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Correlates of HPV vaccine uptake in school-based routine vaccination of preadolescent girls in Norway: A register-based study of 90,000 girls and their parents



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ABSTRACT

Objective. To assess demographic, socioeconomic and behavioural correlates of HPV vaccination of preadolescent girls in a publicly funded, school-based vaccination programme.

Methods. Data for all Norwegian girls born 1997–1999, eligible for routine school-based HPV vaccination in 2009–2011 (n = 90,842), and their registered mother and father, were merged from national registries. Correlates of girl vaccination status were analysed by unadjusted and multivariable logistic regression.

Results. In total, 78.2% of the girls received the first dose of the HPV vaccine, 74.6% received three doses, and 94.8% received the MMR vaccine. Correlates associated with initiation of HPV vaccination included parental age, income and education, maternal occupational status and cervical screening attendance, and girl receipt of the MMR vaccine. Rates of completion of HPV vaccination among initiators were high, and disparities in completion were negligible. Maternal and paternal correlates of daughter HPV vaccination status were similar.

Conclusions. Routine school-based vaccination generally provides equitable delivery, yet some disparities exist. Information campaigns designed to reach the sub-groups with relatively low vaccine uptake could reduce disparities. In none of the sub-groups investigated did uptake of the HPV vaccine approach that of the MMR vaccine, further demonstrating a general potential for improvement in HPV vaccine uptake.

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Introduction

Human papillomavirus (HPV) can cause cervical cancer (Bosch et al., 2002) as well as other cancer forms (zur Hausen, 2009) and genital warts (Aubin et al., 2008). Vaccination against HPV types 6, 11, 16 and 18, which cause most cervical cancers and genital warts, has been available since 2006. The HPV vaccine has been shown to be generally safe (Arnheim-Dahlstrom et al., 2013; Slade et al., 2009) and effective (Baandrup et al., 2013; Leval et al., 2013; Paavonen et al., 2009; Villa et al., 2007), but the uptake (i.e. the proportion vaccinated in the targeted population) is low in many countries that have included the HPV vaccine in their national immunisation programme (Markowitz et al., 2012).

The correlates of HPV vaccine uptake may differ between vaccination settings. Opportunistic uptake of the HPV vaccine is strongly associated

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with high socioeconomic status (Leval et al., 2013). Socioeconomic status, ethnicity, previous uptake of other childhood vaccines, maternal age and maternal screening attendance may also be associated with catch-up vaccination of adolescent girls and young women (Poole et al., 2012; Rondy et al., 2010; Steens et al., 2013). Few large studies have addressed potential disparities in school-based routine HPV vaccination of preadolescent girls (Fisher et al., 2013). This vaccination delivery approach is particularly appropriate because preadolescent girls are the primary target for most HPV vaccination programmes (Markowitz et al., 2012), as vaccine efficacy is highest among young individuals naive to the HPV vaccine types (Villa et al., 2007). Moreover, a school-based setting typically achieves the highest uptake (Hofstetter and Rosenthal, 2014) and may reduce inequalities in uptake (Poole et al., 2012), although some studies indicate that disparities related to socioeconomic status, ethnicity and other demographic characteristics may still exist (Fisher et al., 2014; Ogilvie et al., 2010; Sinka et al., 2014). Additional studies are needed to assess the performance of HPV vaccination in this setting, and potentially, to guide strategies for improving HPV vaccine uptake.

By merging high-quality individual data from multiple national registries, we aim to investigate demographic, socioeconomic and behavioural correlates of routine school-based HPV vaccination of preadolescent girls in Norway. Since involvement in child health-related decision making

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may differ between mothers and fathers (Zvara et al., 2013), we investigate maternal and paternal characteristics separately.

Methods

Vaccination setting

The Norwegian childhood vaccination programme (Trogstad et al., 2012) is administered by the municipality health services, who are obliged by law to provide the included vaccines to all children living in Norway. HPV vaccination was included in the programme in 2009. Girls born in 1997 were the first eligible birth cohort. Three doses of the HPV vaccine is offered free of charge at school to girls in the seventh grade. The vaccine is usually given at months 0, 2 and 6 by the school nurse during school hours. Among other vaccines, the childhood immunisation programme also offers vaccination against MMR (measles, mumps and rubella combined) in the sixth grade. Vaccination is optional, and the vaccinee and their parents/guardians have to consent to vaccination. Written consent is not required, but is encouraged for vaccination of school children. The Norwegian Institute of Public Health has issued HPV vaccine information letters and consent forms in several languages.

Study population

Girls who were born in 1997, 1998 or 1999, and who were resident in Norway during the entire school-year they were offered the HPV vaccine through the programme, were eligible for this study. All Norwegian citizens have a unique personal identification number (PIN), which is used in registries. The National registry contains the PINs for every individual who is or has been resident in Norway. We used the National registry (October 2013 version) to identify all females born between 01.01.1997 and 31.12.1999 (n = 97,269). To avoid inclusion of girls who were not or may not have been offered the HPV vaccine, we excluded a total of 6427 girls based on dates of death, emigration, immigration, or registry irregularities, resulting in 90,842 girls meeting the inclusion criteria. Through the National registry, a mother was identified for 90,540 eligible girls, and a father was identified for 88,565 eligible girls. These girl-mother and girl-father pairs were included in the analyses of initiation of HPV vaccination. For the analyses of completion of HPV vaccination, we exclude ed all girls who did not initiate vaccination, resulting in samples of 70,870 and 69,306 girls for the analyses addressing associations with maternal and paternal characteristics, respectively (Fig. 1).

Registry data

The PIN was used to obtain and to merge individual data from various registries. To ensure data protection, PINs were managed by authorized registry personnel only, and were replaced by running numbers before data was made available for analyses.

