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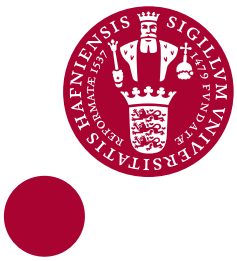

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Published in:
Preventive Medicine Reports

DOI:
10.1016/j.pmedr.2018.02.005

Publication date:
2018

Document version
Publisher's PDF, also known as Version of record

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Citation for published version (APA):
Suppli, C. H., Dreier, J. W., Rasmussen, M., Andersen, A. M. N., Valentiner-Branth, P., Mølbak, K., & Krause, T. G. (2018). Sociodemographic predictors are associated with compliance to a vaccination-reminder in 9692 girls age 14, Denmark 2014–2015. *Preventive Medicine Reports*, *10*, 93-99. https://doi.org/10.1016/j.pmedr.2018.02.005

Download date: 26. sep.. 2020

Preventive Medicine Reports 10 (2018) 93–99

Contents lists available at ScienceDirect

Preventive Medicine Reports

journal homepage: www.elsevier.com/locate/pmedr

Sociodemographic predictors are associated with compliance to a vaccination-reminder in 9692 girls age 14, Denmark 2014–2015

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ARTICLE INFO

Keywords:
Vaccination
Immunization
Socioeconomic factors

ABSTRACT

We aimed to identify sociodemographic predictors of compliance after receiving a personalised reminder on lacking vaccinations against MMR (Measles, Mumps, Rubella) and/or HPV (Human Papilloma Virus) among parents of Danish adolescent girls.

A nationwide register-based study, including all 14-year-old girls (15 May 2014–14 May 2015) lacking either MMR, HPV-vaccination or both. Vaccination-compliance following a postal reminder was modelled using multivariable logistic regression and included the following socio-demographic predictors: maternal age, education, employment and ethnicity. Birth order, number of siblings, family-structure, location of residence, and household income.

The parents of 9692 girls received a reminder. Out of 4940 exclusively lacking an HPV-vaccine, 15.3% were subsequently vaccinated. Among 2026 only lacking an MMR vaccination, 8.5% were vaccinated. Among 2726 girls lacking both, 5% received an HPV, 4.4% an MMR and 5.4% received both vaccinations. We identified sociodemographic differences between reminderletter-compliers and non-compliers, also according to vaccination types. Non-western descendants were more likely to receive HPV-vaccination, although the association was only significant for those who only lacked HPV (OR 2.02, 95% 1.57–2.59). For girls only lacking an MMR, regional differences were identified. Among girls lacking both vaccines, girls of mothers with intermediate (OR 0.63, 0.42–0.95) or basic education (OR 0.43, 0.24–0.75) were less likely to be vaccinated compared to girls of higher educated mothers.

Reminders were in particular effective in increasing HPV uptake among immigrants of non-Western ethnicity. We found reminders to be less effective among less educated mothers whose daughters lacked both vaccines. To increase the coverage in this group, additional interventions are needed.

1. Introduction

Childhood immunization is one of the most powerful and cost-effective of all health interventions and prevents illness and saves millions of lives every year. (World Health Organization, Unicef, 2009).

Despite the proven safety and efficacy of vaccines, immunization rates remain suboptimal in many European countries, and some vaccine-preventable diseases are not sufficiently controlled (Muscat, 2011; WHO regional Office Europe, 2017).

The national immunization program (NIP) of Denmark is a voluntary and free-of-charge program with an overall high childhood vaccination uptake that exceeds 85% for most vaccines. The General Practitioners (GPs) administer vaccines during "Well child visits" which start at 5 weeks, 5 and 12 months and at 2, 3, 4 and 5 years of age. Lastly, there are two visits around 12 years of age (Sundhed.dk, n.d.).

Recent data on vaccination uptake in Denmark shows that coverage of the second vaccine against measles, mumps and rubella (MMR2) given at 4 years of age remains stable around 88% (figures for birth cohort 2012). On the other hand, coverage of first Human Papillomavirus vaccination (HPV1) has dropped from a historical high of 92% (birth cohorts 1998–2000) to a non-satisfactory coverage of 57% (birth cohort of 2004) (SSI, n.d.), following a public media

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https://doi.org/10.1016/j.pmedr.2018.02.005
Received 30 September 2017; Received in revised form 6 February 2018; Accepted 11 February 2018
Available online 23 February 2018
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discussion about concerns of HPV-vaccine safety in Denmark in the period 2015–16.

