HPV Prevention and Control Board

Online Technical Meeting

Reinforcing HPV Vaccination and Cervical Cancer Screening and Treatment

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Antwerp, Belgium

BACKGROUND DOCUMENT

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Introduction

Meeting objectives:

- Increasing access to HPV vaccination
  - Discuss experiences and opportunities to sustain/reinforce/implement HPV vaccination in different regions across the world, in general and during the Covid-19 pandemic.
  - Discuss innovations that may help to achieve access targets such as, improved vaccination schedules, single dose, training and communication of Health Care Workers, etc.
  - Review successful country examples with increased access to vaccination and high vaccination coverage.
  - Discuss need for future research and trials.
  - Discuss lessons learnt from Covid-19 and how these opportunities can be leveraged to increase access to vaccination.
- Increasing access to cervical cancer screening and treatment
  - Discuss experiences and opportunities to sustain/reinforce/implement screening and treatment programs across different regions in the world, in general and during the Covid-19 pandemic.
  - Discuss innovations that may help to achieve access targets such as, self-sampling, availability of HPV tests, point of care screening technology, artificial intelligence-based screening, digitally reaching out to women, etc.
  - Review successful country examples with increased access to screening and treatment.
  - Discuss need for future research and trials.
  - Discuss lessons learnt from Covid-19 and how to leverage these opportunities to increase access to cervical cancer screening and treatment.

Target audience:

- Projects and organisation representatives involved in HPV control and prevention
- Representatives of health organisations involved in the prevention and control of HPV and/or other health issues
- HPV prevention and control Board advisors

Purpose of the background document

This background document provides an overview of articles related to the meeting and a concise bibliography of speakers.

The document should not be considered as an exhaustive report of scientific articles related to the themes of the meeting.

Inclusion of references in this document does not indicate that the Executive Secretariat agrees with the content or correctness of the content. The first objective of this list is to give an overview of what has been published on this topic.

Part 1: References based on a Pubmed search by Topic

Sustaining/Reinforcing HPV Vaccination

A PubMed search was performed with the following selection criteria: [Immunization] AND [Vaccine Coverage] AND [Covid-19], [Immunization] AND [Vaccine Coverage] AND [Covid-19] AND [HPV vaccine], [Vaccination] AND [Covid-19] AND [HPV] OR [Human papillomavirus] AND [Re-start], [Vaccination] AND [Covid-19] AND [HPV], [title/abstract published in the last one year. 234, 7, 0 and 22 items were retrieved respectively and a relevant manual selection of 13 publications between 2020-2021 based on title and abstract was made, and imported into Endnote. Some of the references retrieved were more relevant to the next session.

Abel, M. K., W. K. Huh and J. K. Chan (2020). "Human papillomavirus: The other invisible enemy". Gynecol Oncol 158(2): 254-255.

{ d Z Á } Œ o] • Á } Œ l] v P Á] š Z µ v ‰ Œ v š (Œ À } Œ v • ‰ v] v vaccine for COVID- í õ X { E Œ o Ç ï ô í U ñ ì ì ‰ } ‰ o Á } Œ o Á]] -relate(Œ } u Z µ u v v Œ •] v î ì í ô • ‰] š • (v ((š] À À] v X { t] š Z š Z u } u v š µ u pandemic, we can improve vaccine implementation.

Arbyn, M., M. Gultekin, P. Morice, P. Nieminen, M. Cruickshank, P. Poortmans, D. Kelly, M. Poljak, C. Bergeron, D. Ritchie, D. Schmidt, M. Kyrgiou, A. Van den Bruel, L. Bruni, P. Basu, F. Bray and E. Weiderpass (2021). "The European response to the WHO call to eliminate cervical cancer as a public health problem". Int J Cancer 148(2): 277-284.

The age-standardised incidence of cervical cancer in Europe varies widely by country (between 3 and 25/100000 women-years) in 2018. Human papillomavirus (HPV) vaccine coverage is low in countries with the highest incidence and screening performance is heterogeneous among European countries. A broad group of delegates of scientific professional societies and cancer organisations endorse the principles of the WHO call to eliminate cervical cancer as a public health problem, also in Europe. All European nations should, by 2030, reach at least 90% HPV vaccine } À Œ P u } v P P] Œ o • Ç š Z P } (í ñ 0 Œ Œ • v d •] } u Ç • U] (} • š organised population-based HPV-based screening and achieve 70% of screening coverage in the target age group, providing also HPV testing on self-samples for nonscreened or underscreened women; and to manage 90% of screen-positive women. To guide member states, a group of scientific professional societies and cancer organisations engage to assist in the rollout of a series of concerted evidence-based actions. European health authorities are requested to mandate a group of experts to develop the third edition of European Guidelines for Quality Assurance of Cervical Cancer prevention based on integrated HPV vaccination and screening and to monitor the progress towards the elimination goal. The occurrence of the COVID-19 pandemic, having interrupted prevention activities temporarily, should not deviate stakeholders from this ambition. In the immediate postepidemic phase, health professionals should focus on high-risk women and adhere to cost-effective policies including self-sampling.

Benjamin-Chung, J. and A. Reingold (2021). "Measuring the Success of the US COVID-19 Vaccine Campaign: It's Time to Invest in and Strengthen Immunization Information Systems". Am J Public Health: e1-e3.

With the recent US Food and Drug Administration approval of the Pfizer-BioNTech and Moderna SARS-CoV-2 vaccines, the United States has begun COVID-19 vaccine dissemination. The vaccination program is historic in its massive scope and complexity. It requires accurate, real-time estimates of vaccine coverage to assess progress toward achieving herd immunity. Under Operation Warp Speed, the US Centers for Disease Control and Prevention (CDC) has constructed a federal database, or "data lake," to monitor vaccine coverage nationwide and ensure that recipients receive both of the necessary doses. The data lake will be managed separately from existing state and local

immunization information systems (IISs), which house vaccine data in all 50 states, five cities, the District of Columbia, and eight territories. In an open letter to the Director of the CDC in late 2020, four organizations representing immunization managers and public health officials expressed concerns about the plan to include vaccine recipients' personal identifier information in the data lake.(1) They also urged stronger coordination with IISs. (Am J Public Health. Published online ahead of print Feburary 18, 2021: e1-e3. https://doi.org/10.2105/AJPH.2021.306177).

Bonanni, P., I. F. Angelillo, A. Villani, P. Biasci, S. Scotti, R. Russo, T. Maio, G. Vitali Rosati, M. Barretta, E. Bozzola, P. Castiglia, G. Chiamenti, G. Conforti, M. Conversano, A. Ferro, F. Francia, P. G. Macrì and C. Azzari (2021). "Maintain and increase vaccination coverage in children, adolescents, adults and elderly people: Let's avoid adding epidemics to the pandemic: Appeal from the Board of the Vaccination Calendar for Life in Italy: Maintain and increase coverage also by organizing vaccination services and reassuring the population." Vaccine 39(8): 1187-1189.

The Board of the Vaccination Calendar for Life (Bonanni et al., 2014, 2017) [1,2]), a coalition of four major scientific and professional societies of public health physicians, pediatricians and general practitioners in Italy, made an appeal to health authorities in order to sustain vaccination in COVID-19 times. The five pillars to maintain and increase vaccination coverage at all ages are described as follows: 1) Guarantee paediatric vaccination coverage to all newborns and paediatric boosters and adolescent immunizations, not interrupting active calls and scheduled sessions. 2) Re-organise the way paediatric and adolescent vaccinations are offered. 3) Set-up recovery programs for vaccinations not carried out after the start of the COVID-19 emergency. 4) Provide the preparation of tenders for the supply of flu vaccines with suitable quantities to increase coverage in all Regions and Autonomous Provinces with extreme urgency. 5) Prepare plans to increase coverage for influenza, pneumococcal, tetanus diphtheria and shingles. The Board of the Calendar for Life appeals to the National and Local Health Authorities for a strong and coordinated commitment in favor of the widest offer and acceptance of vaccinations, whose vital importance for collective health is now even more evident to all, in order to avoid that delays in the necessary initiatives should add damage from other epidemics to those suffered by our population due to the COVID-19 pandemic.

Dinleyici, E. C., R. Borrow, M. A. P. Safadi, P. van Damme and F. M. Munoz (2021). "Vaccines and routine immunization strategies during the COVID-19 pandemic." Hum Vaccin Immunother 17(2): 400-407.

Severe acute respiratory syndrome coronavirus 2 related disease (COVID-19) is now responsible for one of the most challenging and concerning pandemics. By August 2020, there were almost 20 million confirmed cases worldwide and well over half-million deaths. Since there is still no effective treatment or vaccine, non-pharmaceutical interventions have been implemented in an attempt to contain the spread of the virus. During times of quarantine, immunization practices in all age groups, especially routine childhood vaccines, have also been interrupted, delayed, re-organized, or completely suspended. Numerous high-income as well as low- and middle-income countries are now experiencing a rapid decline in childhood immunization coverage rates. We will, inevitably, see serious consequences related to suboptimal control of vaccine-preventable diseases (VPDs) in children concurrent with or following the pandemic. Routine pediatric immunizations of individual children at clinics, mass vaccination campaigns, and surveillance for VPDs must continue as much as possible during pandemic.

Franceschi, S., T. Gallo, C. Panato, F. Gongolo and A. Franzo (2020). "Coverage of HPV vaccination programme in Friuli Venezia Giulia Region (Northern Italy)." Epidemiol Prev 44(5-6): 378-384.

OBJECTIVES: to assess the completeness and timeliness of Human papillomavirus (HPV) vaccination programme in Friuli Venezia Giulia (FVG) Region (Northern Italy), notably by monitoring 2-dose coverage among girls before they turn 15 years old (referred to as "at 15") in each year between 2009 and 2018 and making a preliminary evaluation of coverage among boys at 13 years in

2016-2018. DESIGN: retrospective study. SETTING AND PARTICIPANTS: for each vaccine recipient, demographic information and history of HPV vaccine uptake from the digital FVG Vaccination Registry updated as of 31.12.2018 were extracted. Numerator data comprised all doses allocated to FVG residents. Age-specific denominators were derived from the FVG census in each examined year. Coverage estimates for the year 2018 were also provided by number of doses. MAIN OUTCOME MEASURES: coverage for a full course of HPV vaccine, defined as 2 doses in girls and boys younger than age 15 years but 3 doses in less young women. RESULTS: In FVG 52,217 females had received >=1 dose since 2008 and 12,152 males since 2015. >=2-dose coverage in girls at 15 increased from 42% in 2009 to 76% in 2015 and slightly declined afterwards (69% in 2018). In 2008, 3-dose coverage was 65%, 74%, and 59% in females aged 16-17, 18-19, and 20-26 years, respectively. In the same year, 2-dose coverage in boys at 13 years was 54%, similar to the coverage in girls at 13 years (57%). CONCLUSIONS: this paper shows the achievements of routine and catch-up HPV vaccination in FVG. While coverage in girls at 15 years of age peaked in 2015 and slightly diminished in subsequent years, the coverage in boys at 13 in 2018 had already approached the coverage in same-age girls (57%). On account of the signs of weakening in girls' coverage, campaigns in support to HPV vaccination must be repeated, especially in favour of the most cost-effective group, i.e., girls before 15 years of age. The heavy burden posed by the COVID-19 emergency on other prevention-related activities makes a better targeted use of HPV vaccination even more necessary.

