

Project title: School-based HPV-counselling and -vaccination. A user-centred intervention targeting children and parents with ethnic minority background.

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Project group:

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Lene Seibæk: RN, PhD, associate professor at University of Aarhus, professor at University of Greenland, and senior researcher at the Department of Gynaecology and Obstetrics plus Research Centre for Patient Involvement at Aarhus University Hospital.



Project description

Background

Every year, almost 900 are diagnosed with HPV-related cancer in Denmark (DK) (1). This even though HPV-related cancers are considered the most preventable cancer forms due to effective vaccination. HPV-vaccination (HPVV) (Gardasil 9®) is estimated to protect against 90% of all cervical cancers (2,3) and protects against all other HPV-related cancer forms as well (4). In DK a gender-neutral HPVV program was implemented as part of the children vaccination-program in 2019.

Although overall HPVV coverage is generally high in DK (80%), it is lower among ethnic minorities (5). Thus, immigrants have an overall lower HPVV coverage than native Danes (79% vs. 93%), with country specific variation as low as 65% (5). Adding to this, some ethnic minority women, have a high level of combined non-attendance in HPVV and screening at 30% compared to 10% for native Danes (6). Furthermore 25% of all boys in DK does not get HPVV regardless of their ethnic background (7). The reasons for non-attending HPVV are complex and covers insufficient awareness, cultural taboos related to the genital area and sexuality, emotional barriers such as fear that vaccination could lead to promiscuity, and finally a general mistrust in general practitioners (GPs) (8,9)

School-based HPVV can improve participation (10) and coverage among children of all ethnicities (11). Studies have shown positive attitudes towards counselling supporting school-based vaccination (12), but to increase the attendance of ethnic minority children, communication needs to follow examined guidelines regarding communicating with ethnic minority citizens concerning health issues (13, 14). Communication needs to be uniform, simple, and in ethnic minority languages. The environment must be trustworthy and reliable, and the information is best adopted if visual, with an opportunity for repetition (15).

Hypotheses and aims

Hypothesis 1: It is possible to improve participation in HPVV in DK when combining HPV-counselling with school-based vaccination compared to GP-based vaccination.

- Aim 1: To improve HPVV coverage among pupils attending schools with high concentration of non-native pupils. We anticipate improving HPVV among ethnic minority pupils with at least 10%-point, and among native Danish pupils with at least 5%-point.

Hypothesis 2: It is possible to improve participation in HPVV among siblings to enrolled pupils, solely by improving HPV knowledge and awareness among their parents.

- Aim 2: To improve HPVV coverage among siblings to enrolled pupils.

Hypothesis 3: A close cooperation with user-representatives will improve feasibility and implementation.

- Aim 3: To develop and evaluate targeted counselling material concerning HPV and HPVV for parents and children with various ethnical backgrounds, eligible for national implementation.

Materials and methods

Theoretical framework



The intervention is developed according to Complex Interventions Framework (16, 17). Complex interventions contain several interacting components, and the guideline deals with development, assessment of feasibility, implementation, and evaluation (Figure 1). To operationalize the elements of the intervention, we have applied a Logic Model, a graphic tool that illustrates the relationship between activities and intended outcome (18, 19). By this, we have combined theoretical knowledge and components of the intervention to accommodate to possible challenges in implementation (Table 1).

Research design, study and control population

The intervention is conducted as a non-randomized implementation study (Figure 2). The intervention will be implemented schoolyear 2022/23. The intervention group consist of 640 children (11-13 years old) at 5 schools with > 25% ethnic minority pupils, located in Aarhus (Table 2). The control population will be approximately 2560 children comparable in age and regions with similar high concentration of ethnic minority populations.

Developed intervention

The intervention consists of following core elements. For timeline, see Table 3.

- 1) Scholl-based parental HPV-counselling
- 2) Scholl-based pupil HPV-counselling
- 3) Scholl-based HPVV

Counselling-material have been developed according to existing knowledge of communication to ethnic minority parents regarding health issues (15, 20). We have developed mainly video and animation, which also help to ensure methodological rigor. All developed material has been validated and adapted in cooperation with users-representatives. To support implementation, the counselling process is designed to demand only few school-professional resources (21).