Suboptimal vaccination coverage results from a variety of challenges and obstacles acting on different subgroups of the population. These vary from vaccine to vaccine with specific challenges in the different age groups. Ethnicity, low parental socioeconomic status and education, older age of the child, younger maternal age, large family size, late birth order, forgetfulness, sick child delays, and delayed well child visits have been associated with suboptimal compliance to vaccinations (Falagas and Zarkadoulia, 2008; Luman et al., 2003; Strine et al., 2003; Tabacchi et al., 2016).

The literature describes two qualitatively different groups of parents to non-vaccinated children (Leask et al., 2014; Leask et al., 2012). The first are "conscientious objectors" or hesitant parents with expressed concerns about immunization. These parents may decline, delay or be selective in the vaccines they accept and tend to be more affluent and educated (Dubé et al., 2013). The second group comprises families experiencing barriers to access, which may relate to social disadvantage, cultural or logistical barriers (Smith et al., 2004).

Other factors of importance for vaccination uptake include the organisational structures around the vaccination programme as well as personal experience with vaccine-preventable diseases (Falagas and Zarkadoulia, 2008; Glatman-freedman and Nichols, 2012). Investigations of risk factors for non-compliance to reminders on lacking vaccinations may inform future strategies and interventions to increase vaccination coverage.

Systematic reviews show that several interventions are effective in increasing vaccination uptake (Briss et al., 2000; Harvey et al., 2015; Jacobson and Szilagyi, 2009). Reminder/recall may be particularly useful for adolescents who tend to visit medical providers less frequently than younger children, and have been shown to receive less preventive visits (Rand et al., 2007; Suh et al., 2012). New technology such as text messaging and other electronic messages can be especially effective in adolescents (Crocker-Buque et al., 2016).

To increase compliance with the NIP, the Danish parliament decided from May 2014 to issue written reminders to parents of children who lack one or more vaccinations. Vaccination-reminders are issued when the child turns 2, 6 1/2 and 14 years. The vaccination-reminders have been found to increase the vaccination-coverage of MMR2 with 5 percentage point in children at 7 years (Suppli et al., 2017).

However, it is unknown whether there is sociodemographic inequality in compliance with this health intervention and whether it differs by vaccination. Tseng et al. investigated the efficacy of sending letters reminding on cervical cancer screening and found a lower response in women in lower socioeconomic groups (Tseng et al., 2000).

By merging high-quality individual data from multiple national registries, we investigated demographic and socio economic predictors of vaccination compliance with the aims to identify at risk groups of non-compliance to vaccination reminders. A personalised reminder letter concerning HPV and MMR vaccination was sent to parents of Danish girls aged 14 years.

2. Methods and materials

2.1. Study design and study population

We carried out a register-based study including all girls born in Denmark from 15 May 2000 to 14 May 2001, who lacked at least one HPV or MMR-vaccination at their 14th birthday and received a reminder. From national registers, we obtained information on socio-demographic predictors and vaccines given in the following 6 months. Data were linked using the unique Danish civil registration number (CRS). Demographic characteristics and indicators of socioeconomic status included maternal age, maternal education level, family-structure (one- or two-parent household), household income level, place of residence, birth order of the girl, and number of siblings. The reference group was selected as the largest proportion within each socio-demographic predictor. All determinants excluding maternal age and birth order were extracted at the girls 14th birthday. We only included girls alive and living in Denmark in the full study period. Information on emigrations and deaths was extracted from the Danish Civil Registration System.

2.1.1. The Danish Vaccination Register (DDV)

The DDV contains information on all vaccinations given in the NIP to children born from 1996 and onwards. For reimbursement purposes, GPs report all vaccination information to the Health Region. From the health regions, the data is imported into the DDV register. The register contains information such as: date of vaccination, a unique personal identification number (CRS number) of the recipient, name and ID of the vaccine, and identification on the GP (Grove Krause et al., 2012). Since February 2013, citizens have had access to their own vaccination status online. Health professionals have accessed their patients' vaccination status from the NIP since 1996. In case of an under-registration of previously given vaccines, both patients and doctors can add such historical vaccinations online. Patient registered information is included in the register after validation by a doctor.