Gilkey, M. B., R. A. Bednarczyk, M. A. Gerend, M. L. Kornides, R. B. Perkins, D. Saslow, J. Sienko, G. D. Zimet and N. T. Brewer (2020). "Getting Human Papillomavirus Vaccination Back on Track: Protecting Our National Investment in Human Papillomavirus Vaccination in the COVID-19 Era" J Adolesc Health 67(5): 633-634.

Masresha, B. G., R. Luce, Jr., M. E. Shibeshi, B. Ntsama, A. N'Diaye, J. Chakauya, A. Poy and R. Mihigo (2020). "The performance of routine immunization in selected African countries during the first six months of the COVID-19 pandemic" Pan Afr Med J 37(Suppl 1): 12.

INTRODUCTION: following the declaration of the COVID-19 pandemic on 11 March 2020, countries started implementing strict control measures, health workers were re-deployed and health facilities re-purposed to assist COVID-19 control efforts. These measures, along with the public concerns of getting COVID-19, led to a decline in the utilization of regular health services including immunization. METHODS: we reviewed the administrative routine immunization data from 15 African countries for the period from January 2018 to June 2020 to analyze the trends in the monthly number of children vaccinated with specific antigens, and compare the changes in the first three months of the COVID-19 pandemic. RESULTS: thirteen of the 15 countries showed a decline in the monthly average number of vaccine doses provided, with 6 countries having more than 10% decline. Nine countries had a lower monthly mean of recipients of first dose measles vaccination in the second quarter of 2020 as compared to the first quarter. Guinea, Nigeria, Ghana, Angola, Gabon, and South Sudan experienced a drop in the monthly number of children vaccinated for DPT3 and/or MCV1 of greater than 2 standard deviations at some point in the second quarter of 2020 as compared to the mean for the months January-June of 2018 and 2019. CONCLUSION: countries with lower immunization coverage in the pre-COVID period experienced larger declines in the number of children vaccinated immediately after the COVID-19 pandemic was declared. Prolonged and significant reduction in the number of children vaccinated poses a serious risk for outbreaks such as measles. Countries should monitor coverage trends at national and subnational levels, and undertake catch-up vaccination activities to ensure that children who have missed scheduled vaccines receive them at the earliest possible time.

Miyoshi, A., Y. Ueda and T. Kimura (2020). "Contemplating HPV vaccination in Japan during the time of COVID-19." Hum Vaccin Immunother: 1-2.

The Coronavirus Disease 2019 (COVID-19) pandemic has been growing, including in Japan where it has been estimated that as many as 3.1% of patients positive for new CoV strain SARS-CoV-2 might die of COVID-19-related respiratory failure. Meanwhile, human papillomavirus (HPV) is spreading in Japan. The fatality rate for HPV-associated cancers after infection with HPV is as much as that for COVID-19 in Japan, although the time to disease is much longer for HPV. Among advanced countries, the cervical cancer screening rate in Japanese females is very low. The Japanese Ministry of Health, Labor and Welfare (MHLW) suspended its official recommendation for HPV vaccination in June 2013 due to alleged adverse post-vaccination events in several young girls, such as chronic pain and motor impairment, which were repeatedly reported in the media. Subsequently, the rate for vaccinating girls plummeted from approximately 70% to the current rate of 1% or less. Women should accept HPV vaccination for the eventual prevention of cervical cancer with the same passion they are for COVID-19 testing.

Olorunsaiye, C. Z., K. K. Yusuf, K. Reinhart and H. M. Salihu (2020). "COVID-19 and Child Vaccination: A Systematic Approach to Closing the Immunization Gap." Int J MCH AIDS 9(3): 381-385.

The COVID-19 pandemic threatens to set back major successes that have been achieved in global vaccine initiatives. We conducted a rapid review and synthesis of the literature on immunization provision and Utilization since the onset of the COVID-19 pandemic. A total of 11 papers comprising peer-reviewed articles and key policies and guidelines, published between January 1 and June 15, 2020, were analyzed. Widespread disruptions of routine immunization and vaccination campaigns were reported leaving millions of children worldwide at risk of measles outbreaks. We present an expanded model of the World Health Organization's Global Routine Immunization Strategic Plan (GRISP) action areas as a tool to help countries quickly adapt to immunization challenges in the presence of COVID-19 and close the emerging immunization coverage gaps.

Sato, A. P. S. (2020). "Pandemic and vaccine coverage: challenges of returning to schools." Rev Saude Publica 54: 115.

Since March 2020, Brazil has faced the pandemic of the coronavirus disease 2019 (Covid-19), which has severely modified the way in which the population lives and uses health services. As such, face-to-face attendance has dropped dramatically, even for child vaccination, due to measures of social distancing to mitigate the transmission of the virus. Several countries have recorded a substantial drop in vaccination coverage in children, especially of those under two years of age. In Brazil, administrative data indicate the impact of the covid-19 pandemic on this downward trend, which was already an important challenge of the National Immunization Program in recent years. Many children will be susceptible to immunopreventable diseases, which reinforces the need to assess the vaccine status of schoolchildren before returning to face-to-face classes.
Publisher: Abstract available from the publisher.
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Saxena, S., H. Skirrow and H. Bedford (2020). "Routine vaccination during covid-19 pandemic response." Bmj 369: m2392.

Tsu, V. D., D. S. LaMontagne, P. Atuhebwe, P. N. Bloem and C. Ndiaye (2021). "National implementation of HPV vaccination programs in low-resource countries: Lessons, challenges, and future prospects." Prev Med 144: 106335.

More than 90% of cervical cancer deaths occur in low- and middle-income countries (LMICs), which have limited capacity to mount the comprehensive national screening and precancer treatment programs that could prevent most of these deaths. The development of vaccines against the human papillomavirus (HPV) has dramatically altered the landscape of cervical cancer prevention. As of mid-2020, 56 LMICs (41% of all LMICs) have initiated national HPV vaccination programs. This paper reviews the experience of LMICs that have introduced HPV vaccine into their national programs, key

lessons learned, HPV vaccination sustainability and scale-up challenges, and future mitigation measures. As international guidance evolved and countries accumulated experience, strategies for national introduction shifted with regard to target groups, delivery site and timing, preparation and planning, communications and social mobilization, and ultimately monitoring, supervision and evaluation. Despite the successes that LMICs have been able to achieve in reaching large proportions of eligible girls, there are still considerable challenges countries encounter in overcoming rumors, reaching out-of-school girls, completing the vaccine series, estimating target populations, monitoring program performance, and assuring vaccination sustainability. New opportunities, such as the entry of additional vaccine manufacturers and ongoing studies to evaluate one-dose delivery, could help overcome the outstanding barriers to higher coverage and financial sustainability. Effective use of the experience to date and advances on the horizon could enable all LMICs to move towards the coverage levels that are needed to achieve eventual elimination.

Potential Future Approaches for HPV Vaccination

A PubMed search was performed with the following selection criteria: [Human papillomavirus] AND [one dose] AND [Vaccination], title/abstract published in the last 5 years.202 items were retrieved respectively and a relevant manual selection of 15 publications were between 2021-2016 made considering relevancy to the meeting and the topics and imported into Endnote.

Acuti Martellucci, C., S. Nomura, D. Yoneoka, P. Ueda, J. Brotherton, K. Canfell, M. Palmer, L. Manzoli, P. Giorgi Rossi, A. De Togni, C. Palmonari, A. Califano, E. Saito, M. Hashizume and K. Shibuya (2021). "Human papillomavirus vaccine effectiveness within a cervical cancer screening programme: cohort study." Bjog 128(3): 532-539.

OBJECTIVE: To assess the effectiveness of an HPV vaccination programme in reducing the risk of cervical abnormalities identified at subsequent screening. DESIGN: Retrospective cohort study using administrative health data. SETTING: General population of Ferrara Province, Italy. POPULATION: Female residents born in 1986-1993 and participating in the organized cervical screening programme in 2011-2018, who were eligible for HPV vaccination in catch-up cohorts. METHODS: Logistic regression to evaluate the potential association between abnormal cervical cytology and one, two, three or at least one dose of HPV vaccine. MAIN OUTCOME MEASURES: Cervical abnormalities, as predicted by low-grade or high-grade cytology, by number of vaccine doses, stratified by age. RESULTS: The sample consisted of 7785 women (mean age 27.5 years, SD 2.3). Overall, 391 (5.0%) were vaccinated wit Z H í } • v ô õ ï ~ í í X ñ 9 • Z v } Œ u o Ç š } o } P Ç X t } u v Œ vaccine dose were significantly less likely to have an abnormal cytology (adjusted odds ratio 0.52; 95% confidence interval 0.34-0.79). Similar results were observed for women receiving a single dose, for both bivalent and quadrivalent vaccines, and applying buffer periods (excluding cytological outcomes within 1 month, 6 months and 1 year of the first dose). CONCLUSIONS: In the context of an organised cervical screening programme in Italy, catch-up HPV vaccination almost halved the risk of cytological abnormalities. TWEETABLE ABSTRACT: Among Ferrara women, vaccination against human papillomavirus halved the risk of screening cervical abnormalities.

Baandrup, L., C. Dehlendorff and S. K. Kjaer (2020). "One-Dose Human Papillomavirus Vaccination and the Risk of Genital Warts: A Danish Nationwide Population-based Study." Clin Infect Dis.

BACKGROUND: Increasing evidence suggests that 1-dose human papillomavirus (HPV) vaccination may protect significantly against HPV-related disease. We provide nationwide, real-world data on the risk of genital warts (GWs) after <3 vaccine doses. METHODS: All Danish women born in 1985-2003 were identified, and individual-level vaccination data were retrieved. The cohort was followed up for first occurrence of GWs until 31 December 2016. Using Poisson regression, we calculated incidence rates (IRs) of GWs per 100 000 person-years and IR ratios (IRRs) with corresponding 95% confidence intervals (CIs) for GWs, according to vaccination status, age at first dose, and calendar time. RESULTS: The cohort comprised 1 076 945 girls and women, of whom 485 408 were vaccinated. For girls initiating vaccination at age 12-14 years and 15-16 years, 1-dose vaccine effectiveness (VE) was 71% (IRR = 0.29; 95% CI, .22-.38) and 62% (0.38; .29-.49), respectively, compared with unvaccinated girls. In the same age groups, 2-dose VE was 78% (IRR, 0.22; 95% CI, .18-.26) and 68% (0.32; .26-.38), respectively. After 2009, the IRRs for 3 versus 1 dose and 2 versus 1 dose increased towards unity over calendar time, being 0.69 (95% CI, .57-.84) and 0.86 (.68-1.08) in 2016, respectively. CONCLUSIONS: In this study, 1 or 2 doses of quadrivalent HPV vaccine was associated

with substantial p Œ } š š] } v P] v • š ' t •] v P] Œ o • À] v š -dose VEP G í ò Ç approached that of 3 or 2 doses over calendar time, probably reflecting the impact of herd protection.