Parental counselling

- A. Oral presentation (10 min) explaining HPV and HPVV. It will be given by the PhD-student at first school-parent meeting, with ethnic minority ambassadors present.
- B. A simple printed presentation will be available in text and pictures (in Arabic, Turkish, Somali, English and Danish).
- C. The oral presentation will be available as a video texted in Arabic, Turkish, Somali, English and Danish. It will be accessible in a Facebook-group, solely for parents included in the intervention.

To all parents not attending the school-parent meeting we will send all written material and opportunity to submit for participation to both 'e-boks' and by letter with a stamped return-envelope.

Pupil counselling

- A. In a school-nurse setting, it will consist of an animation (3 min), which illustrates facts about HPV and vaccination. The storytelling is a conversation between two kids, diverse in gender and ethnicity and contains subjects as nervousness.
- B. The children will get a tote bag with a postcard, supporting the facts given in the animation and with an opportunity to submission by parents. This as a contact from child to parent, a known pathway for information in especially families with ethnic minority background.



C. The school-nurse will facilitate a conversation about vaccination and nervousness, using 5 question-cards.

School-based HPVV

First vaccination (HPVV1) will be offered after element 1-2 have been completed; the second (HPVV2) will be offered minimum five months later. Both will be given at pre-defined dates during school hours by qualified doctors and nurses. Dates will be visible on posters at school and reminder will be sent to parents via AULA and text messages if this is selected by parents when submitting their child for vaccination.

Evaluation plan

Quantitative outcome

Primary: HPVV coverage between intervention and control group as a total and stratified by ethnicity.
Secondary: HPVV coverage for siblings of included pupils compared to an age- and area matched control group.

Qualitative evaluation

Parents' and school professionals' perceptions of the intervention will be qualitatively evaluated by focus-group interviews. The participants will be strategically selected among attending and non-attending, and represent various schools, cultural and socio-economic conditions. The interviews will be framed by a semi-structured interview guide, and data will be analysed and validated consecutively with Malterud's text analytical method (22).

Power calculation

We have enrolled 5 schools, corresponding to approximately 640 children. 2560 children will be allocated to the control group (1:4 ratio). In both groups, roughly half of these children will be native Danes and the other half will be ethnic minorities. Estimating that minority pupils have a HPVV coverage of 65%, the study will be able to detect a difference of approximately 10 percent points in vaccination coverage between intervention and control group in the stratified analyses with a risk of type 1 error of 5% and type 2 error of 10% (power 90%).

Data sources and statistical analysis

The intervention has been identified by The Municipality of Aarhus and the control group will be identified in the Danish Civil Registration System, as will parents and siblings to both intervention and control groups. Information on children's ethnicity, and demographic and socioeconomic status on parents will be obtained from Statistics Denmark. Data on HPVV 1 and 2 will be collected from The Danish National Health Service Register through the Danish Health Data Authority.

Demographic and socioeconomic characteristics will be presented as numbers and proportions and differences between intervention and control groups tested using Pearson's chi-squared test. Regression analyses will be used to estimate the relative risk of not being vaccinated between intervention and control group. If differences between intervention and control group are identified, both crude and adjusted estimates will be presented with 95% confidence intervals. All analyses will be performed using STATA V.17.

Ethical Considerations



The project will be conducted in accordance with the Good Clinical Practice Guidelines, and is reported to the Data Protection Agency in Central Denmark Region (ref.nr. 761330, 1-16-02-494-21) and Central Denmark Region's Committees on Biomedical Research (1-10-72-274-21). Parents must submit their child for vaccination via written informed consent. HPVV will be offered at pre-defined dates during school hours and provided by qualified medical professionals according to existing guidelines. Each HPVV will be registered in The National Danish Childhood Vaccination Register. All data will be handled according to the EU's General Data Protection Regulation and all sensitive information will be handled with 'e-boks', and REDcap. The municipality of Aarhus will provide personal data on intervention group in order to perform the invention and data processing agreement about disclosure has been concluded. Interviews will be executed in accordance with the Helsinki Declaration's rules on voluntariness and anonymity.

Research plan

Anne Katrine Leonhard will be daily project manager and overall project leader. The PhD will follow the estimated timeline as shown in Figure 3, included already completed preparation scholarship.

