightly bent).**
4. **Relax, spread the labia with one hand, and with the other hand insert the cotton tip of the swab into the vagina. If it does not enter easily, try a slightly different angle.**
5. **Gently push the swab up into the vagina until physically it cannot go any further, at least 2.5 inches.**
6. **Rotate the swab inside the vagina for three full rotations, keeping the swab as far into the vagina as possible.**
7. **Withdraw the swab, being very careful not to touch the floor or any other surface.**
8. **Place the swab directly into the tube that is provided (leaving the tube in the styrofoam holder).**
9. **Leave the tube, swab, and styrofoam holder in the room for the Research Nurse after you are dressed.**



APPENDIX 6: ADDITIONAL TABLES

Table 6.1: Comparison of demographic, lifestyle, reproductive and sexual history characteristics between women who consented to participate in the study and those that refused (n=106).

Characteristic	Women who consented (n = 92) n (%)	Women who refused (n = 14) n (%)	P-value
Age (mean(SD)	33.17 (11.12)	35.65 (11.02)	0.44[a]
Marital Status			
Single	41 (44.6)	5 (35.7)	0.62[b]
Married or living with partner	47 (51.1)	8 (57.1)	
Missing	4 (4.3)	1 (7.1)	
Education level			
Less than Grade 9	23 (25.0)	4 (28.6)	0.90 [b]
Grade 9 or higher	63 (68.5)	9 (64.3)	
Missing	6 (6.5)	1 (7.1)	
Employed			
No	23 (25.0)	2 (14.3)	0.51 [b]
Yes	63 (68.5)	12 (85.7)	
Missing	6 (6.5)	0 (0.0)	
Smoker			
No	19 (20.7)	2 (14.3)	0.85 [b]
Yes	69 (75.0)	12 (85.7)	
Missing	4 (4.3)	0 (0.0)	
Use alcohol			
No	29 (31.5)	3 (21.4)	0.59 [b]
Yes	59 (64.1)	10 (71.4)	
Missing	4 (4.3)	1 (7.1)	
Lifetime deliveries (mean (SD))	2.06 (1.92)	1.64 (1.22)	0.44[a]
Current use of birth control			
No	50 (54.3)	7 (50.0)	0.91 [b]
Yes	37 (40.2)	6 (42.9)	
Missing	5 (5.4)	1 (7.1)	
History of Pap test in previous 3 years			
No	31 (33.7)	7 (50.0)	0.53 [b]
Yes	59 (64.1)	7 (50.0)	
Missing	2 (2.2)	0 (0.0)	
Self reported history of STI			
No	27 (29.3)	5 (35.7)	0.52 [b]
Yes	61 (66.3)	8 (57.1)	
Missing	4 (4.3)	1 (7.1)	
Age at 1st sexual intercourse	**14.58 (1.77)**	**16.73 (1.19)**	**0.0002[a]**
Lifetime number of partners			
0-4	28 (30.4)	5 (35.7)	0.66 [b]
5-9	22 (23.9)	5 (35.7)	
10+	27 (29.3)	3 (21.4)	
Missing	15 (16.3)	1 (7.1)	
Lifetime number of sexual partners			
Less than 10	50 (54.3)	10 (71.4)	0.56 [b]
10 or more	27 (29.3)	3 (21.4)	
Missing	15 (16.3)	1 (7.1)	

Note: [a]: Student's T-test, [b]: Fisher exact test

Table 6.2: Type-specific HPV prevalence in self-collected and provider-collected samples grouped by species (n=86).

HPV type	No. of positive samples		Difference in no. of positive samples (Self – Provider)	Prevalence from self-collection (%)	Prevalence from provider-collection (%)
	Self	Provider			
Species α1					
42	4	0	+4	4.65	0
Species α3					
61	3	3		3.49	3.49
62	11	5	+6	12.79	5.81
72	4	3	+1	4.65	3.49
81	4	3	+1	4.65	3.49
83	2	2		2.33	2.33
84	4	1	+3	4.65	1.16
89	5	3	+2	5.81	3.49
Species α5					
26	2	2		2.33	2.33
51	4	1	+3	4.65	1.16
69	0	0		0	0
82	0	0		0	0
Species α6					
53	2	1	+1	2.33	1.16
56	4	1	+3	4.65	1.16
66	5	4	+1	5.81	4.65
Species α7					
18	3	2	+1	3.49	2.33
39	3	1	+2	3.49	1.16
45	2	3	- 1	2.33	3.49
59	7	2	+5	8.14	2.33
68	1	1		1.16	1.16
70	7	5	+2	8.14	5.81
Species α8					
40	2	1	+1	2.33	1.16
Species α9					
16	4	5	- 1	4.65	5.81
31	2	3	- 1	2.33	3.49
33	0	1	- 1	0	1.16
35	0	0		0	0
52	4	4		4.65	4.65
58	7	6	+1	8.14	6.98
67	2	1	+1	2.33	1.16
Species α10					
6	2	0	+2	2.33	0
11	0	0		0	0
55	3	1	+2	3.49	1.16
Species α11					
34	1	1		1.16	1.16
73	2	1	+1	2.33	1.16
Species α13					
54	3	2	+1	3.49	2.33
Species α15					
71	0	0		0	0