Batmunkh, T., M. T. Dalmau, M. E. Munkhsaikhan, T. Khorolsuren, N. Namjil, U. Surenjav, Z. Q. Toh, P. V. Licciardi, F. M. Russell, S. M. Garland, K. Mulholland and C. von Mollendorf (2020). "A single dose of quadrivalent human papillomavirus (HPV) vaccine is immunogenic and reduces HPV detection rates in young women in Mongolia, six years after vaccination." Vaccine 38(27): 4316-4324.

BACKGROUND: Emerging observational evidence suggests a single-dose of human papillomavirus (HPV) vaccine may be protective against vaccine-targeted HPV infection and associated cervical dysplasia. We aimed to demonstrate whether a single dose of quadrivalent HPV (4vHPV) vaccine was immunogenic and reduced HPV detection rates in young women in Mongolia. We also assessed knowledge and attitudes regarding HPV and the HPV vaccine. METHODS: A retrospective paired cohort study was undertaken to evaluate the effect of a single dose of 4vHPV, given at age 11-17 years in 2012, on HPV detection rates, when compared with unvaccinated women. Real time PCR was performed on self-administered vaginal swabs for HPV detection. An immunological analysis detecting neutralising antibodies (NAb) to high-risk HPV (HRHPV) genotypes 16 and 18 was performed on sera from a subset of 58 participants. Questionnaires evaluated knowledge, attitudes and self-swab acceptability. FINDINGS: A total of 475 women (mean age 20.4 years ± 1.6) were recruited; 118 vaccinated and 357 unvaccinated women. The prevalence of vaccine-targeted HRHPV16 and 18 was reduced by 92% (95%CI 44-99%) in the vaccinated (1·1%) compared with the unvaccinated (15.4%) group. The percentage of non-vaccine HPV genotypes was similar between vaccinated (26.5%) and unvaccinated (26.7%) groups. Approximately 90% and 58% of vaccinated women remained seropositive after six years for HRHPV16 and 18, respectively, with neutralising antibody levels 5- and 2-fold higher than unvaccinated women ($p < 0.001$). INTERPRETATION: One dose of 4vHPV vaccine reduces vaccine-targeted HPV genotypes, six years following vaccination, with high levels of HR genotype seropositivity among young Mongolian women.

Bergman, H., B. S. Buckley, G. Villanueva, J. Petkovic, C. Garritty, V. Lutje, A. X. Riveros-Balta, N. Low and N. Henschke (2019). "Comparison of different human papillomavirus (HPV) vaccine types and dose schedules for prevention of HPV-related disease in females and males." Cochrane Database Syst Rev 2019(11).

BACKGROUND: Uptake of human papillomavirus (HPV) vaccine remains low in many countries, although the bivalent and quadrivalent HPV vaccines given as a three-dose schedule are effective in the prevention of precancerous lesions of the cervix in women. Simpler immunisation schedules, such as those with fewer doses, might reduce barriers to vaccination, as may programmes that include males. OBJECTIVES: To evaluate the efficacy, immunogenicity, and harms of different dose schedules and different types of HPV vaccines in females and males. SEARCH METHODS: We conducted electronic searches on 27 September 2018 in Ovid MEDLINE, the Cochrane Central Register of Controlled Trials (CENTRAL) (in the Cochrane Library), and Ovid Embase. We also searched the WHO International Clinical Trials Registry Platform, and ClinicalTrials.gov (both 27 September 2018), vaccine manufacturer websites, and checked reference lists from an index of HPV studies and other relevant systematic reviews. SELECTION CRITERIA: We included randomised controlled trials (RCTs) with no language restriction. We considered studies if they enrolled HIV-negative males or females aged 9 to 26 years, or HIV-positive males or females of any age. DATA COLLECTION AND ANALYSIS: We used

methods recommended by Cochrane. We use the term 'control' to refer to comparator products containing an adjuvant or active vaccine and 'placebo' to refer to products that contain no adjuvant or active vaccine. Most primary outcomes in this review were clinical outcomes. However, for comparisons comparing dose schedules, the included RCTs were designed to measure antibody responses (i.e. immunogenicity) as the primary outcome, rather than clinical outcomes, since it is unethical to collect cervical samples from girls under 16 years of age. We analysed immunogenicity outcomes (i.e. geometric mean titres) with ratios of means, clinical outcomes (e.g. cancer and intraepithelial neoplasia) with risk ratios or rate ratios and, for serious adverse events and deaths, we calculated odds ratios. We rated the certainty of evidence with GRADE. MAIN RESULTS: We included 20 RCTs with 31,940 participants. The length of follow-up in the included studies ranged from seven months to five years. Two doses versus three doses of HPV vaccine in 9- to 15-year-old females Antibody responses after two-dose and three-dose HPV vaccine schedules were similar after up to five years of follow-up (4 RCTs, moderate- to high-certainty evidence). No RCTs collected clinical outcome data. Evidence about serious adverse events in studies comparing dose schedules was of very low-certainty owing to imprecision and indirectness (three doses 35/1159; two doses 36/1158; 4 RCTs). One death was reported in the three-dose group (1/898) and none in the two-dose group (0/899) (low-certainty evidence). Interval between doses of HPV vaccine in 9- to 14-year-old females and males Antibody responses were stronger with a longer interval (6 or 12 months) between the first two doses of HPV vaccine than a shorter interval (2 or 6 months) at up to three years of follow-up (4 RCTs, moderate- to high-certainty evidence). No RCTs collected data about clinical outcomes. Evidence about serious adverse events in studies comparing intervals was of very low-certainty, owing to imprecision and indirectness. No deaths were reported in any of the studies (0/1898, 3 RCTs, low-certainty evidence). HPV vaccination of 10- to 26-year-old males In one RCT there was moderate-certainty evidence that quadrivalent HPV vaccine, compared with control, reduced the incidence of external genital lesions (control 36 per 3081 person-years; quadrivalent 6 per 3173 person-years; rate ratio 0.16, 95% CI 0.07 to 0.38; 6254 person-years) and anogenital warts (control 28 per 2814 person-years; quadrivalent 3 per 2831 person-years; rate ratio 0.11, 95% CI 0.03 to 0.38; 5645 person-years). The quadrivalent vaccine resulted in more injection-site adverse events, such as pain or redness, than control (537 versus 601 per 1000; risk ratio (RR) 1.12, 95% CI 1.06 to 1.18, 3895 participants, high-certainty evidence). There was very low-certainty evidence from two RCTs about serious adverse events with quadrivalent vaccine (control 12/2588; quadrivalent 8/2574), and about deaths (control 11/2591; quadrivalent 3/2582), owing to imprecision and indirectness. Nonavalent versus quadrivalent vaccine in 9- to 26-year-old females and males Three RCTs were included; one in females aged 9- to 15-years (n = 600), one in females aged 16- to 26-years (n = 14,215), and one in males aged 16- to 26-years (n = 500). The RCT in 16- to 26-year-old females reported clinical outcomes. There was little to no difference in the incidence of the combined outcome of high-grade cervical epithelial neoplasia, adenocarcinoma in situ, or cervical cancer between the HPV vaccines (quadrivalent 325/6882, nonavalent 326/6871; OR 1.00, 95% CI 0.85 to 1.16; 13,753 participants; high-certainty evidence). The other two RCTs did not collect data about clinical outcomes. There were slightly more local adverse events with the nonavalent vaccine (905 per 1000) than the quadrivalent vaccine (846 per 1000) (RR 1.07, 95% CI 1.05 to 1.08; 3 RCTs, 15,863 participants; high-certainty evidence). Comparative evidence about serious adverse events in the three RCTs (nonavalent 243/8234, quadrivalent 192/7629; OR 0.60, 95% CI 0.14 to 2.61) was of low certainty, owing to imprecision and indirectness. HPV vaccination for people living with HIV Seven RCTs reported on HPV vaccines in people with HIV, with two small trials that collected data about clinical outcomes. Antibody responses were higher following vaccination with either bivalent or quadrivalent HPV vaccine than with control, and these responses could be demonstrated to have been maintained for up to 24 months in children living with HIV (low-certainty evidence). The evidence about clinical outcomes and harms for HPV

vaccines in people with HIV is very uncertain (low- to very low-certainty evidence), owing to imprecision and indirectness. AUTHORS' CONCLUSIONS: The immunogenicity of two-dose and three-dose HPV vaccine schedules, measured using antibody responses in young females, is comparable. The quadrivalent vaccine probably reduces external genital lesions and anogenital warts in males compared with control. The nonavalent and quadrivalent vaccines offer similar protection against a combined outcome of cervical, vaginal, and vulval precancer lesions or cancer. In people living with HIV, both the bivalent and quadrivalent HPV vaccines result in high antibody responses. For all comparisons of alternative HPV vaccine schedules, the certainty of the body of evidence about serious adverse events reported during the study periods was low or very low, either because the number of events was low, or the evidence was indirect, or both. Post-marketing surveillance is needed to continue monitoring harms that might be associated with HPV vaccines in the population, and this evidence will be incorporated in future updates of this review. Long-term observational studies are needed to determine the effectiveness of reduced-dose schedules against HPV-related cancer endpoints, and whether adopting these schedules improves vaccine coverage rates.

Brady, A. M., E. B. Walter, L. E. Markowitz, E. R. Unger and G. Panicker (2020). "Delayed dosing intervals for quadrivalent human papillomavirus vaccine do not reduce antibody avidity." Hum Vaccin Immunother 16(8): 1802-1807.

The quadrivalent HPV vaccine (4vHPV) was originally recommended as a three-dose series (0/2/6 months), though delays in completing the series frequently occur. We previously found delayed dosing in girls resulted in similar or higher antibody titers compared to on-time dosing. Archived sera from 262 healthy females aged 9-18 recruited from pediatric clinics were tested to determine if delayed dosing intervals affected antibody avidity. Avidity index (AI; ratio of IgG Ab bound in the treated and untreated sample) was determined pre- and post-dose 3 4vHPV for each participant using a modified multiplex ELISA. Data were grouped by dosing intervals: (1) on-time dose 2 and 3, (2) delayed dose 2 and on-time dose 3, (3) on-time dose 2 and delayed dose 3, (4) delayed dose 2 and 3. Overall, mean AI was highest for HPV16 and lowest for HPV6. As expected, AI did not differ between groups 1 & 3 or groups 2 & 4 pre-dose 3, however, for most types mean AI was significantly higher both pre- and post-dose 3 for groups with delayed dose 2. For all types, mean AI was higher post-dose 3 in all delayed dosing groups compared to group 1. One month post-dose 3, there was a positive but Á l } Œ Œ o š] } v š Á v / • v v š] } Ç š] š Œ (} Œ , W s ò ~ Œ A ì X î ñ X ì ï ó ì • U , W s í ò ~ Œ A ì X í í U ‰ A X ì õ ï ð 0 0 1). Our findings suggest longer intervals between doses result in higher antibody avidity, providing further evidence that delayed dosing of 4vHPV does not hinder the immune response.