2.2. The reminder system

The reminder system was implemented 15 May 2014. All children who turn two, 6 1/2 and 14 years lacking at least one vaccination in the childhood vaccination programme are identified in DDV. Parents are reminded on all vaccinations in the NIP except lacking pneumococcal conjugate or Haemophilus influenzae B vaccinations. The reminder is sent to the parent in custody of the child. If the parents have joint custody but do not share the same address, the reminder is sent to both parents (Krause et al., 2015). Information on all written reminders is saved in a database. (See appendix 1 for generic reminder letter).

2.3. Demographic factors

The selection of potential socio-demographic predictors was based on prior knowledge of predictors for vaccination uptake in Denmark (Fernández de Casadevante et al., 2016; Sundhedsstyrelsen, 2007; Widgren et al., 2011) and as measures describing different aspects of the socio-economic position of the family.

- Maternal age at time of birth (< 25 years, 25–34 and ≥35), from the Danish Civil Registration System (Pedersen, 2011).
- Maternal educational level at the daughter's 14th birthday (higher defined as bachelor degree or more), intermediate (high school level) and basic, from the Population's Education Register (Jensen and Rasmussen, 2011).
- Maternal ethnicity, categorised by place of birth (Danish born, western-immigrant and non-western immigrant), from the Danish Civil Registration System (Pedersen, 2011).
- Maternal level of employment (no unemployment, up to 26 weeks of unemployment and > 26 weeks of unemployment), from the Integrated Labour Market Statistics Register (Timmermans, 2010).
- Maternal birth order of the girl, (first, second and third or later), from The Medical Birth Register (Knudsen and Olsen, 1998).
- Number of siblings, both older and younger (0, 1, 2 and 3 or more), from the Population Statistics Register (Statistics_Denmark, 2016).
- Place of residence at the time of the reminder, by the five regions of Denmark (Nomenclature of Territorial Units for Statistics, level 2, from the Danish Civil Registration System (Pedersen, 2011)).
- Family-structure (two parent and single parent household), from The Population Statistics Register (Statistics_Denmark, 2016).
- Household income level in 2014 (0–20, 21–40, 41–60, 61–80 and 81–100 percentiles), from The Income Statistics Register (Baadsgaard and Quitzau, 2011).

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2.4. Outcome variables

We defined three endpoints: (i) vaccination with MMR during the six months after reminder, (ii) vaccination with HPV, and (iii) vaccination with both MMR and HPV.

2.5. Statistical analysis

All variables were defined a priori and kept in the multivariable model. Logistic regression models were used to estimate crude and adjusted odds ratios (ORs and aORs) and their corresponding 95% confidence intervals (CIs) to examine the effect of sociodemographic characteristics on compliance to the reminder. Separate models were specified for a) uptake of MMR among girls only lacking MMR, b) uptake of HPV among girls only lacking HPV, c) uptake only of MMR among girls lacking MMR and HPV, d) uptake only of HPV among girls lacking MMR and HPV, and finally e) uptake of both MMR and HPV, among girls lacking MMR and HPV. Likelihood ratio tests were used to assess model fit when the predictors were individually removed from the full model. Analyses were performed using Stata (version 14 StataCorp, 2013).

3. Results

This study included 9692 girls who turned 14 years between 15 May 2014 and 14 May 2015; 4940 lacked one or more HPV-vaccine, 2026 lacked only one or more MMR-vaccine and 2726 lacked both HPV and MMR-vaccines. A large proportion of the girls resided in the Capital Region (31.7%), 85.7% had Danish-born mothers; 88% had mothers that were employed in the previous year and for 40.3% their mothers had a higher education.

Table 1 shows the number of registered vaccines in the six-month-period following the reminder. Overall, 14% of the girls responded to the reminder by receiving at least one vaccine. We registered 1042 HPV and 442 MMR-vaccinations in the study group. Overall, we found the highest response in girls lacking only an HPV (15.3%) and girls only lacking an MMR (8.5%). Among girls who lacked both vaccines, the highest response was seen in girls who received both an HPV and MMR -vaccine (5.4%).