Supervisors

Lene Seibæk will be main supervisor, responsible for the qualitative methods and overall project. Sara Badre-Esfahani will contribute as project leader as well as co-supervisor. Lone Kjeld Petersen will be responsible clinician and co-supervisor. Mette Bach Larsen will be responsible for the quantitative methods and co-supervisor.

Collaborators and user-representatives

From the Municipality of Aarhus, Department of Children and Youth, we have a consultant dedicated to the project. The project has been approved by Alderman Thomas Medom, and May-Britt Kullberg, leader of the department, are close collaborator. Two school-nurses are user-representatives.

"Neighbourhood mothers" is a national volunteer organization of minority women trained in health, family and the Danish society. They constitute a large group of user-representatives. 10 mothers and children with various ethnic and social background are user-representatives, as well as 2 health professionals with cultural insight. "Sex og Samfund" has contributed with consultation regarding counselling material.

Perspectives

The perspectives of initiating school-based HPPV, is to create equal opportunities for participation in primary prevention from HPV-related cancer for all children living in DK. Results from this study may be used in future preventive interventions, and material can be used in future school-based vaccination programs.

We expect that the intervention will contribute to minimize misinformation and taboos related to HPVV among ethnic minority families, causing the intervention to indirectly benefit the HPVV attendance of the family's other children, and contribute to reduce inequality in health care.

This project is the first step in a larger project with an overall aim to improve HPV-related cervical cancer prevention among minority groups in DK, which takes place in a cross regional collaboration



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between Aarhus University Hospital, Odense University Hospital and Randers Regional Hospital (Figure 4).



Figures

Figure 1: Key elements in developing and evaluating complex interventions according to the Complex Interventions Framework (17).

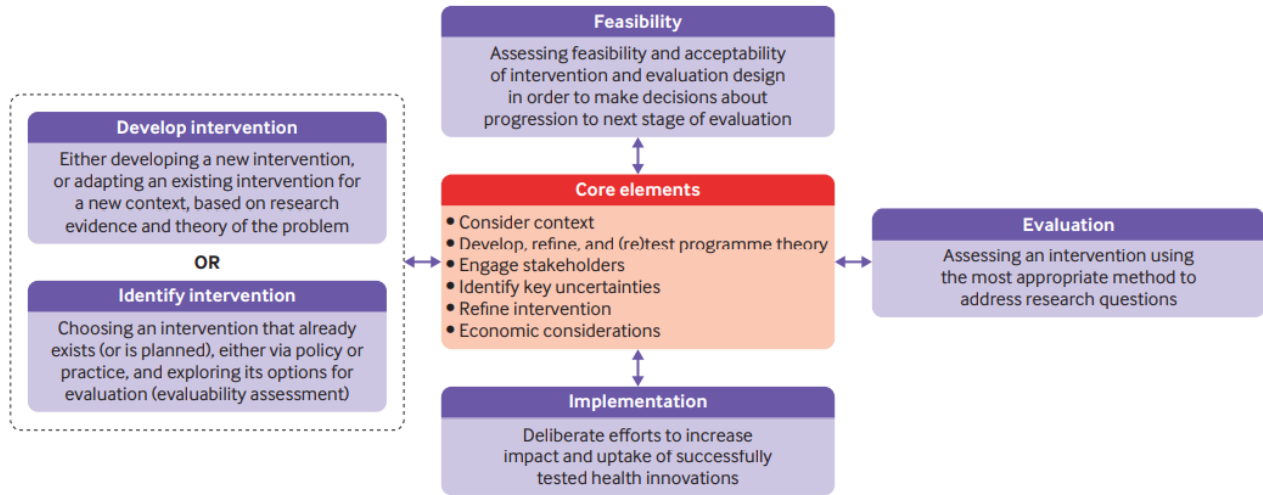




Figure 2: quasi-experimental design.