Brotherton, J. M., A. Budd, C. Rompotis, N. Bartlett, M. J. Malloy, R. L. Andersen, K. A. Coulter, P. W. Couvee, N. Steel, G. H. Ward and M. Saville (2019). "Is one dose of human papillomavirus vaccine as effective as three?: A national cohort analysis." Papillomavirus Res 8: 100177.

AIM: Prophylactic human papillomavirus (HPV) vaccines are highly effective at preventing pre-cancerous cervical lesions when given in a three-dose schedule. Some post-hoc trial data suggest that one dose prevents HPV infection. If one dose could prevent pre-cancerous cervical lesions, then global cervical cancer prevention would be greatly facilitated. We assessed the effectiveness of quadrivalent HPV vaccine by number of doses against cervical intraepithelial neoplasia (CIN) 2 or 3/adenocarcinoma-in-situ (AIS)/cancer in Australia up to seven years post vaccination. METHODS: We

linked registry data from all 8 jurisdictional cervical screening registers, with the national HPV vaccination register, death index and cancer registers for all Australian women aged 15 or under when eligible for vaccine who screened between April 2007 (when vaccination commenced) and 31 December 2014. We performed Cox proportional hazard regression, adjusted a priori for age, socioeconomic status, and area of residence, to estimate hazard ratios of histologically confirmed CIN2/CIN3/AIS/cancer. RESULTS: We included 250,648 women: 48,845 (19·5%) unvaccinated, 174,995 (69·8%) had received three doses, 18,190 (7·3%) two doses and 8,618 (3·4%) one dose. The adjusted hazard ratio was significantly lower for all dose groups compared to unvaccinated women (1 dose 0·65 (95%CI 0·52-0·81), 2 doses 0·61 (0·52-0·72) and 3 doses 0·59 (0·54-0·65).) With adjustment for age at vaccination amongst the vaccinated group, the adjusted hazard ratios for one dose and two dose recipients were comparable to three dose recipients (one dose 1.01 (95%CI 0.81-1.26), two doses 1.00 (0.85-1.17).) Multiple sensitivity analyses, including use of different dose assignment methods, produced consistent findings. Comparison with a historical cohort of age matched women showed that the result was not due to herd protection alone. CONCLUSIONS: One dose had comparable effectiveness as two or three doses in preventing high-grade disease in a high coverage setting. These findings support the hypothesis that one dose vaccination may be a viable strategy when working towards the global elimination of cervical cancer.

Gilca, V., C. Sauvageau, G. Panicker, G. De Serres, M. Ouakki and E. R. Unger (2019). "Antibody persistence after a single dose of quadrivalent HPV vaccine and the effect of a dose of nonavalent vaccine given 3-8 years later - an exploratory study." Hum Vaccin Immunother 15(2): 503-507.

The objective of this study was to assess the persistence of antibodies after a single dose of quadrivalent HPV vaccine (4vHPV) and the effect of a dose of nonavalent HPV vaccine (9vHPV) given 3-8 years later. Such data might be of interest in the decision-making process regarding the 2-dose course completion in non-compliant vaccinees in jurisdictions which switched from 4vHPV to 9vHPV. Girls who previously received a single dose of 4vHPV were eligible to participate. Blood specimens were collected just before and one month post-9vHPV administration. The specimens were tested by ELISA for the presence of antibodies to 9 HPV types included in the 9vHPV. Thirty-one girls aged 13-18 years (mean 15.5 years) participated in the study. Pre-9vHPV administration, all participants were seropositive to 4 HPV types included in 4vHPV and 58%-87% were seropositive to the five other HPV types included in the 9vHPV. GMTs were 6.1 AU/ml, 7.7 AU/ml, 20.1 IU/ml and 6.3 IU/ml to HPV6, HPV11, HPV16 and HPV18, respectively. The GMTs for the other five HPV types varied from 1.0 to 2.9 AU/ml. One month post-9vHPV administration all 31 participants were seropositive to all 9 HPV types with a 36.1 to 89.1-fold increase of GMTs. High seropositivity rates observed several years after a single dose of 4vHPV and 100% seropositivity after a dose of 9vHPV suggest that this schedule might be used in non-compliant vaccinees or when switching immunization programs from 4vHPV to 9vHPV.

Gilca, V., C. Sauvageau, G. Panicker, G. De Serres, J. Schiller, M. Ouakki and E. R. Unger (2019). "Long intervals between two doses of HPV vaccines and magnitude of the immune response: a post hoc analysis of two clinical trials." Hum Vaccin Immunother 15(7-8): 1980-1985.

The objective of this analysis was to compare the anti-HPV GMTs and their distribution after a 6-month or a 3-8 -y interval between two HPV vaccine doses. The results from two clinical trials, conducted by the same team in the same region, with serological assays performed at the same laboratory using the same ELISA methodology were compared. In the first study, 173 9-10-y-old girls and boys received two doses of 9vHPV vaccine at a 6-month interval; in the second study, 31 girls vaccinated with one dose of 4vHPV at the age of 9-14 y received a dose of 9vHPV 3-8 y later (mean

5.4 y). In both studies, blood samples were collected before and 1 month post second dose. Despite large differences in the time since the first dose, all subjects (100%) were seropositive to the common 4 HPV types (6, 11, 16 and 18) to both vaccines, with comparable GMTs and titer distributions before the second dose. One month post second dose, the GMTs increased 40-91-fold for those with a 6-month interval between doses and 60-82-fold for those with a 3-8-y interval. Titer distributions after the booster dose were comparable in the two studies. These results indicate that 2-dose HPV vaccination schedules with an interval of several years could be used for pre-adolescents. Intervals longer than 6 months may facilitate logistics for immunization programs and could be useful during periods of vaccine shortage or as a transition while the effectiveness of a one-dose schedule is being evaluated.

Kreimer, A. R., J. N. Sampson, C. Porras, J. T. Schiller, T. Kemp, R. Herrero, S. Wagner, J. Boland, J. Schussler, D. R. Lowy, S. Chanock, D. Roberson, M. S. Sierra, S. H. Tsang, M. Schiffman, A. C. Rodriguez, B. Cortes, M. H. Gail, A. Hildesheim, P. Gonzalez and L. A. Pinto (2020). "Evaluation of Durability of a Single Dose of the Bivalent HPV Vaccine: The CVT." J Natl Cancer Inst 112(10): 1038-1046.

BACKGROUND: The authors investigated the durability of vaccine efficacy (VE) against human papillomavirus (HPV)16 or 18 infections and antibody response among nonrandomly assigned women who received a single dose of the bivalent HPV vaccine compared with women who received multiple doses and unvaccinated women. METHODS: HPV infections were compared between HPV16 or 18-À] v š Á } u v P í ô š } î ñ 0 Ç Œ • Á Z } Œ] À } v ~ E 0 A 0 í í î • U š Á } doses, and age- and geography- u š Z µ v À] v š Á } u v ~ E 0 A 0 í ó ô • µ š Z o } v P of the Costa Rica HPV Vaccine Trial. Cervical HPV infections were measured at two study visits, approximately 9 and 11 years after initial HPV vaccination, using National Cancer Institute next-generation sequencing TypeSeq1 assay. VE and 95% confidence intervals (CIs) were estimated. HPV16 or 18 antibody levels were measured in all one- and two-dose women, and a subset of three-dose women, using a virus-like particle-based enzyme- o] v l] u u µ v } • } Œ v š • • Ç ~ v 0 A 0 ð ð ô • X Median follow-up for the HPV- À] v š P Œ } µ ‰ Á • í í X ï 0 Ç Œ • ~] í ý š ó Œ Ç µ Œ š } o C and did not vary by dose group. VE against prevalent HPV16 or 18 infection was 80.2% (95% CI = 70.7% to 87.0%) among three-dose, 83.8% (95% CI = 19.5% to 99.2%) among two-dose, and 82.1% (95% CI = 40.2% to 97.0%) among single-dose women. HPV16 or 18 antibody levels did not qualitatively decline between years four and 11 regardless of the number of doses given, although one-dose titers continue to be statistically significantly lower compared with two- and three-dose titers. CONCLUSION: More than a decade after HPV vaccination, single-dose VE against HPV16 or 18 infection remained high and HPV16 or 18 antibodies remained stable. A single dose of bivalent HPV vaccine may induce sufficiently durable protection that obviates the need for more doses.

Lazcano-Ponce, E., M. Carnalla-Cortés, T. Barrientos-Gutiérrez, L. Torres-Ibarra, A. Cruz-Valdez, J. Salmerón and M. Hernández-Ávila (2018). "The effect of a booster dose of HPV tetravalent vaccine after 51 months: implications for extended vaccination schedules." Salud Publica Mex 60(6): 666-673.

OBJECTIVE: To asses the non-inferiority between two differ- ent vaccination schedules one month after the administration of the third dose. MATERIALS AND METHODS: We evaluated the anti-HPV 16/18 antibody titers induced by quadrivalent HPV vaccine administered using two different schedules in girls 9 to 10-year-old girls: a traditional (0-2-6) and an alterna- tive (0-6-50). Blood samples

were collected at month 7, 21 and 51. RESULTS: The antibody geometric mean titer ratios one month after the application of the third dose -month 51 for the alternative and month 7 for the traditional- were 1.55 for HPV16 (95%CI, 1.15-2.08) and 1.53 for HPV18 (95%CI, 1.12-2.09). The seropositive rate was above 99% in both groups. CONCLUSIONS: The application of an alternative 3-dose schedule in 9 to 10-year-old girls induces a non-inferior immune response compared to the standard one month after the last dose. Further research is needed to understand the minimal number of doses and their timing to provide the best coverage for HPV infection.

Markowitz, L. E., A. L. Naleway, N. P. Klein, R. M. Lewis, B. Crane, T. D. Querec, A. Hsiao, L. Aukes, J. Timbol, S. Weinmann, G. Liu, M. Steinau and E. R. Unger (2020). "Human Papillomavirus Vaccine Effectiveness Against HPV Infection: Evaluation of One, Two, and Three Doses." J Infect Dis 221(6): 910-918.