Table 2 shows the distribution of sociodemographic factors in 9692 Danish 14 year old girls six months after receiving written reminders. The table includes the likelihood ratio test, p-values for each socio-demographic determinant and the odds ratios (OR) for vaccination with HPV, MMR or both.

Many of the socio-demographic characteristics examined in this study, had little or no effect on vaccination-compliance to the reminder. Birth order and number of siblings, family structure, household income, mother's age, and unemployment showed no effect.

Mother's ethnicity had a strong predictive value for girls who only lacked HPV-vaccination. Here, we found a two-fold increase in vaccination-compliance for girls with non-western mothers (OR 2.02, 1.57–2.59).

The same tendency was seen for receiving a HPV-vaccination among those who also lacked MMR-vaccination although the likelihood ratio test was not significant.

The educational level was found to predict reminder-compliance in girls receiving both vaccinations, with higher response in the group with higher education. Girls having a mother with intermediate or basic education were less likely to be vaccinated (OR 0.63, 0.42–0.95) and (OR 0.43, 0.24–0.75) respectively. The same tendency was seen for receiving a HPV-vaccination among those only lacking HPV although the likelihood ratio test was not significant.

Girls only lacking an MMR-vaccination, were less likely to be vaccinated when living in the North Denmark (OR 0.21, 0.09–0.49), Central Denmark (OR 0.48, 0.31–0.73), Southern Denmark (OR 0.62, 0.40–0.98) or Zealand region (OR 0.47, 0.28–0.81) as compared to the Capital region.

4. Discussion

This study showed that vaccination-compliance after a personalised written reminder was affected by socio-demographic determinants and that these effects depend on the specific vaccines that were missing.

The strongest association was seen for girls only lacking HPV-vaccination, where we saw a twofold likelihood of receiving the vaccination in girls with non-western immigrant descent. The same pattern was seen for receiving a HPV-vaccination among those who also lacked MMR-vaccination although the likelihood ratio test was not significant. This finding may be related to the public discussion concerning the safety of HPV vaccines. These discussions occurred on social media platforms and public media (TV, newspapers, etc.) in Danish, from 2015 until 2016. Hence, it is possible that parents of non-Western ethnicity, who are not part of this discourse, may easily be convinced of vaccination by a personal reminder, whereas parents with Danish as their mother tongue may need more persuasion due to the expressed concerns about the safety of HPV-vaccination.

On the other hand, we found a decreased likelihood of MMR-vaccination reminder-compliance in girls living outside the Capital Region. This could be related to the fact that MMR-vaccination uptake in the Capital region consistently has been lower than the rest of the country. Hence, some parents of the Capital region may be “the low hanging fruits” that respond to the reminder, and do not represent conscientious objectors. Internationally, several studies have shown lower vaccination rates among inner-city or urban children providing pockets of poor coverage allowing for high susceptibility for vaccine-preventable disease (Finney Rutten et al., 2017; Wright and Polack, 2006).

Even though the correlation was only found to be significant for the group of girls lacking and receiving both vaccines, it is interesting to note that education was positively correlated with reminder-compliance in all groups except the group only lacking MMR-vaccination. The reasons for this may be manifold. We have no way to know if the reminder letter was opened, read and understood by all the parents, It is conceivable that the chance of reading and understanding a two-page letter from a public organisation increases by increased levels of education. More research is needed to investigate utilising various communication platforms as reminder tools.

Many of the socio-demographic characteristics examined in this study, had little or no effect on vaccination-compliance after the reminder. Contrary to previous studies of vaccination predictors, we did not find any effects of maternal birth order (Falagas and Zarkadoulia, 2008) and number of siblings (Ogilvie et al., 2010), family structure (Pearce et al., 2008; Vandermeulen et al., 2008), household income

Table 1
The number of vaccinations administered in the six-month-follow-up after a written reminder to 9692 14-year-old girls lacking either an HPV-vaccination, an MMR-vaccination or both, Denmark from 15 May 2014 to 14 May 2015.