Girl vaccination status was obtained from the Norwegian immunisation registry (SYSVAK), from which we requested all dates of HPV and MMR vaccinations. Age and region of residence in the year of scheduled HPV vaccination was obtained from the National registry. For each mother and father, we requested the following data from Statistics Norway, referring to the year of scheduled HPV vaccination of the daughter: marital status, education, total income (the sum of income from work, properties, taxable and tax-free transfers),



Fig. 1. The study populations for analyses of HPV vaccination in Norway 2009-2011.

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Table 1

Odds ratios^a for initiation and completion of routine HPV vaccination among 12–13 year old girls in Norway 2009–2011 by mother and daughter characteristics.

	Initiation				Completion among initiators			
	N ^b	% initiated	Unadjusted OR (99% CI)	Adjusted ^c OR (99% CI)	N ^b	% completed	Unadjusted OR (99% CI)	Adjusted ^c OR (99% CI)
Mother's age								
<35	9854	80.0	1.06 (0.99,1.14)	1.16 (1.07,1.26)	7888	95.0	0.89 (0.77,1.04)	
35–39	26,012	79.8	1.05 (0.99,1.10)	1.09 (1.03,1.15)	20,767	95.0	0.89 (0.80,1.00)	
40-44	32,872	79.1	1.00 (reference)	1.00 (reference)	25,995	95.5	1.00 (reference)	
45-49	16,993	75.5	0.82 (0.77,0.86)	0.80 (0.76,0.85)	12,831	95.4	0.98 (0.86,1.12)	
>=50	4809	70.5	0.63 (0.58,0.69)	0.64 (0.59,0.71)	3389	95.6	1.03 (0.82,1.30)	
Mother's marital status								
Unmarried	18,956	79.3	1.08 (1.02,1.14)	1.03 (0.98,1.09)	15,028	95.0	0.90 (0.81,1.01)	
Married/Registered Partner	56,142	78.0	1.00 (reference)	1.00 (reference)	43,791	95.5	1.00 (reference)	
Divorced/Separated/Widowed	14,459	78.8	1.05 (0.99,1.11)	1.01 (0.95,1.08)	11,387	95.0	0.90 (0.80,1.03)	
Mother's education								
None/Primary only	1215	83.3	1.35 (1.10,1.65)	1.76 (1.40,2.21)	1012	95.5	1.08 (0.73,1.60)	1.33 (0.86,2.03)
Lower secondary	15,878	77.9	0.96 (0.90,1.02)	1.08 (1.01,1.15)	12,376	94.9	0.95 (0.83,1.07)	0.98 (0.86,1.12)
Upper secondary & post-secondary non-tertiary	35,267	78.7	1.00 (reference)	1.00 (reference)	27,756	95.1	1.00 (reference)	1.00 (reference)
Undergraduate	30,043	78.2	0.97 (0.92,1.02)	0.88 (0.83,0.93)	23,484	95.7	1.15 (1.03,1.29)	1.12 (0.98,1.28)
Post-graduate	6538	76.6	0.89 (0.82,0.96)	0.75 (0.68,0.82)	5008	95.6	1.11 (0.91,1.34)	1.01 (0.81,1.26)
Mother's total income (NOK)								
<200,000	9591	70.3	0.59 (0.55,0.63)	0.63 (0.58,0.68)	6743	94.8	0.89 (0.76,1.04)	0.96 (0.80,1.16)
200,000-349,999	29,012	77.2	0.84 (0.80,0.89)	0.84 (0.79,0.88)	22,408	95.2	0.97 (0.87,1.08)	0.99 (0.88,1.11)
350,000-499,999	33,790	80.1	1.00 (reference)	1.00 (reference)	27,062	95.4	1.00 (reference)	1.00 (reference)
500,000-699,999	12,654	81.2	1.07 (1.00,1.15)	1.11 (1.04,1.20)	10,269	95.3	0.98 (0.85,1.13)	1.00 (0.86,1.16)
>=700,000	4820	82.0	1.13 (1.02,1.25)	1.27 (1.14,1.42)	3950	96.5	1.32 (1.05,1.67)	1.39 (1.08,1.78)
Mother's occupational status								
Employed: Managers/Professionals/Associates	34,698	79.7	1.04 (0.99,1.09)	1.04 (0.98,1.11)	27,661	95.7	1.13 (1.02,1.25)	1.05 (0.92,1.20)
Employed: Other	39,598	79.1	1.00 (reference)	1.00 (reference)	31,328	95.2	1.00 (reference)	1.00 (reference)
Unemployed	1251	77.1	0.89 (0.75,1.06)	0.98 (0.81,1.18)	965	94.2	0.82 (0.57,1.18)	0.84 (0.57,1.23)
Outside of workforce ^d	14,256	73.2	0.72 (0.68,0.77)	0.81 (0.76,0.87)	10,441	94.8	0.92 (0.81,1.05)	0.98 (0.84,1.14)
Mother's country of birth								
Norway	76,256	78.5	1.00 (reference)	1.00 (reference)	59,862	95.4	1.00 (reference)	
Old EU ^e /EEA/EFTA, USA, Canada, Australia, NZ	3309	73.5	0.76 (0.69,0.84)	0.88 (0.78,0.98)	2433	95.2	0.95 (0.74,1.22)	
Newer EU & other Europe ^f	2752	77.8	0.96 (0.85,1.08)	1.04 (0.90,1.19)	2140	94.9	0.90 (0.69,1.16)	
Africa	1793	72.2	0.71 (0.62,0.81)	0.76 (0.64,0.90)	1294	95.4	1.00 (0.71,1.41)	
Asia	5104	82.5	1.29 (1.17,1.42)	1.44 (1.29,1.62)	4211	94.9	0.91 (0.75,1.10)	
Central and South America	472	73.1	0.74 (0.57,0.97)	0.76 (0.57,1.02)	345	93.3	0.68 (0.39,1.19)	
Number of children in mother's household								
0	2147	80.3	1.08 (0.93,1.25)	1.20 (1.03,1.40)	1725	94.6	0.83 (0.62,1.10)	0.88 (0.65,1.18)
1	15,359	76.6	0.86 (0.82,0.92)	0.92 (0.87,0.98)	11,767	94.9	0.87 (0.77,0.99)	0.91 (0.80,1.04)
2	40,957	79.1	1.00 (reference)	1.00 (reference)	32,404	95.5	1.00 (reference)	1.00 (reference)
3	23,726	79.1	1.00 (0.95,1.06)	0.99 (0.93,1.04)	18,779	95.5	1.00 (0.89,1.12)	0.97 (0.87,1.09)
>=4	/368	/5.1	0.79 (0.74,0.86)	0.80 (0.74,0.87)	5531	94.9	0.88 (0.74,1.05)	0.88 (0.73,1.06)
Mother's recent cervical screening history								
Not attended screening in the past 4 years	18,390	75.5	0.83 (0.79,0.87)	0.86 (0.81,0.91)	13,890	94.8	0.88 (0.78,0.98)	0.94 (0.84,1.06)
Has attended in past 4 years, recent result normal	70,564	78.9	1.00 (reference)	1.00 (reference)	55,659	95.4	1.00 (reference)	1.00 (reference)
Has attended in past 4 years, recent result abnormal	1586	83.3	1.33 (1.12,1.59)	1.28 (1.07,1.53)	1321	95.4	0.99 (0.71,1.40)	1.08 (0.76,1.54)
Daughter received the combined MMR vaccine								
Yes	85,901	80.1	1.00 (reference)		68,836	95.7	1.00 (reference)	
No	4639	43.8	0.19 (0.18,0.21)		2034	82.9	0.22 (0.19,0.26)	
Daughter's region of residence								
East	43,118	78.4	1.00 (reference)	1.00 (reference)	33,813	94.8	1.00 (reference)	1.00 (reference)
South	5643	78.9	1.03 (0.94,1.13)	1.04 (0.95,1.15)	4454	96.4	1.48 (1.19,1.84)	1.49 (1.19,1.86)
West	20,074	78.7	1.02 (0.96,1.07)	0.99 (0.94,1.05)	15,799	95.5	1.17 (1.04,1.32)	1.17 (1.04,1.33)
Middle	12,726	76.1	0.88 (0.83,0.93)	0.85 (0.79,0.90)	9690	96.0	1.31 (1.13,1.52)	1.33 (1.14,1.55)
North	8969	79.3	1.05 (0.98,1.13)	1.02 (0.95,1.10)	7109	95.4	1.14 (0.98,1.34)	1.17 (0.99,1.37)
Daughter's year of birth								
1997	30,420	72.0	1.00 (reference)	1.00 (reference)	21,895	96.4	1.00 (reference)	1.00 (reference)
1998	29,904	80.4	1.60 (1.52,1.68)	1.63 (1.55,1.71)	24,045	96.6	1.07 (0.94,1.22)	1.05 (0.92,1.21)
1999	30,216	82.5	1.84 (1.74,1.93)	1.86 (1.76,1.96)	24,930	93.0	0.50 (0.44,0.56)	0.48 (0.43,0.54)