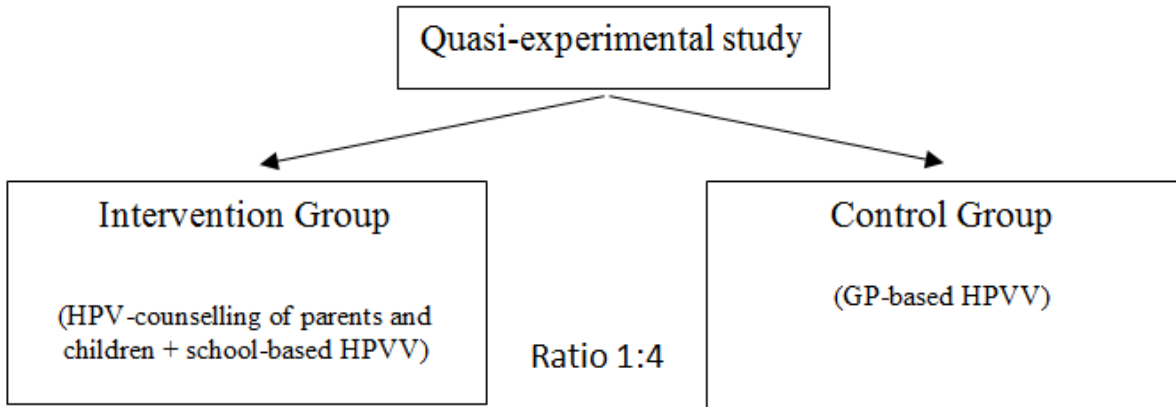
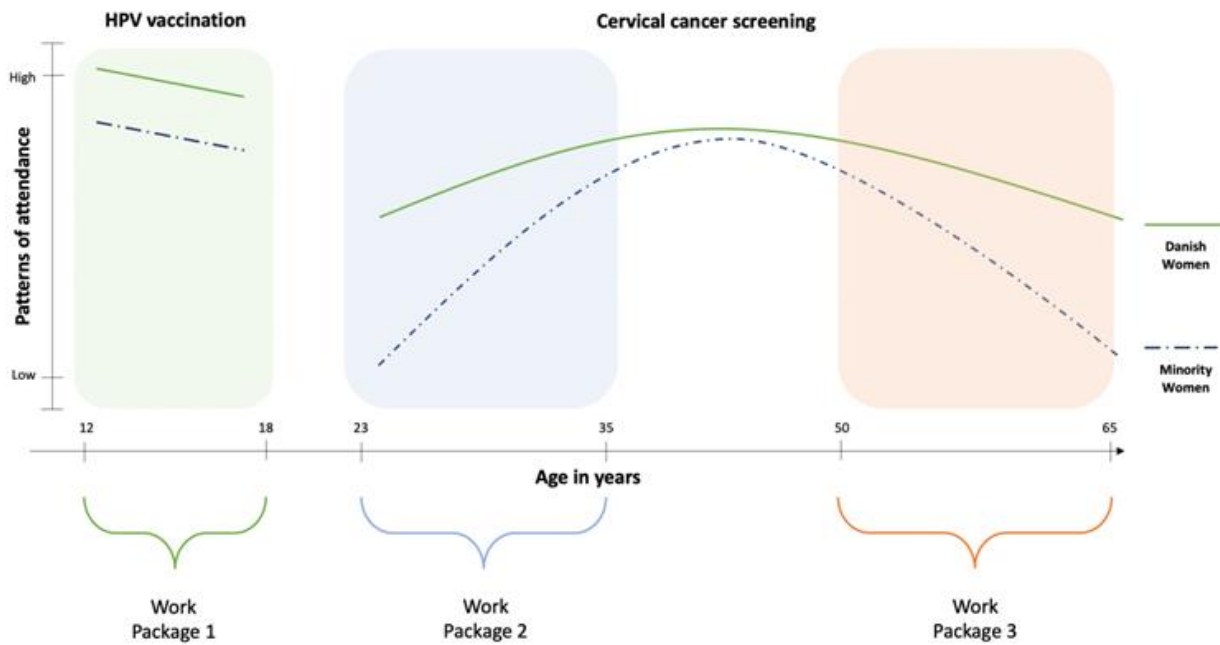


Figure 3: Timeframe, PhD.

Months	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36												
Years	1												2												3																							
Intervention	[Green bar]																																															
Schoolbased counselling	[Black bar]			[Green bar]																																												
School-based HPVV	[Black bar]			[Black bar]			[Black bar]			[Green bar]																																						
Implementation analysis	[Black bar]												[Green bar]																																			
Modelling process and outcomes	[Black bar]												[Black bar]						[Green bar]																													
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Surveillance and monitoring	[Black bar]												[Green bar]																																			
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Publications	[Black bar 1]												[Black bar 2]												[Black bar 3]																							
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Figure 4: Overview over patterns of attendance in HPVV and cervical cancer screening among Danish and minority women according to age as well as focus and age intervals in three studies. Study 1, which is the centre of this application, aims to improve HPVV coverage among minority children in Denmark (green box), study 2 aims to improve cervical cancer screening among young minority women in Denmark (blue box) and study3 aims to improve cervical cancer screening among older minority women in Denmark (orange box).