	Total	Girls lacking HPV-vaccination n = 4940	Girls lacking MMR-vaccination n = 2026	Girls lacking HPV- & MMR-vaccination n = 2726
Receiving only HPV	894	757 (15.3%)		137 (5.0%)
Receiving only MMR	294		173 (8.5%)	121 (4.4%)
Receiving both HPV and MMR	148			148 (5.4%)

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Table 2
The distribution of sociodemographic factors, the Likelihood Ratio Test p-values and the odds ratios (OR) for vaccination with HPV, MMR or both in 9692 Danish 14-year-old girls in the six months follow up period after receiving a written reminder, Denmark 15 May 2014 to 14 May 2015.

OR for vaccination by sociodemographic variables, six month after receiving a reminder		Girls only lacking HPV n = 4940	Girls only lacking MMR n = 2026	Girls lacking both HPV and MMR n = 2726		
		Receipt of HPV vaccine	Receipt of MMR vaccine	Receipt of MMR and HPV vaccine	Receipt of MMR vaccine	Receipt of HPV vaccine
Number of vaccines administered		757	173	148	121	137
Total[c] n = 9692		OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Mothers' age	% (n)[a]	[b]p = 0.5969	p = 0.1466	p = 0.1095	p = 0.8140	p = 0.8296
> 35	16.3 (1580)	0.82 (0.82–1.32)	0.73 (0.44–1.20)	1.06 (0.65–1.74)	1.01 (0.59–1.75)	0.86 (0.51–1.45)
25–34	67.9 (6580)	1	1	1	1	1
< 25	15.8 (1531)	1.05 (0.82–1.33)	0.66 (0.40–1.12)	1.73 (1.05–2.83)	0.83 (0.46–1.49)	1.05 (0.61–1.79)
Mothers' ethnicity	% (n)	p = 0.0000	p = 0.9660	p = 0.2578	p = 0.6768	p = 0.0733
Danish born	85.7 (8306)	1	1	1	1	1
Western immigrant	2.4 (233)	0.82 (0.45–1.48)		1.54 (0.59–3.99)	1.65 (0.58–4.72)	0.76 (0.18–3.17)
Non-western immigrant	11.9 (1153)	2.02 (1.57–2.59)	1.01 (0.59–1.74)	1.54 (0.87–2.72)	1.0 (0.47–2.11)	1.96 (1.11–3.45)
Family structure	% (n)	p = 0.8833	p = 0.2010	p = 0.7082	p = 0.8273	p = 0.0894
Two-parent household	71.9 (6969)	1	1	1	1	1
Single-parent household	27.5 (2665)	1.02 (0.82–1.27)	1.33 (0.86–2.05)	0.92 (0.99–2.65)	1.06 (0.64–1.75)	1.50 (0.94–2.39)
Birth order	% (n)	p = 0.2969	p = 0.1056	p = 0.1087	p = 0.0740	p = 0.8213
First child	42.1 (4080)	1	1	1	1	1
Second	35.8 (3470)	1.15 (0.95–1.38)	0.87 (0.61–1.25)	1.02 (0.66–1.57)	0.66 (0.43–1.02)	1.06 (0.70–1.61)
Third or later	21.9 (2123)	1.15 (0.90–1.47)	0.58 (0.35–0.97)	1.62 (0.99–2.65)	0.57 (0.32–1.02)	0.90 (0.53–1.54)