 ^a Logistic regression model estimates.
^b Sample sizes refer to unadjusted models, and differ between variables due to missing values. ^a Adjusted for all variables in the table except for MMR vaccination and variables with all Cls overlapping unity in the unadjusted model (N initiation = 87,705, N completion = 68,974).
^d Outside of workforce refers to those who are in education, retired or stay-at-home parents.
^e Countries who joined the EU before 2004.
^f Countries who joined the EU in 2004/2007 & European countries outside of EU/EEA/EFTA.

occupational status, country of birth and number of children in household. For each mother, we also used the Cytology registry to obtain individual information on cervical screening attendance and result during the four years prior to 15 August of the scheduled year of HPV vaccination of the daughter. Norway has an organized cervical screening programme which recommends screening once every three years. The proportion of missing values per sociodemographic variable retrieved from Statistics Norway ranged from 0.7% to 1.8% for mothers and 1.4%–2.4% for fathers. Individuals with a missing value for any model variable were excluded from that model, thus sample sizes differed according to the variables included in each model.

Statistical analyses

To address correlates of vaccine uptake, we used logistic regression with vaccination status as binary dependent variable, and report odds ratios (OR) with 99% confidence intervals (CI). HPV vaccine initiation was defined as having received at least one dose of the vaccine. HPV vaccine completion was defined as having received all three recommended doses of the vaccine. Maternal and paternal characteristics were addressed separately. Selection of independent variables was guided by findings in previous studies (Fisher et al., 2013; Kumar and Whynes, 2011; Spencer et al., 2013; Widgren et al., 2011). We report bivariate (unadjusted) estimates for independent variable. We also report mutually adjusted multivariable estimates for independent variables with at least one bivariate CI not overlapping unity. However, since correlates of MMR and HPV vaccine uptake were similar, MMR vaccine status was not included in multivariable models to avoid collinearity. Statistical computing was performed with Stata MP version 13.1.