BACKGROUND: Highly effective human papillomavirus (HPV) vaccines are used in many national programs in 3- or 2-dose schedules. We examined HPV vaccine effectiveness against HPV prevalence by number of doses. METHODS: We collected residual liquid-based cytology samples from US women aged 20-29 years who were screened for cervical cancer. Women continuously enrolled from 2006 through the specimen collection date were analyzed. Specimens were tested using the Linear Array assay. We analyzed prevalence of quadrivalent HPV vaccine (4vHPV) types (HPV 6,11,16,18) and other HPV-type categories and determined prevalence ratios (PRs) and 95% confidence intervals (CIs) for 1, 2, and 3 compared with no vaccine doses. RESULTS: Among 4269 women, 1052 (24.6%) were unvaccinated, 2610 (61.1%) received 3 doses, 304 (7.1%) received 2 doses, and 303 (7.1%) received 1 dose. The 4vHPV-type prevalence was 7.4% among unvaccinated women compared with 1.7%, 1.0%, and 1.0% among 1-, 2-, and 3-dose recipients. Among women vaccinated š G í ô Ç Œ • U i µ 2 š and 3 doses were 0.06 (95% CI, 0.01-0.42), 0.05 (95% CI, 0.01-0.39), and 0.06 (95% CI, 0.04- ì X í î • X K E > h ^ / K E ^ W u } v P Á } u v Á Z } Œ] À š Z] Œ (estimated HPV vaccine effectiveness was high regardless of number of doses.

Orumaa, M., S. K. Kjaer, C. Dehlendorff, C. Munk, A. O. Olsen, B. T. Hansen, S. Campbell and M. Nygård (2020). "The impact of HPV multi-cohort vaccination: Real-world evidence of faster control of HPV-related morbidity." Vaccine 38(6): 1345-1351.

BACKGROUND: In 2009, both Norway and Denmark initiated routine quadrivalent human papillomavirus vaccination (qHPV) for 12-year-old girls; however, Denmark also introduced free-of-charge multi-cohort vaccination for older age groups in 2008. We aim to describe trends in genital warts (GWs) incidence rates (IRs) among men and women and qHPV vaccine coverage among women in Norway and Denmark in 2006-2015. METHODS: We linked multiple national health registries in Norway and Denmark via national personal identifiers to access data on GWs incidence and qHPV vaccination among women and men aged 12-35 years residing in Norway and Denmark in 2006-2015. We calculated age-specific and age-standardized GWs IRs, GWs IR trends before (2006-2009) and after (2009-2015) the implementation of qHPV vaccination, and qHPV vaccine coverage among women. RESULTS: In Norway and Denmark together, there were more than 200,000 cases of incident GWs and over 710,000 girls got at least one dose of qHPV vaccine during the study period. The total qHPV coverage in Norway and Denmark in 2015 was among women aged 12-35 years 24% and 70%, respectively. GWs IRs in Norway and Denmark decreased annually in 2009-2015 among women by 4.8% (95% confidence interval: 4.3 to 5.3) and 18.0% (95%CI: 17.5 to 18.6), respectively, and among men 1.9% (95%CI: 1.4 to 2.4) and 10.7% (95%CI: 10.3 to 11.2), respectively. In Denmark, GWs IRs decreased rapidly among both sexes and all age groups after qHPV vaccination, while Norway showed only a modest decrease. CONCLUSION: Rapid decline in HPV-related morbidity is feasible with high coverage of multi-cohort vaccination. However, the decision to vaccinate a single cohort of 12-years-

old girls only will postpone HPV-related disease control by at least a decade. Thus countries planning HPV vaccination programs should also initiate multi-cohort vaccination for faster disease control.

Pasmans, H., T. M. Schurink-Van't Klooster, M. J. M. Bogaard, D. M. van Rooijen, H. E. de Melker, M. J. P. Welters, S. H. van der Burg, F. R. M. van der Klis and A. M. Buisman (2019). "Long-term HPV-specific immune response after one versus two and three doses of bivalent HPV vaccination in Dutch girls." Vaccine 37(49): 7280-7288.

BACKGROUND: In view of further reduction of HPV vaccination schedules, gaining more insight into humoral and cellular immune responses after a single HPV vaccine is of great interest. Therefore, these responses were evaluated after different doses of the bivalent (2v) HPV-vaccine in girls. METHODS: Blood was collected yearly up to seven years post-vaccination with one-, two- or three- } • • } (š Z î À , W s À] v -type-specific IgG and IgA antibody levels, IgG-isotypes and avidity indexes were measured by a virus-like-particle-based multiplex-immuno-assay for two vaccine and five non-vaccine HPV types. HPV-type-specific memory B-cell numbers- and T-cell cytokine responses were determined in a subpopulation. RESULTS: HPV-type-specific antibody concentrations were significantly lower in one- than in two- and three-dose vaccinated girls but remained stable over seven years. The lower antibody response coincided with reduced HPV-type-specific B- and T-cell responses. There were no differences in both the IgG subtypes and the avidity of the HPV16-specific antibodies between the groups. CONCLUSIONS: One-dose of the 2vHPV vaccine is immunogenic, but results in less B- and T-cell memory and considerable lower antibody responses when compared with more doses. Therefore, at least of some of girls receiving the one-dose of the vaccination might be at higher risk for waning immunity to HPV in the long-term.

Toh, Z. Q., J. Kosasih, F. M. Russell, R. Reyburn, J. Fong, E. Tuivaga, F. T. Ratu, C. D. Nguyen, S. Matanitobua, L. A. H. Do, T. Menheniott, I. H. Frazer, S. M. Garland, E. K. Mulholland and P. V. Licciardi (2019). "Selective Persistence of HPV Cross-Neutralising Antibodies following Reduced-Dose HPV Vaccine Schedules." Vaccines (Basel) 7(4).

The duration of cross-neutralising antibody responses (cross-NAb) following HPV immunisation is unknown. We compared cross-NAb responses in cohort of girls who were either unimmunised or had received immunisation with one, two or three doses of 4vHPV (Gardasil(®),Merck Inc.) six years earlier, before and one month after a booster dose of 2vHPV (Cervarix(®), GSK). NAb to potentially cross-reactive HPV genotypes 31, 33, 45, 52 and 58 were measured using a HPV pseudovirion-based neutralisation assay. Girls who had previously received at least one dose of 4vHPV had significantly higher NAb titres for HPV31 when compared with unimmunised girls, whereas no difference in NAb titre was observed for four other genotypes (33, 45, 52 and 58). Following a single further immunisation with 2vHPV, NAb titres to each of the five tested HPV genotypes were comparable for girls who previously received one, two or three doses of 4vHPV, and were significantly higher than for previously unimmunised girls. Immunisation with one, two or three doses of 4vHPV induced NAb to HPV31 that persisted for six years, but there was no persistence of NAb to HPV33, 45, 52 or 58. Our results suggest that one or two doses of 4vHPV may provide long-term protection against HPV31.

Whitworth, H. S., K. E. Gallagher, N. Howard, S. Mounier-Jack, G. Mbwanji, A. R. Kreimer, P. Basu, H. Kelly, M. Drolet, M. Brisson and D. Watson-Jones (2020). "Efficacy and immunogenicity of a single dose of human papillomavirus vaccine compared to no vaccination or standard three and two dose vaccination regimens: A systematic review of evidence from clinical trials." Vaccine 38(6): 1302-1314.

OBJECTIVES: This study aimed to systematically review the literature on the efficacy and immunogenicity of single-dose HPV vaccination compared to no vaccination or multi-dose schedules among vaccine trial participants. METHODS: Medline, EMBASE, Global Health Database and Cochrane Central Register of Controlled Trials were searched for publications and conference abstracts (dated January 1999-August 2018) using MeSH and non-MeSH terms for human papillomavirus AND vaccines AND (immunogenicity OR efficacy/effectiveness) AND dosage. Search results were screened against pre-specified eligibility criteria. Data were extracted from included articles, and a narrative synthesis conducted on efficacy against HPV16/18 infection and humoral immunogenicity. RESULTS: Seven of 6,523 unique records identified were included in the review. Six were nested observational studies of participants randomised to receive two or three doses in three large HPV vaccine trials, in which some participants did not complete their allocated schedules. One small pilot study prospectively allocated participants to receive one or no vaccine dose. Frequency of HPV16/18 infection was low (e.g. <1% for 12-month-persistent infection) in all vaccinated participants up to seven years post vaccination and did not significantly differ by number of doses ($p > 0.05$ in all cases). Frequency of infection was significantly lower in one-dose recipients compared to unvaccinated controls ($p < 0.01$ for all infection endpoints in each study). HPV16/18 seropositivity rates were high in all HPV vaccine recipients (100% in three of four studies reporting this endpoint), though antibody levels were lower with one compared to two or three doses. CONCLUSIONS: This review supports the premise that one HPV vaccine dose may be as effective in preventing HPV infection as multi-dose schedules in healthy young women. However, it also highlights the paucity of available evidence from purpose-designed, prospectively-randomised trials. Results from ongoing clinical trials assessing the efficacy and immunogenicity of single-dose HPV vaccination compared to currently-recommended schedules are awaited.

Lessons learnt from Covid-19: Leveraging Opportunities for HPV Vaccination and Cervical cancer screening and treatment

A PubMed search was performed with the following selection criteria: [HPV] OR [human papilloma virus] AND [Covid-19] AND [Opportunities], [HPV] OR [human papilloma virus] AND [cervical cancer] AND [Covid-19] AND [Innovation], [HPV] AND [cervical cancer] AND [Covid-19] AND [Innovation] AND [lessons learnt], [HPV] AND [cervical cancer screening] OR [cervical cancer treatment] AND [Covid-19] AND [opportunities], [HPV] AND [cervical cancer] AND [Covid-19], [cervical cancer] AND [covid-19] AND [tracing] AND [opportunities],title/abstract published in the last one year. 4, 2, 0, 7, 13 and items were retrieved respectively and a relevant manual selection of 14 publications between 2020-2021 based on title and abstract was made, and imported into Endnote. Some of the references were taken from PubMed search for other similar topics in the background document

Abeler, J., M. Bäcker, U. Buermeyer and H. Zillessen (2020). "COVID-19 Contact Tracing and Data Protection Can Go Together." JMIR Mhealth Uhealth 8(4): e19359.

We discuss the implementation of app-based contact tracing to control the coronavirus disease (COVID-19) pandemic and discuss its data protection and user acceptability aspects.

Ajenifuja, K. O., J. Belinson, A. Goldstein, K. T. Desai, S. de Sanjose and M. Schiffman (2020). "Designing low-cost, accurate cervical screening strategies that take into account COVID-19: a role for self-sampled HPV typing?" Infect Agent Cancer 15: 61.