Tables

Table 1: Logic Model of intervention “School-based HPV-counselling and -vaccination”

RESSOURCES	ACTIVITIES/ PRODUCTS	CLIENTS	RESULTS		
			Short-term ”Attitude”	Intermediate ”Behavior”	Long-term ”Conditions”
<p><u>Human</u> <i>Theory and development of intervention</i></p> <ul style="list-style-type: none"> - Neighbourhood mothers - The municipality of Aarhus - School nurses - Negin Jaafar <p><i>Intervention</i></p> <ul style="list-style-type: none"> - School nurses - School teachers - Vaccination staff - The municipality of Aarhus - Neighbourhood mothers 	<p><u>Parent counselling</u></p> <ul style="list-style-type: none"> - Oral, 15 min. - Movie (oral performance) <p><u>Pupils education</u></p> <ul style="list-style-type: none"> - Movie (animation, facts) - In writing_(postcard) - Script for school nurses - Question cards <p><u>Additional effort</u></p> <ul style="list-style-type: none"> - letter with stamped envelope <p><u>HPV-vaccination, first</u></p> <ul style="list-style-type: none"> - Poster with short information (for parents, at school) - Script for vaccinators - Guideline for vaccination <p><u>HPV-vaccination, second</u></p> <ul style="list-style-type: none"> - Script for vaccinators - Guideline for vaccination 	<p>Pupils in fourth, fifth and sixth grade and their parents, at schools in the Municipality of Aarhus with 25% or more pupils with ethnical minority background.</p>	<p><u>Parents</u></p> <ul style="list-style-type: none"> - Change of behavior (increased HPV-vaccinated pupils) - Awareness - Perception of relevance - Knowledge - Understanding - Motivation for screening <p><u>Pupils</u></p> <ul style="list-style-type: none"> - Change of behavior (increased HPV-vaccinated pupils) - Own provision - Knowledge - Understanding - Motivation - Positive interaction between students towards vaccination 	<p><u>Parents</u></p> <ul style="list-style-type: none"> - Change of behavior (Women participate in screening) - Ambassadors and advice of HPV-vaccination in local environment - Decision about other children getting HPV-vaccinated <p><u>Pupils</u></p> <ul style="list-style-type: none"> - Positive influence of related children by positive mention of HPV-vaccination and prevention of disease by vaccination 	<p><u>Parents</u></p> <ul style="list-style-type: none"> - Change in environmental tradition for HPV-vaccination - Less taboos related HPV and HPV-vaccination - Reduced fear of sexual behavior after HPV-vaccination due to change of focus - Change in culture about prevention of disease - Increased awareness about other cancer-preventing offers (breast, colon etc.) <p><u>Pupils</u></p> <ul style="list-style-type: none"> - Change in future behavior by increased attendance to both screening and vaccination of children in future generations. - Increased talk and awareness about HPV and HPV-vaccination. <p><u>Society</u></p> <ul style="list-style-type: none"> - Increased focus and interest regarding school-based vaccination



Assumptions and contextual factors

Environment

- **Anti-first-mover environment. Need for ambassadors locally.**
- **High trust to volunteers and health professionals (not GP's).**
- **High trust to school and school-nurses.**
- Positive mention by role-models and in media will benefit the outcome

Culture

- **Storytelling about preventing disease is more effective than focus on HPV being a sexual transmitted disease and best given before debut of sexual activity.**
- **Fear of change in sexual behavior after HPV-vaccination.**
- Broad presentation of ethnicities and authorities in project group and cooperators benefits the outcome of the project.
- Information pathway from child to parent

Intervention – form and materials

- **Minimal information about project will benefit the outcome → the less information and material, more manageable and larger participation to vaccination.**
- **The more uniform the intervention is, the stronger are our scientific methods.**
- **Nervousness among pupils must be taken into account. Minimal nervousness → more gets vaccinated.**
- Counselling of both parents and pupils will cause positive attitude to vaccination.
- Animation is the best platform for pupils
- Pupils want facts about HPV, cancer and vaccination.
- Pupils will have positive interaction between one another regards vaccination and counteract nervousness.
- We will not cluster and provoke anti-vaccination behavior by being progressive.