Results

Initiation of HPV vaccination

HPV vaccination was initiated by 78.2% of all girls included in the study. The likelihood of vaccination decreased with increasing maternal age (Table 1). Girls with mothers older than age 50 at the time of their daughter's scheduled vaccination had a particularly low likelihood of initiation compared to girls with younger mothers (adjOR: 0.64, CI: 0.59, 0.71). Compared to girls with mothers of intermediate education levels, HPV vaccine initiation was higher among girls whose mothers had the lowest education, and lower for girls whose mothers had the highest education (Table 1). In contrast, HPV vaccine initiation generally increased with increasing maternal income (Table 1). Compared to girls with mothers of intermediate income, initiation was particularly low among girls with mothers in the lowest income bracket (adjOR: 0.63, CI: 0.58, 0.68). HPV vaccine initiation was lower among girls with mothers who were outside the workforce compared to girls with mothers who were currently employed (adjOR: 0.81, CI: 0.76, 0.87, Table 1). Maternal marital status was not strongly associated with initiation of HPV vaccination (Table 1).

There was considerable variation in HPV vaccine uptake by parental country of birth. For instance, mothers from Vietnam had daughters with an uptake exceeding ten percentage points of the population average, while mothers from Somalia and Germany had daughters with uptake lower than ten percentage points below the population average (Table 2). In the multivariable model, girls with mothers from Africa had a somewhat lower likelihood of initiation (adjOR: 0.76, CI: 0.64, 0.90), and girls with mothers from Asia had a higher likelihood of initiation (adjOR: 1.44, CI: 1.29, 1.62), compared to girls with Norwegian mothers (Table 1). Compared with a two-child household, mothers with four or more children, as well as mothers with a single child, were somewhat less likely to have their daughters initiate HPV vaccination, while mothers with no children in their household had daughters with a higher rate of initiation (Table 1). Mother's recent cervical screening history was also associated with daughter initiation of HPV vaccination. Compared with mothers who had a normal test at the last screening visit, non-attendees had daughters with a lower likelihood of initiating HPV vaccination, and mothers who had an abnormal test at the last screening visit had daughters with a higher likelihood of initiating HPV vaccination (Table 1). In total, 94.8% of the girls received the combined MMR vaccine. Girls who had not received the MMR vaccine were far less likely to initiate HPV vaccination (OR: 0.19, CI: 0.18, 0.21, Table 1).

Region of residence was not a very strong predictor of HPV vaccine initiation, although the uptake was somewhat lower in the middle region compared to the other regions (Table 1). Initiation of HPV vaccination was higher for girls born in 1998 and 1999 than for girls born in 1997 (Table 1).

The model estimates of the unadjusted and the adjusted models differed somewhat more for the education variable than for the other variables, indicating confounding. Since education and income were moderately correlated (Spearman $r_s = 0.43$, p < 0.0001), we performed additional multivariable models stratified by income level, which showed that education was negatively associated with initiation in each of the three lowest categories of income, but no association with education was found in the two highest income categories (not shown). We also performed a separate model for girls with mothers of Norwegian descent, since they were poorly represented at the lowest education level. This analysis confirmed that, relative to the intermediate reference level, girls with highly educated Norwegian mothers had a significantly lower likelihood of initiation of HPV vaccination. However, no significant differences were found for the two lowest levels of education (not shown).

The analyses addressing associations between paternal characteristics and initiation of HPV vaccination (Table 3) largely showed the same patterns as described for the mother-daughter pairs (Table 1). However, the differences observed were often somewhat smaller in the paternal analyses. Moreover, occupational status was not significantly associated with daughter initiation of HPV vaccination in the paternal multivariable model.

Completion of HPV vaccination

Completion of all three recommended vaccine doses was achieved for 74.6% of all girls included in the study, and for 69.4, 77.6, and 76.7% of the 1997, 1998 and 1999 cohorts, respectively. Among girls who initiated HPV vaccination, 95.3% completed the vaccine series.

Among girls who initiated HPV vaccination, there was little variation in completion across the categories of each included characteristic.

Table 2

Crude rates of initiation of HPV vaccination among 12–13 year old girls in Norway 2009–2011 by parental country of birth^a.

	Mothers		Fathers		
Country	N	% vaccinated (99% CI)	N	% vaccinated (99% CI)	
Vietnam	500	90.6 (86.6,93.5)	460	90.2 (86.1,93.5)	
Thailand	516	87.8 (83.5,91.1)	19	73.7 (41.8,93.8)	
Kosovo	371	87.3 (82.1,91.2)	397	85.6 (80.6,89.8)	
Afghanistan	318	85.8 (80.0,90.2)	291	88.7 (83.1,93.0)	
Pakistan	810	84.3 (80.7,87.3)	869	81.7 (78.1,85.0)	
Turkey	416	84.1 (78.9,88.2)	461	80.5 (75.3,85.0)	
Iran	305	81.6 (75.2,86.7)	429	77.6 (72.0,82.6)	
Iraq	646	81.1 (76.8,84.8)	646	81.4 (77.2,85.2)	
Philippines	463	80.6 (75.4,84.9)	106	84.9 (73.9,92.6)	
Poland	699	80.5 (76.4,84.1)	476	79.8 (74.7,84.4)	
Sri Lanka	498	80.5 (75.5,84.7)	537	79.5 (74.7,83.8)	
Sweden	886	79.1 (75.4,82.4)	761	76.0 (71.7,79.8)	
Norway	76,322	78.5 (78.1,78.9)	74,745	78.5 (78.2,78.9)	
Denmark	517	77.8 (72.7,82.1)	451	77.8 (72.4,82.7)	
Bosnia-Herzegovina	261	75.1 (67.5,81.4)	265	75.1 (67.6,81.6)	
US	431	74.9 (69.2,80.0)	423	70.4 (64.4,76.0)	
Costa Rica	370	71.1 (64.6,76.8)	155	69.7 (59.3,78.8)	
UK	254	69.7 (61.7,76.6)	406	76.6 (70.8,81.8)	
Germany	395	65.1 (58.6,71.0)	397	76.1 (70.1,81.4)	
Somalia	746	63.9 (59.3,68.3)	607	62.9 (57.7,67.9)	

^a The 20 most frequent countries of birth among mothers.