BACKGROUND: We propose an economical cervical screening research and implementation strategy designed to take into account the typically slow natural history of cervical cancer and the severe but hopefully temporary impact of COVID-19. The commentary introduces the practical validation of some critical components of the strategy, described in three manuscripts detailing recent project results in Asia and Africa.The main phases of a cervical screening program are 1) primary screening of women in the general population, 2) triage testing of the small minority of women that screen positive to determine need for treatment, and 3) treatment of triage-positive women thought to be at highest risk of precancer or even cancer. In each phase, attention must now be paid to safety in relation to SARS-CoV-2 transmission. The new imperatives of the COVID-19 pandemic support self-sampled HPV testing as the primary cervical screening method. Most women can be reassured for several years by a negative test performed on a self-sample collected at home, without need of clinic visit and speculum examination. The advent of relatively inexpensive, rapid and accurate HPV DNA testing makes it possible to return screening results from self-sampling very soon after specimen collection, minimizing loss to follow-up. Partial HPV typing provides important risk stratification useful for triage of HPV-positive women. A second "triage" test is often useful to guide management. In lower-resource settings, visual inspection with acetic acid (VIA) is still proposed but it is inaccurate and poorly reproducible, misclassifying the risk stratification gained by primary HPV testing. A deep-learning based approach to recognizing cervical precancer, adaptable to a smartphone camera, is being validated to improve VIA performance. The advent and approval of thermal ablation permits quick, affordable and safe, immediate treatment at the triage clinic of the majority of HPV-positive, triage-positive women. CONCLUSIONS: Overall, only a small percentage of women in cervical screening programs need to attend the hospital clinic for a surgical procedure, particularly when screening is targeted to the optimal age range for detection of precancer rather than older ages with decreased visual screening performance and higher risks of hard-to-treat outcomes including invasive cancer.

Finley, C., M. J. Dugan, J. K. Carney, W. S. Davis, T. V. Delaney, V. C. Hart, B. W. Holmes, G. S. Stein, R. Katrick, H. Morehouse, B. Cole, L. S. Bradford, M. B. Boardman, H. Considine, N. C. Kaplan, M. Plumpton, L. Schadler, J. J. Smith and K. McAllister (2021). "A Peer-Based Strategy to Overcome HPV Vaccination Inequities in Rural Communities: A Physical Distancing-Compliant Approach." Crit Rev Eukaryot Gene Expr 31(1): 61-69.

The human papilloma virus (HPV) vaccine is the world's first proven and effective vaccine to prevent cancers in males and females when administered pre-exposure. Like most of the US, barely half of Vermont teens are up-to-date with the vaccination, with comparable deficits in New Hampshire and Maine. The rates for HPV vaccine initiation and completion are as low as 33% in rural New England. Consequently, there is a compelling responsibility to communicate its importance to unvaccinated teenagers before their risk for infection increases. Messaging in rural areas promoting HPV vaccination is compromised by community-based characteristics that include access to appropriate medical care, poor media coverage, parental and peer influence, and skepticism of science and medicine. Current strategies are predominantly passive access to literature and Internet-based information. Evidence indicates that performance-based messaging can clarify the importance of HPV vaccination to teenagers and their parents in rural areas. Increased HPV vaccination will significantly contribute to the prevention of a broadening spectrum of cancers. Reducing rurality-based inequities is a public health priority. Development of a performance-based peer-communication intervention can capture a window of opportunity to provide increasingly effective and sustained HPV protection. An effective approach can be partnering rural schools and regional health teams with a program that is nimble and scalable to respond to public health policies and practices compliant with COVID-19 pandemic-related modifications on physical distancing and interacting in the foreseeable future.

Finney Rutten, L. J., X. Zhu, A. L. Leppin, J. L. Ridgeway, M. D. Swift, J. M. Griffin, J. L. St Sauver, A. Virk and R. M. Jacobson (2021). "Evidence-Based Strategies for Clinical Organizations to Address COVID-19 Vaccine Hesitancy." Mayo Clin Proc 96(3): 699-707.

The success of vaccination programs is contingent upon irrefutable scientific safety data combined with high rates of public acceptance and population coverage. Vaccine hesitancy, characterized by lack of confidence in vaccination and/or complacency about vaccination that may lead to delay or refusal of vaccination despite the availability of services, threatens to undermine the success of coronavirus disease 2019 (COVID-19) vaccination programs. The rapid pace of vaccine development, misinformation in popular and social media, the polarized sociopolitical environment, and the inherent complexities of large-scale vaccination efforts may undermine vaccination confidence and increase complacency about COVID-19 vaccination. Although the experience of recent lethal surges of COVID-19 infections has underscored the value of COVID-19 vaccines, ensuring population uptake of COVID-19 vaccination will require application of multilevel, evidence-based strategies to influence behavior change and address vaccine hesitancy. Recent survey research evaluating public attitudes in the United States toward the COVID-19 vaccine reveals substantial vaccine hesitancy. Building upon efforts at the policy and community level to ensure population access to COVID-19 vaccination, a strong health care system response is critical to address vaccine hesitancy. Drawing on the evidence base in social, behavioral, communication, and implementation science, we review, summarize, and encourage use of interpersonal, individual-level, and organizational interventions within clinical organizations to address this critical gap and improve population adoption of COVID-19 vaccination.

Gorin, S. N. S., M. Jimbo, R. Heizelman, K. M. Harmes and D. M. Harper (2021). "The future of cancer screening after COVID-19 may be at home." Cancer 127(4): 498-503.

During the coronavirus disease 2019 (COVID-19) pandemic, cancer screening decreased precipitously; home screening for colorectal cancer diminished less than that for colonoscopy and breast and cervical cancer screening. The authors have highlighted approaches for home cancer screening in addition to telemedicine.

Kazi, A. M., S. A. Qazi, S. Khawaja, N. Ahsan, R. M. Ahmed, F. Sameen, M. A. Khan Mughal, M. Saqib, S. Ali, H. Kaleemuddin, Y. Rauf, M. Raza, S. Jamal, M. Abbasi and L. K. Stergioulas (2020). "An Artificial Intelligence-Based, Personalized Smartphone App to Improve Childhood Immunization Coverage and Timelines Among Children in Pakistan: Protocol for a Randomized Controlled Trial." JMIR Res Protoc 9(12): e22996.

BACKGROUND: The immunization uptake rates in Pakistan are much lower than desired. Major reasons include lack of awareness, parental forgetfulness regarding schedules, and misinformation regarding vaccines. In light of the COVID-19 pandemic and distancing measures, routine childhood immunization (RCI) coverage has been adversely affected, as caregivers avoid tertiary care hospitals or primary health centers. Innovative and cost-effective measures must be taken to understand and deal with the issue of low immunization rates. However, only a few smartphone-based interventions have been carried out in low- and middle-income countries (LMICs) to improve RCI. OBJECTIVE: The primary objectives of this study are to evaluate whether a personalized mobile app can improve children's on-time visits at 10 and 14 weeks of age for RCI as compared with standard care and to determine whether an artificial intelligence model can be incorporated into the app. Secondary objectives are to determine the perceptions and attitudes of caregivers regarding childhood vaccinations and to understand the factors that might influence the effect of a mobile phone-based app on vaccination improvement. METHODS: A mixed methods randomized controlled trial was designed with intervention and control arms. The study will be conducted at the Aga Khan University Hospital vaccination center. Caregivers of newborns or infants visiting the center for their children's 6-week vaccination will be recruited. The intervention arm will have access to a smartphone app with text, voice, video, and pictorial messages regarding RCI. This app will be developed based on the findings of the pretrial qualitative component of the study, in addition to no-show study findings, which will explore caregivers' perceptions about RCI and a mobile phone-based app in improving RCI coverage. RESULTS: Pretrial qualitative in-depth interviews were conducted in February 2020. Enrollment of study participants for the randomized controlled trial is in process. Study exit interviews will be conducted at the 14-week immunization visits, provided the caregivers visit the immunization facility at that time, or over the phone when the children are 18 weeks of age. CONCLUSIONS: This study will generate useful insights into the feasibility, acceptability, and usability of an Android-based smartphone app for improving RCI in Pakistan and in LMICs. TRIAL REGISTRATION: ClinicalTrials.gov NCT04449107; https://clinicaltrials.gov/ct2/show/NCT04449107. INTERNATIONAL REGISTERED REPORT IDENTIFIER (IRRID): DERR1-10.2196/22996.

Kolesnyk, P., T. Frese, S. Vinker, I. Shushman, A. Zharkova, N. Messaadi, A. Kolesnyk and S. Bayen (2021). "Steps towards implementing evidence-based screening in family medicine in Ukraine: SWOT-analysis of an approach of multidimensional empowerment." BMC Fam Pract 22(1): 20.

BACKGROUND: The purpose of this study is to forward the implementation of an operational evidence-based state screening program of common diseases in Ukraine, where currently no state-based and evidence-based screening (EBS) exists. EBS should be performed by Family Doctors in a primary care setting and concern prevalent diseases in adults, such as: obesity (BMI), hypertension (BP measurement), diabetes (glycaemia), dyslipidemia (cholesterol/lipids), colon cancer

(FOBT/colonoscopy), breast cancer (mammography), STIs (chlamydia, syphilis), HIV, HBV, HCV (i.e. serology or other rapid tests), HPV (swabs), cervical cancer (test Pap). depression (i.e., PHQ-9), and smoking (i.e., Fagerstrom). METHODS: Four needs-based research actions were led among citizens and healthcare professionals, based on multidimensional empowerment. Internal Strengths and Weaknesses of the ongoing implementation process were identified through these studies, whereas external Opportunities and Threats were determined by the present socio-cultural and political context. This SWOT analysis is likely to guide future state-based initiatives to accomplish EBS implementation in Ukraine. RESULTS: Internal Strengths are the bottom-up multidimensional empowerment approach, teaching of EBS and the development of an internet-based platform "Screening adviser" to assist shared decision making for person-centred EBS programs. Internal Weaknesses identified for the Family Doctors are a heterogeneous screening and the risk of decreasing motivation to screen. External Opportunities include the ongoing PHC reform, the existent WONCA and WHO support, and the existence of EBS programs in Europe. External Threats are the lack of national guidelines, not fully introduced gate keeping system, the vulnerable socio-economic situation, the war situation in the East of Ukraine and the Covid-19 pandemic. CONCLUSIONS: We started EBS implementation through research actions, based on a multidimensional empowerment of citizens, HCP and in EBS pathways involved stakeholder teams, to foster a sustainable operational human resource to get involved in that new EBS pathway to implement. The presented SWOT-analysis of this ongoing implementation process allows to plan and optimize future steps towards a state based and supports EBS program in Ukraine.

Lim, A. W. W. (2021). "Will COVID-19 Be the Tipping Point for Primary HPV Self-Sampling?" Cancer Epidemiol Biomarkers Prev 30(2): 245-247.

Self-sampling is poised to be a disruptor for cervical screening. So far, cancer screening has been a causality of COVID-19; however, the opposite may transpire for self-sampling. Self-sampling enables socially distanced cervical screening with an outreach that extends to underserved populations. As evidence mounts that self-sampling is noninferior to clinician-taken samples, the focus for self-sampling is now as a primary screening option for all women. Now, we have evidence from a modeling study (using Australia as an exemplar) to suggest that program effectiveness with primary self-sampling would be better than the current program, even if sensitivity is lower. Regulatory issues, suitable triage strategies, and clear communication about self-sampling are hurdles yet to be overcome. Nevertheless, existing evidence coupled with COVID-19 could be the tipping point for wider introduction of self-sampling.See related article by Smith et al., p. 268.