External Factors

- Eventual circumstances due to COVID-19 such as homeschool.
- Negative media attention of HPV
- Another project in the local community regarding vaccination (COVID-19), risk of double-nudging.
- Religious focus on sexual transmitted HPV-infection, and hereby increased fear of change in sexual behavior, possibly by senior religious figure.

Table 2: Schools and classes

No.	School	%-minority pupils	Participating classes	Total pupils
1	Ellehøjskolen	91%	5 th and 6 th grade	64
2	Møllevangskolen	46%	4 th , 5 th and 6 th grade	127
3	Skjoldhøjskolen	38%	4 th , 5 th and 6 th grade	130
4	Bakkegårdsskolen	30%	4 th , 5 th and 6 th grade	114
5	Sabro-Korsvejskolen	25%	4 th , 5 th and 6 th grade	201
	TOTAL	46% (Mean)		636

Table 3: Timeline of intervention

End of schooyear 2021/2022			Schooyear 2022/2023												
May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun		
			SCHOOL-BASED HPV-INTERVENTION												
First contact															
			Second contact												
			Parental counselling												
			Social media platform												
					Pupil education					Parental brush-up					
					HPVV1 2 weeks before: Aula 1 day before: Text					HPVV2 2 weeks before: Aula 1 day before: Text					
			Extra effort												

First contact	Via aula. "Offer to get HPV-vaccination during school-hours next schooyear. More information after the summer holidays".
Second contact	Via aula. "Offer to get HPV-vaccination durin school-hours this schooyear. More information at upcoming school-parental meeting" Included date for HPV1. Included link to exlusive social media page.
Parental counselling	School-parental meeting (local ambassadours present) Oral presentation and HPV-counselling by healthcare professional (10-15 min). Written material translated to minority languages. Possibility to give consent.
Social media platform	Exclusive for included parents. Coitaing brieft information. Film with parental counselling (1:1 as oral presentation). Link for consent.
Extra effort	E-boks and written letter with all written material included stamped return-envelope. Neighbourhood mothers as ambassabours in local community and at included schools.
Pupil education	In school hours by school nurse. Animation (3 min): facts about HPV and vaccination. Totebag with postcard. Schoolnurse: forum for sharing thoughts , experience with vaccination.
Parents brush-up	Brief update via aula. Included date for HPV2.
HPVV1	School-based vaccination by healthcare professionals. 2 weeks before: reminder at aula. Link to consent. 1 day before: reminder by text.
HPVV2	School-based vaccination by healthcare professionals. 2 weeks before: reminder at aula. Link to consent. 1 day before: reminder by text.