Several correlates of initiation were not associated with completion, and the models addressing maternal (Table 1) and paternal characteristics (Table 3) generally showed similar results. However, if the girl had not received the MMR vaccine, her likelihood of completion was considerably lower than if she had received the vaccine. Moreover, the completion rates were slightly lower in the eastern region as compared to the other regions of Norway, and lower in 1999 than in the two preceding years. A higher completion rate was observed for the highest level of maternal income (Table 1), and a lower completion rate was observed for the lowest level of paternal income (Table 3).

Table 3

Odds ratios^a for initiation and completion of routine HPV vaccination among 12–13 year old girls in Norway 2009–2011 by father and daughter characteristics.

	Initiation				Completion among initiators			
	N ^b	% initiated	Unadjusted OR (99% CI)	Adjusted ^c OR (99% CI)	N ^b	% completed	Unadjusted OR (99% CI)	Adjusted ^c OR (99% CI)
Father's age								
<35	3344	80.0	1.05 (0.94,1.19)	1.08 (0.95,1.22)	2675	95.1	0.95 (0.74,1.21)	
35-39	16.810	80.0	1.06 (1.00.1.13)	1.09 (1.02.1.16)	13.456	95.2	0.98 (0.86,1,11)	
40-44	31.070	79.1	1.00 (reference)	1.00 (reference)	24.584	95.3	1.00 (reference)	
45-49	22,678	78.1	0.94 (0.89 0.99)	0.93 (0.88 0.98)	17 703	95.6	1.06 (0.94.1.20)	
>=50	14 663	743	0.76 (0.72 0.81)	0.77(0.720.82)	10,888	95.3	0.99 (0.86 1.13)	
	1 1,005	7 1.5	0.70 (0.72,0.01)	0.77 (0.72,0.02)	10,000	55.5	0.00 (0.00,1.10)	
Father's marital status								
Unmarried	17,818	79.3	1.09 (1.04,1.15)	1.11 (1.04,1.18)	14,135	94.9	0.87 (0.78,0.98)	0.93 (0.82,1.06)
Married/registered partner	55,695	77.8	1.00 (reference)	1.00 (reference)	43,349	95.5	1.00 (reference)	1.00 (reference)
Divorced/separated/widowed	13,223	79.1	1.08 (1.01,1.15)	1.22 (1.13,1.31)	10,459	95.1	0.91 (0.80,1.04)	1.03 (0.88,1.21)
Father's education								
None/primary only	746	82.3	1.24 (0.96,1.59)	1.41 (1.07,1.86)	614	96.4	1.34 (0.77,2.36)	
Lower secondary	16,448	78.7	0.98 (0.93,1.04)	1.02 (0.96,1.09)	12,950	95.0	0.95 (0.84,1.07)	
Upper secondary & post-secondary non-tertiary	42,001	79.0	1.00 (reference)	1.00 (reference)	33,177	95.2	1.00 (reference)	
Undergraduate	18,921	76.9	0.89 (0.84,0.94)	0.90 (0.84,0.95)	14,556	95.6	1.09 (0.96,1.23)	
Post-graduate	9236	77.0	0.89 (0.83,0.96)	0.91 (0.84,0.99)	7114	95.8	1.14 (0.96,1.34)	
Father's total income (NOK)								
<200,000	4329	72.6	0.73 (0.66,0.80)	0.78 (0.69,0.87)	3143	93.7	0.72 (0.58,0.88)	0.76 (0.60,0.96)
200,000-349,999	12,301	77.5	0.94 (0.88,1.01)	0.95 (0.88,1.03)	9528	94.9	0.89 (0.77,1.03)	0.92 (0.79,1.08)
350,000–499,999	27,032	78.5	1.00 (reference)	1.00 (reference)	21,214	95.4	1.00 (reference)	1.00 (reference)
500,000–699,999	22,598	79.3	1.05 (0.99,1.11)	1.04 (0.98,1.10)	17,916	95.6	1.04 (0.92,1.18)	1.06 (0.93,1.21)
>=700,000	20,589	78.8	1.02 (0.96,1.08)	1.04 (0.98,1.11)	16,230	95.7	1.06 (0.93,1.21)	1.08 (0.94,1.25)
Father's occupational status								
Employed: managers/professionals/associates	34 906	784	0.98 (0.94.1.03)	1 00 (0 94 1 05)	27 381	95.6	1 08 (0 97 1 19)	1.06 (0.95.1.18)
Employed: managers/protessionals/associates	/1 880	787	1.00 (reference)	1.00(0.54, 1.05)	32 082	05.3	1.00 (0.57, 1.15) 1.00 (reference)	1.00 (0.55,1.10)
Unemployed	1225	77.8	0.95 (0.79.1.13)	1.00 (101010100)	953	95.0	0.93 (0.63 1.36)	1.00 (10101000)
Outside of workforce ^d	8707	76.2	0.86 (0.80.0.93)	0.96 (0.89 1.05)	6635	94.4	0.33(0.33,1.30) 0.83(0.720.97)	1.07(0.71,1.55) 1.00(0.84120)
outside of workforce	0707	70.2	0.00 (0.00,0.00)	0.50 (0.05,1.05)	0055	54.4	0.05 (0.72,0.57)	1.00 (0.04,1.20)
Father's country of birth								
Norway	74,745	78.5	1.00 (reference)	1.00 (reference)	58,706	95.3	1.00 (reference)	
Old EU ^e /EEA/EFTA, USA, Canada, Australia, NZ	3316	73.8	0.77 (0.69,0.85)	0.83 (0.74,0.93)	2447	95.3	0.98 (0.76,1.26)	
Newer EU & Other Europe ^f	2165	78.2	0.98 (0.85,1.12)	1.00 (0.86,1.17)	1692	95.8	1.12 (0.81,1.53)	
Africa	1662	71.6	0.69 (0.60,0.79)	0.77 (0.66,0.90)	1190	95.7	1.09 (0.75,1.58)	
Asia	4170	81.4	1.19 (1.08,1.33)	1.31 (1.16,1.47)	3394	95.2	0.97 (0.79,1.21)	
Central and South America	339	72.6	0.72 (0.53,0.99)	0.77 (0.55,1.07)	246	94.3	0.81 (0.40,1.65)	
Number of shildren in father's household								
Number of children in father's nousenoid	12 101	77.4	0.00 (0.04.0.05)	0.02 (0.77.0.00)	10 127	045	0.77 (0.60.0.00)	0.02 (0.00 0.00)
1	13,101	77.4	0.89 (0.84,0.95)	0.83(0.77,0.90)	10,137	94.5	0.77 (0.68,0.89)	0.82 (0.69,0.96)
1	12,970	77.3	0.89(0.84,0.95)	0.88(0.82,0.94)	10,034	95.3	0.92(0.79,1.06)	0.93(0.80,1.07)
2	34,301	79.3	1.00 (reference)	1.00 (reference)	27,187	95.7	1.00 (reference)	
3	20,273	79.1	0.99(0.94, 1.05)	0.98(0.93, 1.04)	16,041	95.6	0.98(0.87,1.12)	0.96(0.85,1.09)
>=4	6086	/4./	0.77 (0.71,0.84)	0.76 (0.70,0.83)	4545	94.9	0.84 (0.69,1.01)	0.83 (0.68,1.00)
Daughter received the combined MMR vaccine								
Yes	84.240	80.1	1.00 (reference)		67.435	95.7	1.00 (reference)	
No	4325	43.3	0.19 (0.18.0.21)		1871	83.1	0.22 (0.19.0.26)	
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Daughter's region of residence								
East	42,126	78.4	1.00 (reference)	1.00 (reference)	33,034	94.9	1.00 (reference)	1.00 (reference)
South	5520	78.9	1.03 (0.94,1.13)	1.01 (0.92,1.11)	4357	96.4	1.46 (1.17,1.83)	1.46 (1.17,1.82)
West	19,628	78.6	1.01 (0.96,1.07)	0.98 (0.93,1.04)	15,426	95.5	1.16 (1.03,1.31)	1.14 (1.01,1.29)
Middle	12,511	76.1	0.88 (0.82,0.93)	0.84 (0.79,0.90)	9519	96.0	1.30 (1.12,1.50)	1.32 (1.13,1.54)
North	8770	79.4	1.06 (0.99,1.14)	1.06 (0.98,1.15)	6965	95.5	1.14 (0.97,1.34)	1.16 (0.99,1.37)
Daughter's year of hirth								
1007	20 280	71.0	1.00 (reference)	1.00 (reference)	21/11/	96.5	1.00 (reference)	1.00 (reference)
1998	20,700	80.4	1.60 (1.52.1.60)	1.00 (1000000)	21,414	96.7	1.00 (101010100)	1.05 (0.02 1.20)
1999	29 535	82.6	185 (176195)	1 88 (1 78 1 98)	23,300	93.0	0.49(0.440.55)	0.48(0.430.54)
1555	20,000	52.0	1.03 (1.70,1.33)	1.00 (1.70,1.30)	24,304	55.0	515 (014,0.55)	(FC.0,CF.0) 0F.0