McDowell, L., S. P. Ng and J. Corry (2020). "COVID-19-An Opportunity for Optimizing Surveillance Protocols During and Beyond the Pandemic: HPV-Associated Oropharyngeal Cancer as an Example of Response-Based Local Surveillance." Int J Radiat Oncol Biol Phys 108(2): 400-403.

Olorunsaiye, C. Z., K. K. Yusuf, K. Reinhart and H. M. Salihu (2020). "COVID-19 and Child Vaccination: A Systematic Approach to Closing the Immunization Gap." Int J MCH AIDS 9(3): 381-385.

The COVID-19 pandemic threatens to set back major successes that have been achieved in global vaccine initiatives. We conducted a rapid review and synthesis of the literature on immunization provision and Utilization since the onset of the COVID-19 pandemic. A total of 11 papers comprising peer-reviewed articles and key policies and guidelines, published between January 1 and June 15, 2020, were analyzed. Widespread disruptions of routine immunization and vaccination campaigns

were reported leaving millions of children worldwide at risk of measles outbreaks. We present an expanded model of the World Health Organization's Global Routine Immunization Strategic Plan (GRISP) action areas as a tool to help countries quickly adapt to immunization challenges in the presence of COVID-19 and close the emerging immunization coverage gaps.

Polaha, J., L. Johnson, M. Quinn and N. Sunderji (2020). "Lessons from the team care playbook: Recommendations for COVID-19 vaccination dissemination and uptake." Fam Syst Health 38(4): 341-345.

For too many of us, the implications of a worldwide pandemic unfolded in graduated stages of understanding that seemed too sluggish for the opponent we faced. For too many of us, even those of us in health care, the unfolding was terrifying; we felt blindsided and unprepared. If coronavirus disease 2019 (COVID-19) were a bully picking a fight, they got the first punch in before we even raised a fist. Now, many rounds in, health care teams will have an opportunity to deploy a new weapon against COVID-19. Vaccines are coming. We do not know when, who will pay for them, or the logistical aspects (e.g., storage and administration). We do not even know how effective they will be. Moreover, we must plan for mass vaccination in a chaotic and politically charged context that bears little resemblance to the ones with which we have experience. Nevertheless, in this fight, vaccines could be our winning blow. We are getting better at working with unknowns and in disrupted environments during COVID-19. We have some time to prepare, and we have some extant knowledge and experience in vaccine distribution and uptake. Health care teams can use these to best their adversary, and we can and should begin now. The aim of this article is to discuss how to mobilize interprofessional teams within systems of care to engage best practices in vaccine dissemination and uptake in the unique COVID-19 context. We begin by discussing challenges to dissemination and uptake and then provide solutions using our experiences in the primary care system. (PsycInfo Database Record (c) 2021 APA, all rights reserved).

Rosa, M. F. F., E. N. da Silva, C. Pacheco, M. V. P. Diógenes, C. Millett, C. A. G. Gadelha and L. M. P. Santos (2021). "Direct from the COVID-19 crisis: research and innovation sparks in Brazil." Health Res Policy Syst 19(1): 10.

BACKGROUND: The coronavirus disease 2019 (COVID-19) pandemic has spread throughout more than 160 countries, infecting millions of people worldwide. To address this health emergency, countries have organized the flow of production and innovation to reduce the impact on health. This article shows the response of the Brazilian scientific community to meet the urgent needs of the public unified health system [SUS], aiming to guarantee universal access to an estimated population of 211 million. By December 2020, Brazil had recorded more than six million cases and approximately 175,000 deaths. METHODS: We collected data on research, development and innovation projects carried out by 114 public universities (plus Oswaldo Cruz Foundation [Fiocruz] and Butantan Institute), as reported on their websites. Additionally, we examined the studies on COVID-19 approved by the National Comission for Research Ethics, as well as those reported on the Ministry of Education website as of May 15, 2020. RESULTS: The 789 identified projects were classified according to research š P } Œ] • • (} o o } Á • W À o } ‰ u v š v] š v Ç } ‰ š]] } v (‰ v Œ } A i 0 î ñ ì • U v] š A Z
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focused on the development and innovation of personal protective equipment, medical devices, diagnostic tests, medicines and vaccines, which were rapidly identified as research priorities by the scientific community. Some promising results have been observed from phase III vaccine trials, one of which is conducted in partnership with Oxford University and another of which is performed with Sinovac Biotech. Both trials involve thousands of volunteers in their Brazilian arms and include technology transfer agreements with Fiocruz and the Butantan Institute, respectively. These vaccines

proved to be safe and effective and were immediately licensed for emergency use. The provision of doses for the public health system, and vaccination, started on January 17, 2021. CONCLUSIONS: The mobilized Brazilian scientific community has generated comprehensive research, development and innovation proposals to meet the most urgent needs. It is important to emphasize that this response was only possible due to decades of investment in research, development and innovation in Brazil. We need to reinforce and protect the Brazilian science, technology and innovation system from austerity policies that disregard health and knowledge as crucial investments for Brazilian society, in line with the constitutional right of universal health access and universal health coverage.

Vogt, T. M., F. Zhang, M. Banks, C. Black, B. Arthur, Y. Kang, P. Lucas and B. Lamont (2020). "Provision of Pediatric Immunization Services During the COVID-19 Pandemic: an Assessment of Capacity Among Pediatric Immunization Providers Participating in the Vaccines for Children Program - United States, May 2020." MMWR Morb Mortal Wkly Rep 69(27): 859-863.

Recent reports suggest that routine childhood immunization coverage might have decreased during the coronavirus disease 2019 (COVID-19) pandemic (1,2). To assess the capacity of pediatric health care practices to provide immunization services to children during the pandemic, a survey of practices participating in the Vaccines for Children (VFC) program was conducted during May 12-20, 2020. Data were weighted to account for the sampling design; thus, all percentages reported are weighted. Among 1,933 responding practices, 1,727 (89.8%) were currently open; 1,397 (81.1%) of these reported offering immunization services to all of their patients. When asked whether the practice would likely be able to accommodate new patients to assist with provision of immunization services through August, 1,135 (59.1%) respondents answered affirmatively. These results suggest that health care providers appear to have the capacity to deliver routinely recommended childhood vaccines, allowing children to catch up on vaccines that might have been delayed as a result of COVID-19-related effects on the provision of or demand for routine well child care. Health care providers and immunization programs should educate parents on the need to return for well-child and immunization visits or refer patients to other practices, if they are unable to provide services (3).

Wang, Z., Y. Kang, F. Yu, F. H. Zhong, K. Huang, X. Zhou, Y. Tang, Y. Zhang, Y. L. Liou and Y. Ma (2021). "TruScreen detection of cervical tissues for high-risk human papillomavirus-infected women during the COVID-19 pandemic." Future Oncol 17(10): 1197-1207.

Aims: To evaluate the efficacy of TruScreen (TS01) for high-risk human papillomavirus (HR-HPV) women compared with other methods in reducing colposcopy referral rates in hospitals. Methods: A single-center, prospective, case-control study was conducted from December 2019 to June 2020. Results: Among 139 (46.2%) HR-HPV-positive patients, 58 were CIN1, 52 were CIN2-3 and 29 had cervical cancer (n = 29). The sensitivity and specificity of detecting CIN2+ by TS01, colposcopy and HPV16/18 testing were 96.3% and 46.4%, 85.2% and 40.5% and 59.3% and 74.1%, respectively. The highest sensitivity was 96.3% at HPV16/18 and TS01 (each positive results), and the highest specificity was 83.6% at HPV16/18 and TS01 (both positive) for CIN2+ compared with the other methods. Conclusion: TS01 is a noninvasive screening method and can be used to diagnose cervical lesions quickly. It is especially suitable as triage tool for HR-HPV-positive women facing SARS-CoV-2 exposure and infection risks in hospital.

Reinforcing/ sustaining Cervical Cancer Screening and Treatment

A PubMed search was performed with the following selection criteria: [screening] AND [human papillomavirus] AND [cervical cancer] AND [coverage] AND [Covid-19], [cervical cancer] AND [covid-19] AND [screening], [cervical cancer] AND [covid-19] AND [screening coverage] AND [restarting] title/abstract published in the last one year. 3, 37, and 0 items were retrieved respectively and a relevant manual selection of 11 publications between 2020-2021 based on title and abstract was made, and imported into Endnote.

Castanon, A., M. Rebolj, F. Pesola and P. Sasieni (2021). "Recovery strategies following COVID-19 disruption to cervical cancer screening and their impact on excess diagnoses." Br J Cancer.

BACKGROUND: The COVID-19 pandemic has disrupted cervical cancer screening services. Assuming increases to screening capacity are unrealistic, we propose two recovery strategies: one extends the screening interval by 6 months for all and the other extends the interval by 36/60 months, but only for women who have already missed being screened. METHODS: Using routine statistics from England we estimate the number of women affected by delays to screening. We used published research to estimate the proportion of screening age women with high-grade cervical intraepithelial neoplasia and progression rates to cancer. Under two recovery scenarios, we estimate the impact of COVID-19 on cervical cancer over one screening cycle (3 years at ages 25-49 and 5 years at ages 50-64 years). The duration of disruption in both scenarios is 6 months. In the first scenario, 10.7 million women have their screening interval extended by 6 months. In the second, 1.5 million women (those due to be screened during the disruption) miss one screening cycle, but most women have no delay. RESULTS: Both scenarios result in similar numbers of excess cervical cancers: 630 vs. 632 (both 4.3 per 100,000 women in the population). However, the scenario in which some women miss one screening cycle creates inequalities-they would have much higher rates of excess cancer: 41.5 per 100,000 delayed for screened women compared to those with a 6-month delay (5.9 per 100,000). CONCLUSION: To ensure equity for those affected by COVID-19 related screening delays additional screening capacity will need to be paired with prioritising the screening of overdue women.

de Pelsemaeker, M. C., Y. Guiot, J. Vanderveken, C. Galant and M. R. Van Bockstal (2021). "The Impact of the COVID-19 Pandemic and the Associated Belgian Governmental Measures on Cancer Screening, Surgical Pathology and Cytopathology." Pathobiology 88(1): 46-55.