Number of siblings	% (n)	p = 0.2109	p = 0.8539	p = 0.4480	p = 0.6953	p = 0.2916
0	17.1 (1657)	1.05 (0.83–1.33)	0.93 (0.59–1.46)	1.02 (0.59–1.76)	0.94 (0.55–1.61)	0.89 (0.50–1.56)
1	47.2 (4575)	1	1	1	1	1
2	25.6 (2481)	1.19 (0.98–1.45)	0.92 (0.61–1.39)	1.17 (0.76–1.81)	0.95 (0.59–1.53)	1.39 (0.91–2.13)
≥3	9.4 (911)	0.91 (0.67–1.24)	1.23 (0.64–2.36)	1.59 (0.91–2.78)	0.61 (0.26–1.43)	0.88 (0.44–1.76)
Mothers' education	% (n)	p = 0.1096	p = 0.1851	p = 0.0067	p = 0.6968	p = 0.7218
Higher	40.3 (3906)	1	1	1	1	1
Intermediate	39.7 (3848)	0.96 (0.82–1.15)	1.39 (0.96–2.02)	0.63 (0.42–0.95)	0.83 (0.53–1.30)	0.95 (0.62–1.47)
Basic	18.0 (1745)	0.76 (0.58–0.99)	1.44 (0.85–2.43)	0.43 (0.24–0.75)	0.97 (0.54–1.72)	1.18 (0.68–2.03)
Place of residence by region	% (n)	p = 0.1500	p = 0.0000	p = 0.0957	p = 0.0833	p = 0.0774
North Denmark	8.4 (814)	1.02 (0.76–1.38)	0.21 (0.09–0.49)	0.68 (0.30–1.55)	1.37 (0.68–2.76)	0.59 (0.23–1.54)
Central Denmark	21.9 (2123)	0.83 (0.66–1.04)	0.48 (0.31–0.73)	0.72 (0.43–1.19)	0.55 (0.31–1.00)	1.37 (0.88–2.14)
Southern Denmark	22.2 (2152)	0.87 (0.70–1.08)	0.62 (0.40–0.98)	1.24 (0.79–1.95)	0.70 (0.40–1.22)	0.77 (0.45–1.32)
Zealand	15.9 (1541)	0.76 (0.58–0.98)	0.47 (0.28–0.81)	0.64 (0.35–1.14)	1.08 (0.65–1.82)	0.67 (0.37–1.21)
Capital	31.7 (3072)	1	1	1	1	1
Household income	% (n)	p = 0.6818	p = 0.7224	p = 0.7822	p = 0.5854	p = 0.6021
0–20 percentile	19.9 (1929)	0.81 (0.58–1.13)	0.97 (0.51–1.84)	1.26 (0.62–2.57)	1.50 (0.69–3.23)	0.69 (0.34–1.38)
21–40 percentile	19.9 (1929)	0.98 (0.73–1.30)	0.71 (0.40–1.26)	1.42 (0.74–2.72)	1.31 (0.64–2.67)	0.61 (0.32–1.17)
41–60 percentile	19.9 (1929)	0.97 (0.74–1.26)	0.85 (0.51–1.40)	1.43 (0.78–2.61)	1.22 (0.63–2.39)	0.68 (0.37–1.24)
61–80 percentile	19.9 (1929)	0.98 (0.76–1.26)	0.87 (0.53–1.43)	1.31 (0.72–2.39)	1.64 (0.89–3.05)	0.70 (0.39–1.26)
81–100 percentile	19.9 (1929)	1	1	1	1	1
Mothers' employment	% (n)	p = 0.8690	p = 0.3276	p = 0.6394	p = 0.8335	p = 0.3021
Employed	88.0 (8529)	1	1	1	1	1
Unemployed < 26 weeks	7.8 (756)	0.93 (0.68–1.26)	0.68 (0.34–1.38)	1.29 (0.73–2.28)	0.81 (0.38–1.69)	0.54 (0.23–1.26)
Unemployed ≥ 26 weeks	3.1 (301)	1.05 (0.68–1.60)	0.59 (0.20–1.69)	0.82 (0.25–2.72)	0.89 (0.27–2.96)	1.00