^a Logistic regression model estimates.

^b Sample sizes refer to unadjusted models, and differ between variables due to missing values.

^c Adjusted for all variables in the table except for MMR vaccination and variables with all CIs overlapping unity in the unadjusted model (N initiation = 85,039, N completion = 67,762). ^d Outside of workforce refers to those who are in education, retired or stay-at-home parents.

^e Countries who joined the EU before 2004.

^f Countries who joined the EU in 2004/2007 & European countries outside of EU/EEA/EFTA.

Discussion

This study shows that publicly funded school-based vaccination generally provides equitable HPV vaccine uptake. However, some disparities in initiation of HPV vaccination were found. The lowest rates and likelihoods of initiation were identified among girls who had not received the MMR vaccine, girls with mothers in the lowest income bracket, and girls with mothers age 50 or above. Girls with parents originating from a subset of foreign countries, and girls with mothers who were outside the workforce also had a relatively low uptake.

A recent meta-analysis did not find strong evidence for differences in HPV vaccination initiation by parental education or income (Fisher et al., 2013). We found opposing effects of parental education and income, which may be explained by the moderate correlation documented between these two variables. In Norway, dispersion in earnings is remarkably low (Haegeland et al., 1999), and the economic returns of higher education are far lower than commonly observed in other countries (OECD, 2014; Reisel, 2013). However, the estimates of the education variable changed markedly with multivariable modelling, implying that education was particularly influenced by other variables that also were associated with vaccine uptake. Further, the effect of education was not consistent across all levels of income. The most striking effect of parental education was not a particularly low uptake at any level of education, but a high uptake at the lowest level of education. In contrast, initiation of HPV vaccination was particularly low in the lowest parental income bracket, which affected many girls. Hence, from a public health perspective, parental income appeared to be a more important predictor of inequality than did parental education.

We confirm previous findings that maternal cervical screening attendance, as well as experience with an abnormal screening result, may influence daughter HPV vaccine uptake (Chao et al., 2009; Spencer et al., 2013). This indicates that maternal knowledge about cervical cancer and/or maternal compliance to preventive public health measures in general may be relevant for daughter uptake of the HPV vaccine. We also confirm (Ogilvie et al., 2010) that having more than three children in the household may reduce the likelihood of HPV vaccine uptake. However, in contrast to some other studies (Sinka et al., 2014; Smith et al., 2011), we did not find strong evidence of socioeconomic disparities in completion of HPV vaccination.