References

- (1) Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2018 Nov;68(6):394-424.
- (2) Serrano B, Alemany L, Ruiz PA, Tous S, Lima MA, Bruni L, et al. Potential impact of a 9-valent HPV vaccine in HPV-related cervical disease in 4 emerging countries (Brazil, Mexico, India and China). *Cancer epidemiology*. 2014;38(6):748.
- (3) Kjaer SK, Nygård M, Sundström K, Dillner J, Tryggvadottir L, Munk C, et al. Final analysis of a 14-year long-term follow-up study of the effectiveness and immunogenicity of the quadrivalent human papillomavirus vaccine in women from four nordic countries. *ClinicalMedicine*. 2020;23:100401.
- (4) Lei J, Ploner A, Elfström KM, Wang J, Roth A, Fang F, et al. HPV Vaccination and the Risk of Invasive Cervical Cancer. *N Engl J Med*. 2020;383(14):1340-8.
- (5) Hertzum-Larsen R, Thomsen LT, Frederiksen K, Kjaer SK. Human papillomavirus vaccination in immigrants and descendants of immigrants in Denmark. *European journal of cancer prevention : the official journal of the European Cancer Prevention Organisation (ECP)*. 2019.
- (6) Badre-Esfahani S, Larsen MB, Seibæk L, Petersen LK, Blaaekær J, Andersen B. Low attendance by non-native women to human papillomavirus vaccination and cervical cancer screening - A Danish nationwide register-based cohort study. *Prev Med Rep*. 2020;19:101106.
- (7) Institut SS. Statistics HPV vaccination 2021 Available from: <https://www.ssi.dk/vaccinationer/boernevaccination/vaccination-mod-livmoderhalskraeft/statistik-om-hpv-vaccination> Accessed 30.1.2022.
- (8) Badre-Esfahani S, Petersen LK, Tatari CR, Blaaekær J, Andersen B, Seibæk L. Perceptions of cervical cancer prevention among a group of ethnic minority women in Denmark-A qualitative study. *PLoS One* 2021 Jun 1;16(6):e0250816.
- (9) Tatari CR, Andersen B, Brogaard T, Badre-Esfahani SK, Jaafar N, Kirkegaard P. Perceptions about cancer and barriers towards cancer screening among ethnic minority women in a deprived area in Denmark - a qualitative study. *BMC Public Health*. 2020 Jun 12;20(1):921. doi: 10.1186/s12889-020-09037-1. PMID: 32532227; PMCID: PMC7291658.
- (10) Feldstein LR, Fox G, Shefer A, Conklin LM, Ward K. School-based delivery of routinely recommended vaccines and opportunities to check vaccination status at school, a global summary, 2008-2017. *Vaccine*. 2020;38(3):680-9.
- (11) Wang J, Ploner A, Sparen P, Lepp T, Roth A, Arnheim-Dahlstrom L, et al. Mode of HPV vaccination delivery and equity in vaccine uptake: A nationwide cohort study. *Prev Med*. 2019;120:26-3



- (12) Davies C, Stoney T, Hutton H, Parrella A, Kang M, Macartney K, et al. School-based HPV vaccination positively impacts parents' attitudes toward adolescent vaccination. *Vaccine*. 2021;39(30):4190-8.
- (13) Voss SS, Nørgaard SK, Chaine M og Valentiner-Branthet P. Which groups of children need a targeted vaccination effort? Determinants for low coverage of vaccines covered by the Danish childhood vaccination program. *Infection Epidemiology and Prevention* [Hvilke grupper af børn har behov for en målrettet vaccinationsindsats? Determinanter for lav dækning af vacciner omfattet af det danske børnevaccinationsprogram. *Infektionsepideimiologi og Forebyggelse*]. 2021.
- (14) Flygtningehjælp Dansk. COVID-19 and ethnic minorities. Mapping of information channels and media [COVID-19 og etniske minoriteter. Kortlægning af informationskanaler og medier]. 2020
- (15) Tatari CR, Andersen B, Brogaard T, Badre-Esfahani S, Jaafar N, Kirkegaard P. The SWIM study: Ethnic minority women's ideas and preferences for a tailored intervention to promote national cancer screening programmes-A qualitative interview study. *Health Expect*. 2021;24(5):1692-700.
- (16) Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M. Developing and evaluating complex interventions: the new Medical Research Council guidance. *Int J Nurs Stud* 2013 May;50(5):587-592.
- (17) Skivington K, Matthews L, Simpson SA, Craig P, Baird J, Blazeby JM, et al. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. *Bmj*. 2021;374:n2061.
- (18) Bonell C, Jamal F, Melendez-Torres GJ, Cummins S. 'Dark logic': theorising the harmful consequences of public health interventions. *J Epidemiol Community Health*. 2015;69(1):95-8.
- (19) Seidl KL, Gingold DB, Stryckman B, Landi C, Sokan O, Fletcher M, et al. Development of a Logic Model to Guide Implementation and Evaluation of a Mobile Integrated Health Transitional Care Program. *Popul Health Manag*. 2021;24(2):275-81.
- (20) Smith Jervelund S, Vinther-Jensen K, Ryom K, Villadsen SF, Hempler NF. Recommendations for ethnic equity in health: A Delphi study from Denmark. *Scand J Public Health*. 2021 Sep 13:14034948211040965. doi: 10.1177/14034948211040965. Epub ahead of print. PMID: 34515598.
- (21) Cooper SC, Davies C, McBride K, et al. Development of a human papillomavirus vaccination intervention for Australian adolescents. *Health Education Journal*. 2016;75(5):610-620. doi:10.1177/0017896915608884
- (22) Malterud K. Systematic text condensation: a strategy for qualitative analysis. *Scand J Public Health* 2012 Dec;40(8):795-805.