[a] The remaining proportion represents missing responses for each covariable.
[b] p-value for Likelyhood ratio test (LR-test).
[c] No marked differences in distribution of covariables by subgroups of missing vaccinations.

(Vandermeulen et al., 2008), mother's age (Widgren et al., 2011), and unemployment (Vandermeulen et al., 2008). This could in part be related to the fact that Denmark is a more homogeneous country than many other study settings with a Gini coefficient around 0.25 in 2014 (Organisation for Economic Co-operation and Development (OECD), n.d.).

We have been unable to identify previous studies investigating socio-economic or demographic variables for vaccination-compliance after a reminder with emphasis on different pathways for the MMR and HPV-vaccinations. Studies investigating mail and telephone reminder and recall interventions have shown low effectiveness in lower income populations (Irigoyen et al., 2006; LeBaron et al., 2004; Szilagyi et al., 2006). Tseng et al. investigated the efficacy of sending patient reminder letters for cervical screenings (Tseng et al., 2000), and found the letters to increase the rate of cervical cancer screenings, yet with less effect in lower socioeconomic groups. This coincides with our findings regarding education.

Evidence is now emerging that the association between under-vaccination and sociodemographic factors is complex. Our results of a higher likelihood of HPV/MMR vaccination in girls from highly educated women reaffirm the classical correlation. This correlation has been seen in vaccination decisions regarding MMR (Tabacchi et al., 2016) and HPV (Finney Rutten et al., 2017; Monnat et al., 2016). This contrasts with findings of vaccine acceptance being less likely in parents with longer educations in the USA and Canada (Constantine and Jerman, 2007; Ogilvie et al., 2010; Rosenthal et al., 2008). A recent meta-analysis did not find strong evidence for differences in HPV-vaccination by parental income or education (Fisher et al., 2013), and a study from Norway found opposing effects of parental education and income (Hansen et al., 2015).

In 2011, Widgren et al. showed that the adherence to MMR-vaccination was a strong determinant for uptake of HPV1 (Widgren et al., 2011), which is very much in line with previous studies on the predictive value of previous vaccination behaviour (Pearce et al., 2009).

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We found that 50% of the girls who received a reminder missed only HPV-vaccination, which is likely due to the current HPV crisis in Denmark. Among those who missed both MMR and HPV-vaccination the uptake was similar after the reminder.

Other signs of clustering of preventive health behaviour have been found. Prevention of cervical cancer is a combination of vaccination and screening (PAP-smear). Studies have shown social inequality in cervical cancer screening (Blackwell et al., 2008; Drolet et al., 2013; Scarinci et al., 2010) as well as knowledge of HPV (Rossi et al., 2014) and HPV-vaccination uptake (Marc et al., 2010). This pattern also extends to the daughters as mothers' intention has been shown to be the strongest predictor of their girls' HPV-vaccination uptake (Alberts et al., 2017). Also, girls of mothers attending regular PAP-smears have a higher likelihood of receiving HPV-vaccinations (Markovitz et al., 2014; Monnat and Wallington, 2013).

De Casadevante et al., found large differences in uptake of the first HPV-vaccination, indicating that some target groups are harder to reach than others. They also hypothesised that this difference was likely to dissipate as the integration occurs where differences between the different population groups seem to vanish (Fernández de Casadevante et al., 2016). In addition to what was mentioned below, the results of a higher effect in girls of non-western descent could be explained by the fact that girls in Denmark of non-native descent are less likely to initiate the HPV-vaccination series (Slåttelid Schreiber et al., 2015), in other words; there is a larger pool of girls to target with the reminder.

4.1. Predictors for compliance after reminder

Social-environmental factors including cultural beliefs as well as social group norms may also play a role (STURM et al., 2005). The debate on HPV-vaccination and suspected adverse events has been fierce over the previous years in Denmark. This could have affected the native Danish population to a higher degree than immigrant mothers and differentiate the reminder effect. We saw no signs of active opting out of HPV-vaccinations with the debate affecting the vaccination choices in this particular group. There were indications of a selective vaccination process in 258 girls (258/2726 = 9.5%) who lacked both HPV and MMR-vaccination. Out of the group, 121 girls received only an MMR-vaccination and 137 received only an HPV-vaccination but the numbers too small to conclude. Nevertheless, this indicates different decision pathways for the two vaccines.

Identifying and understanding the social determinants related to routine childhood vaccination in various countries are important to improve vaccination coverage. Our findings show that these factors are diverse and that the relationship between socio-demographic predictors and childhood vaccination is complex and driven by context. Some social determinants may be similar in countries with any income level while others may be population-specific (Glatman-freedman and Nichols, 2012).

Our findings supplement current knowledge on the social distribution of HPV and MMR-vaccination uptake and regional differences in coverage, particularly in relation to maternal ethnicity.