A family model of two workers/caregivers who share paid and unpaid work equally, is a political goal in many countries. In Norway, the involvement of fathers in daily child care has become substantial (Kitterod and Lappegard, 2012), which may facilitate comparatively more paternal involvement in child health-related decision making (Zvara et al., 2013). Although the associations to HPV vaccine uptake sometimes were slightly weaker in the paternal than in the maternal models in the present study, the patterns were similar, indicating that maternal and paternal sociodemographic characteristics play a similar role for daughter HPV vaccine uptake. Hence, efforts to decrease disparities in HPV vaccine uptake, and to increase the uptake in general, should reach and appeal to mothers and fathers alike. Further studies on father involvement in decisions regarding child HPV vaccine uptake are needed.

Study limitations and strengths

The present study has several strengths that set it apart from studies on HPV vaccine uptake performed in a similar setting in other countries (Fisher et al., 2014; Kumar and Whynes, 2011; Ogilvie et al., 2010; Sinka et al., 2014; Smith et al., 2011; Widgren et al., 2011). We investigate variables registered at the individual level, and all dynamic variables refer to the year of scheduled vaccination. Furthermore, we present data on maternal and paternal characteristics separately, which to our knowledge has not been done before. Another strength of this study is the use of administrative and health registry data that is not self-reported, close to complete and of high validity for the entire population of Norwegian girls eligible for vaccination, and for their parents. The registries used in this study are continuously updated and have standardized routines for retrieval and registration of data, ensuring high data quality (Larsen et al., 2009; Seaboe et al., 2003; Trogstad et al., 2012). The use of population-based registry data in the present study minimizes the potential for selection, misclassification and response bias. However, the analyses presented here do not address causal relationships or identify individual barriers to HPV vaccine uptake in Norway. A range of individual barriers to HPV vaccination, such as receiving inadequate information, perceiving the daughter as too young for the vaccine, and concerns about side effects, have previously been identified in surveys and qualitative studies (Grandahl et al., 2014; Marlow et al., 2007; Waller et al., 2006). Further studies are needed to address how the population-level characteristics addressed here may be associated to individual choices regarding HPV vaccination.

The multivariable models presented include many variables, several of which are correlated, which could introduce overadjustment bias and affect model precision (Schisterman et al., 2009). It is also possible that we did not adjust for all salient confounders (i.e. residual confounding). Moreover, there are likely to be associations between the variables in this comprehensive dataset that were not fully addressed in the models. As such, assessments of the public health relevance of the data presented here should be based on the crude estimates as well as the adjusted estimates. In general, the patterns observed in the corresponding adjusted estimates.

Conclusions

Knowledge from this study may be relevant for other vaccination programmes, and may be useful for the development of strategies to further improve uptake of the HPV vaccine. Although this study shows that alarming disparities in the uptake of the HPV vaccine within a publicly funded school-based delivery system do not exist, some subgroups had a relatively low uptake and contained many girls. Information campaigns designed to reach these groups could improve equity in delivery. Moreover, since the uptake was far lower for the HPV than for the MMR vaccine across all sub-groups investigated, this study also demonstrates a large general potential for improving HPV vaccine uptake.

Author contributions

BTH conceived the study and drafted the manuscript. SC managed all data and performed the analyses. All authors contributed to study design, commented on various drafts and approved the final version of the manuscript.

Conflict of interest statement

BTH, SC and EB declare no conflict of interest. MN has received research grants from MSD/ Merck through the affiliating institute.

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Ethical approval

The study was approved by the Regional committee for medical and health research ethics (reference number: 2013/420/REKsør-østC).

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References

- Arnheim-Dahlstrom, L, Pasternak, B, Svanstrom, H., Sparen, P., Hviid, A., 2013. Autoimmune, neurological, and venous thromboembolic adverse events after immunisation of adolescent girls with quadrivalent human papillomavirus vaccine in Denmark and Sweden: cohort study. Br. Med. J. 347, f5906.
- Aubin, F., Pretet, J.L., Jacquard, A.C., et al., 2008. Human papillomavirus genotype distribution in external acuminata condylomata: a large French national study (EDiTH IV). Clin. Infect. Dis. 47, 610–615.
- Baandrup, L, Blomberg, M., Dehlendorff, C., Sand, C., Andersen, K.K., Kjaer, S.K., 2013. Significant decrease in the incidence of genital warts in young Danish women after implementation of a national human papillomavirus vaccination program. Sex. Transm. Dis. 40, 130–135.
- Bosch, F.X., Lorincz, A., Munoz, N., Meijer, C.J., Shah, K.V., 2002. The causal relation between human papillomavirus and cervical cancer. J. Clin. Pathol. 55, 244–265.
- Chao, C., Slezak, J.M., Coleman, K.J., Jacobsen, S.J., 2009. Papanicolaou screening behavior in mothers and human papillomavirus vaccine uptake in adolescent girls. Am. I. Public Health 99. 1137–1142.
- Fisher, H., Trotter, C.L., Audrey, S., MacDonald-Wallis, K., Hickman, M., 2013. Inequalities in the uptake of human papillomavirus vaccination: a systematic review and metaanalysis. Int. I. Epidemiol. 42, 896–908.
- Fisher, H., Audrey, S., Mytton, J.A., Hickman, M., Trotter, C., 2014. Examining inequalities in the uptake of the school-based HPV vaccination programme in England: a retrospective cohort study. J. Public Health 36, 36–45.
- Grandahl, M., Oscarsson, M., Stenhammar, C., Neveus, T., Westerling, R., Tyden, T., 2014. Not the right time: why parents refuse to let their daughters have the human papillomavirus vaccination. Acta Paediatr. 103, 436–441.
- Haegeland, T., Klette, T.J., Salvanes, K.G., 1999. Declining returns to education in Norway? Comparing estimates across cohorts, sectors and over time. Scand. J. Econ. 101, 555–576.
- Hofstetter, A.M., Rosenthal, S.L., 2014. Factors impacting HPV vaccination: lessons for health care professionals. Expert Rev. Vaccines 13, 1013–1026.
- Kitterod, R.H., Lappegard, T., 2012. A typology of work–family arrangements among dualearner couples in Norway. Fam. Relat. 61, 671–685.
- Kumar, V.M., Whynes, D.K., 2011. Explaining variation in the uptake of HPV vaccination in England. BMC Public Health 11, 172.
- Larsen, I.K., Smastuen, M., Johannesen, T.B., et al., 2009. Data quality at the Cancer Registry of Norway: an overview of comparability, completeness, validity and timeliness. Eur. J. Cancer 45, 1218–1231.
- Leval, A., Herweijer, E., Ploner, A., et al., 2013. Quadrivalent human papillomavirus vaccine effectiveness: a Swedish national cohort study. J. Natl. Cancer Inst. 105, 469–474.
- Markowitz, L.E., Tsu, V., Deeks, S.L., et al., 2012. Human papillomavirus vaccine introduction the first five years. Vaccine 30, F139–F148.
- Marlow, L.A.V., Waller, J., Wardle, J., 2007. Parental attitudes to pre-pubertal HPV vaccination. Vaccine 25, 1945–1952.
- OECD, 2014. Economic Survey Of Norway. OECD, Paris.