4.2. Strengths and limitations of this study

The study is nationwide and included all unvaccinated 14-year-old girls in Denmark in the study period. We investigated variables registered at the individual level and all dynamic variables refer to the year of the reminder. The use of national population-based registry data ensures no loss to follow up and minimises the risk of selection, misclassification and response-biases. We studied the associations between parents' income, mothers' education and other socio-demographic determinants and the uptake of vaccines while controlling for numerous possible confounders. However, we could not address causal relationships or identify individual barriers to HPV or MMR-vaccination. Using quantitative register based studies does not allow for investigations of barriers such as misinformation or concerns about adverse events previously identified in studies (Dubé et al., 2013). Qualitative studies are needed to address the individual decision process after receiving a written reminder-letter. Denmark is a high-income country with a high level of interpersonal and societal trust (Elgar and Aitken, 2011) and a free childhood vaccination schedule. Generalisation to other settings and/or other vaccines may be challenged by the fact that determinants for non-vaccination differ across countries depending on the cultural context and on the structures managing the vaccination programme. To uncover this it is necessary to apply a qualitative approach e.g. as included in the "Tailoring Immunisation Programme" developed by WHO. This has been carried out in England (Public Health England, 2016) and Sweden (Godoy-Ramirez, 2016).

The DDV has been shown to include a underreporting of vaccinations estimated to 3–4 percentage points (Wójcik et al., 2013). Misclassification of vaccination status could lead to parents receiving an irrelevant reminder, which could lead to a decrease in registered effect of the reminder. We have no reason to suspect differential misclassification between HPV and MMR-vaccination.

The multivariable model included variables, which are correlated, and could introduce over adjustment bias affecting the precision of the model. This is particularly the case for maternal education and household income as well as for number of siblings and birth order. All variables were adjusted for each other but the risk of residual confounding exists. Still, we found that the patterns observed in the crude estimates were similar to the patterns in the adjusted estimates. Sample size was limited and the lack of power could result in lacking identification of associations.

We only looked at predictors related to the mother as current international literature supports that the mother is the gatekeeper in the parental clinical decision-making process (Walhart, 2012). There is emerging evidence that paternal determinants play a role in vaccination behaviour (Rammohan et al., 2012). The available data indicate it to be less influential for HPV-vaccination. It is, on the other side conceivable that the relative importance of maternal versus paternal determinants must be high context specific and this needs to be considered in future studies.

Our study group was confined to girls born in Denmark, which excluded the possibility to investigate the associations in refugees and immigrants, a vulnerable groups, well known to be at risk for non-vaccination (Moller et al., 2015).

5. Conclusions

Overall, 14% of girls reminded received at least one vaccine with the highest effect found in girls only lacking HPV.

Among girls who only missed HPV-vaccination the compliance to the reminder was two-fold higher among girls with non-western born mothers, as compared to mothers born in Denmark. This is encouraging as cervical cancer incidence has been shown to have a higher prevalence in ethnic minority groups (Arnold et al., 2010). We found similar uptake of HPV and MMR-vaccination in girls lacking both vaccinations, disregarding the theory of Danish parents being more opposed to the new and less familiar HPV-vaccine. The finding of a lower effect in girls of mother with shorter education as well as girls living outside the capital region indicates the need of supplementary interventions in order to increase vaccination coverage in these groups.

We found that sociodemographic factors were associated with response to vaccination-reminders. Knowledge from this study may be relevant for other countries considering implementing a national reminder system to increase the vaccination coverage.

Conflicts of interest

All authors report no conflicts of interest.

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Acknowledgments

Camilla Hiul Suppli, has received PhD research funding through unrestricted grants from the following private foundations: Axel Muusfeldts fond (3-635), Christian Larsen og Dommer Ellen Larsens legat (9681-3115), Else og Mogen Wedell-Wedellsborgs fond (24-15-1), Familien Hede-Nielsens fond (9681-3159), AP Møller Fonden - Fonden til Lægevidenskabens fremme (14-406), Helsefonden (9681-3095), Illum Fondet (9681-3177), Ole Kirks fond (20-5685) and Rosalie Petersens fond (020432-0001). None has any affiliation that poses a conflict of interest. The study was approved by the Danish Data Inspection Agency according to Danish Legislation.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pmedr.2018.02.005.

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