- Ogilvie, G., Anderson, M., Marra, F., et al., 2010. A population-based evaluation of a publicly funded, school-based HPV vaccine program in British Columbia, Canada: parental factors associated with HPV vaccine receipt. PLoS Med. 7, e1000270.
- Paavonen, J., Naud, P., Salmeron, J., et al., 2009. Efficacy of human papillomavirus (HPV)-16/18 AS04-adjuvanted vaccine against cervical infection and precancer caused by oncogenic HPV types (PATRICIA): final analysis of a double-blind, randomised study in young women. Lancet 374, 301–314.
- Poole, T., Goodyear-Smith, F., Petousis-Harris, H., et al., 2012. Human papillomavirus vaccination in Auckland: reducing ethnic and socioeconomic inequities. Vaccine 31, 84–88.
- Reisel, L., 2013. Is more always better? Early career returns to education in the United States and Norway. Res. Soc. Stratification Mobil. 31, 49–68.
- Rondy, M., van Lier, A., van de Kassteele, J., Rust, L., de Melker, H., 2010. Determinants for HPV vaccine uptake in the Netherlands: a multilevel study. Vaccine 28, 2070–2075.
- Schisterman, E.F., Cole, S.R., Platt, R.W., 2009. Overadjustment bias and unnecessary adjustment in epidemiologic studies. Epidemiology 20, 488–495.
- Seaboe, H.V., Byfuglien, J., Johannessen, R., 2003. Quality issues at statistics Norway. J. Off. Stat. 19, 287–303.
- Sinka, K., Kavanagh, K., Gordon, R., et al., 2014. Achieving high and equitable coverage of adolescent HPV vaccine in Scotland. J. Epidemiol. Community Health 68, 57–63.
- Slade, B.A., Leidel, L., Vellozzi, C., et al., 2009. Postlicensure safety surveillance for quadrivalent human papillomavirus recombinant vaccine. IAMA 302, 750–757.
- Smith, L.M., Brassard, P., Kwong, J.C., Deeks, S.L., Ellis, A.K., Levesque, L.E., 2011. Factors associated with initiation and completion of the quadrivalent human papillomavirus vaccine series in an Ontario cohort of grade 8 girls. BMC Public Health 11, 645.
- Spencer, A.M., Brabin, L., Verma, A., Roberts, S.A., 2013. Mothers' screening histories influence daughters' vaccination uptake: an analysis of linked cervical screening and human papillomavirus vaccination records in the North West of England. Eur. J. Cancer 49, 1264–1272.
- Steens, A., Wielders, C.C., Bogaards, J.A., Boshuizen, H.C., de Greeff, S.C., de Melker, H.E., 2013. Association between human papillomavirus vaccine uptake and cervical cancer screening in the Netherlands: implications for future impact on prevention. Int. J. Cancer 132, 932–943.
- Trogstad, L., Ung, G., Hagerup-Jenssen, M., Cappelen, I., Haugen, I.L., Feiring, B., 2012. The Norwegian immunisation register – SYSVAK. Euro Surveill. 17, 20147.
- Villa, L., Perez, G., Kjaer, S., et al., 2007. Effect of prophylactic human papillomavirus L1 virus-like-particle vaccine on risk of cervical intraepithelial neoplasia grade 2, grade 3, and adenocarcinoma in situ: a combined analysis of four randomised clinical trials. Lancet 369, 1861–1868.
- Waller, J., Marlow, L.A.V., Wardle, J., 2006. Mothers' attitudes towards preventing cervical cancer through human papillomavirus vaccination: a qualitative study. Cancer Epidemiol. Biomarkers 15, 1257–1261.
- Widgren, K., Simonsen, J., Valentiner-Branth, P., Molbak, K., 2011. Uptake of the human papillomavirus-vaccination within the free-of-charge childhood vaccination programme in Denmark. Vaccine 29, 9663–9667.
- zur Hausen, H., 2009. Papillomaviruses in the causation of human cancers a brief historical account. Virology 384, 260–265.
- Zvara, B.J., Schoppe-Sullivan, S.J., Dush, C.K., 2013. Fathers' involvement in child health care: associations with prenatal involvement, parents' beliefs, and maternal gatekeeping. Fam. Relat. 62, 649–661.