INTRODUCTION: The severe acute respiratory syndrome coronavirus 2 caused a pandemic of coronavirus disease 2019 (COVID-19). Unprecedented public health actions were introduced, including social distancing, travel restrictions and quarantine. The Belgian government announced a national emergency plan, thereby postponing all non-urgent medical consultations and operations. This report analyses the impact of these measures on cancer screening, through assessment of the workload of a laboratory for histopathology and cytopathology. METHODS: Data on monthly numbers of histological and cytological samples, immunohistochemistry and molecular tests were extracted from the laboratory information management system. RESULTS: The global histopathological and cytological workload was substantially reduced. The impact on oncology-related surgical procedures was rather limited. The anti-COVID-19 measures significantly diminished all screening-related samples, such as colon biopsies, breast biopsies and cervical cytology, and strongly reduced the number of samples related to "functional" pathology, such as thyroidectomies and gastric biopsies. CONCLUSIONS: Since many health care interventions are reflected in the workload of a pathology laboratory, this study enabled us to identify areas for "deconfinement" health care actions. Our

findings indicate that various areas in medicine were affected, but the impact seemed largest for cancer screening. Health care professionals should assure that consultations related to cancer screening are postponed instead of cancelled.

Feletto, E., P. Grogan, C. Dickson, M. Smith and K. Canfell (2020). "How has COVID-19 impacted cancer screening? Adaptation of services and the future outlook in Australia" Public Health Res Pract 30(4).

The coronavirus disease 2019 (COVID-19) pandemic has caused major disruptions to many aspects of life in Australia and globally. This includes actual and potential future impacts on Australia's three national screening programs for breast, bowel and cervical cancer. These programs aim to improve cancer outcomes through an organised approach to the early detection of cancer and precancer in asymptomatic populations. The design of each program varies according to biological differences in the three cancers, the available screening technology, the target population, and variations in their administration of Australia's federal, state and territory jurisdictions. The observed and potential impacts of COVID-19 on these programs, and on related activities such as the current national enquiry into lung cancer screening feasibility, therefore vary significantly. This article focuses on observed short-term impacts, adaptations and the longer-term outlook for cancer screening in relation to COVID-19. It summarises potential responses to minimise the harms of disruptions caused by COVID-19, and highlights research and policy opportunities in the pandemic response and recovery which could inform and accelerate optimisation of cancer screening in the long term.

Jach, R., M. Mazurec, M. Trzeszcz and M. Zimmer (2020). "Possible deferral of diagnostic and therapeutic procedures for patients with abnormal screening tests results in cervical cancer secondary prevention in current SARS-CoV-2 pandemic Interim guidelines of the Polish Society of Gynecologists and Obstetricians and the Polish Society of Colposcopy and Cervical Pathophysiology" Ginekol Pol 91(7): 428-431.

The Polish Society of Gynecologists and Obstetricians and Polish Society of Colposcopy and Cervical Pathophysiology Interim Guidelines goal at aiding gynecologists in providing a cervical cancer prevention care during the evolving SARS-CoV-2 pan-demic. Presented guidelines were developed on a review of limited data and updated when new relevant publications were revealed. Timing for deferrals of diagnostic-therapeutic procedures were mostly covered in the guidelines. Also, a support for the existing Polish recommendations on abnormal screening results in a subject of minor and major screening abnor-malities terminology were given. The guidelines are obligatory for the specified COVID-19 pandemic period only and they might be changed depending on the new available evidence.

Mantellini, P., F. Battisti, P. Armaroli, P. Giubilato, L. Ventura, M. Zorzi, J. Battagello, P. Sassoli de Bianchi, C. Senore and M. Zappa (2020). "[Oncological organized screening programmes in the COVID-19 era: an Italian survey on accrued delays, reboot velocity, and diagnostic delay estimates]" Epidemiol Prev 44(5-6 Suppl 2): 344-352.

OBJECTIVES: to describe the course of Italian organized cancer screening programmes during the COVID-19 emergency; to provide estimates of the diagnosis of malignant or pre-malignant lesions that will face a diagnostic delay due to the slowing down of screening activities. DESIGN: quantitative survey of aggregated data for each Region and overall for Italy relating to screening tests carried out in the period January-May 2020 compared to those of the same period of 2019; estimate of diagnostic delays starting from the calculation of the average detection rate of the last 3 years available (specific by Region). SETTING AND PARTICIPANTS: Italian mass screening programmes. Data on the tests carried out in the target population of the breast (women 50-69 years old), cervix (women 25-64 years old), and colorectal (women and men 50-69 years old) cancer screening. MAIN OUTCOME MEASURES: the

cumulative delay (in absolute numbers and as a percentage) in the period January-May 2020 compared to the same period of 2019, by Region; the difference of screening tests (in absolute number and in percentage) performed in May 2020 compared to May 2019; the estimate of the fewer lesions diagnosed in 2020 compared with 2019 with relative 95% confidence intervals (95%CI); the 'standard months' of delay (proportion of fewer tests carried out from January to May 2020 for the corresponding number of months). RESULTS: 20 Regions out of 21 participated. In the period January-May 2020, the fewer screening tests performed in comparison with the same period of 2019 were: 472,389 (equal to 53.8%) with an average delay of standard months of 2.7 for mammography screening; 585,287 (equal to 54.9%) with an average delay of standard months of 2.7 for colorectal screening; 371,273 (equal to 55.3%) with an average delay of 2.8 standard months for cervical screening. The estimated number of undiagnosed lesions is 2,201 (95%CI 2,173-2,220) breast cancers; 645 (95%CI 632-661) colorectal carcinomas; 3,890 (95%CI 3,855-3,924) advanced colorectal adenomas and 1,497 (95%CI 1,413-1,586) CIN2 or more serious lesions. CONCLUSIONS: mass screenings need to be restarted as quickly as possible. In order to make up for the delay that is accumulating, it is necessary to provide for wider delivery times, greater resources, and new organizational approaches. It will also be essential to develop communication strategies suitable for promoting participation during this emergency.

Matsuo, K., H. Novatt, S. Matsuzaki, M. S. Hom, A. V. Castaneda, E. Licon, D. J. Nusbaum and L. D. Roman (2020). "Wait-time for hysterectomy and survival of women with early-stage cervical cancer: A clinical implication during the coronavirus pandemic." Gynecol Oncol 158(1): 37-43.

OBJECTIVE: A global pandemic caused by a novel coronavirus (Covid-19) has created unique challenges to providing timely care for cancer patients. In early-stage cervical cancer, postponing hysterectomy for 6-8 weeks is suggested as a possible option in the Covid-19 burdened hospitals. Yet, literature examining the impact of surgery wait-time on survival in early-stage cervical cancer remains scarce. This study examined the association between surgery wait-time of 8 weeks and oncologic outcome in women with early-stage cervical cancer. METHODS: This is a single institution retrospective observational study at a tertiary referral medical center examining women who underwent primary hysterectomy or trachelectomy for clinical stage IA-IIA invasive cervical cancer between 2000 and 2017 (N = 217). Wait-time from the diagnosis of invasive cervical cancer via biopsy to definitive surgery was categorized as: short wait-time (<8 weeks; n = 110) versus long wait-time ~ Hweeks; n = 107). Propensity score inverse probability of treatment weighting was used to balance the measured demographics between the two groups, and disease-free survival (DFS) and overall survival (OS) were assessed. A systematic literature review with meta-analysis was additionally performed. RESULTS: In a weighted model (median follow-up, 4.6 years), women in the long wait-time group had DFS (4.5-year rates, 91.2% versus 90.7%, hazard ratio [HR] 1.11, 95% confidence interval [CI] 0.47-2.59, P = 0.818) and OS (95.0% versus 97.4%, HR 1.47, 95%CI 0.50-4.31, P = 0.487) similar to those in the short wait-time group. Three studies were examined for meta-analysis, and a pooled HR for surgery wait- š] u } (weeks on DFS was 0.96 (95%CI 0.59-1.55). CONCLUSION: Our study suggests that wait-time of 8 weeks for hysterectomy may not be associated with short-term disease recurrence in women with early-stage cervical cancer.

Miller, M. J., L. Xu, J. Qin, E. E. Hahn, Q. Ngo-Metzger, B. Mittman, D. Tewari, M. Hodeib, P. Wride, M. Saraiya and C. R. Chao (2021). "Impact of COVID-19 on Cervical Cancer Screening Rates Among Women Aged 21-65 Years in a Large Integrated Health Care System - Southern California, January 1-September 30, 2019, and January 1-September 30, 2020." MMWR Morb Mortal Wkly Rep 70(4): 109-113.

On March 19, 2020, the governor of California issued a statewide stay-at-home order to contain the spread of SARS-CoV-2, the virus that causes coronavirus disease 2019 (COVID-19).* The } Œ Œ Œ µ • •]] o] š Ç š } v ‰ š] v š š š v v š } µ š ‰ š] v š preventive services such as cervical cancer screening. In-person clinic visits increased when California reopened essential businesses on June 12, 2020.(§) Electronic medical records of approximately 1.5 million women served by Kaiser Permanente Southern California (KPSC), a large integrated health care system, were examined to assess cervical cancer screening rates before, during, and after the stay-at-home order. KPSC policy is to screen women aged 21-29 years every 3 years with cervical cytology alone (Papanicolaou [Pap] test); those aged 30-65 years were screened every 5 years with human papillomavirus (HPV) testing and cytology (cotesting) through July 15, 2020, and after July 15, 2020, with HPV testing alone, consistent with the latest recommendations from U.S. Preventive Services Task Force.(¶) Compared with the 2019 baseline, cervical cancer screening rates decreased substantially during the stay-at-home order. Among women aged 21-29 years, cervical cytology screening rates per 100 person-months declined 78%. Among women aged 30-65 years, HPV test screening rates per 100 person-months decreased 82%. After the stay-at-home order was lifted, screening rates returned to near baseline, which might have been aided by aspects of KPSC's integrated, organized screening program (e.g., reminder systems and tracking persons lost to follow-up). As the pandemic continues, groups at higher risk for developing cervical cancers and precancers should be evaluated first. Ensuring that women receive preventive services, including cancer screening and appropriate follow-up in a safe and timely manner, remains important.

Nogami, Y., Y. Kobayashi, K. Tsuji, M. Yokota, H. Nishio, M. Nakamura, W. Yamagami, T. Morisada, E. Tominaga, K. Banno and D. Aoki (2020). "Impact of the COVID-19 epidemic at a high-volume facility in gynecological oncology in Tokyo, Japan: a single-center experience." J Ovarian Res 13(1): 105.

BACKGROUND: The number of cases of novel coronavirus disease 2019 (COVID-19) in Japan have risen since the first case was reported on January 24, 2020, and 6225 infections have been reported as of June 30, 2020. On April 8, 2020, our hospital began screening patients via pre-admission reverse transcriptase-polymerase chain reaction (RT-PCR) for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and chest computed tomography (CT). Although no patients exhibited apparent pneumonia, treatment delay or changes in treatment plans were required for a few patients based on the results of screening tests. During an emerging infectious disease pandemic, the likelihood of being infected, as well as the disease itself, affects clinical decision making in several ways. We summarized and presented our experience. CASE PRESENTATION: After the introduction of pre-admission screening, RT-PCR and CT were performed in 200 and 76 patients, respectively, as of June 30, 2020. The treatment of five patients, including two patients with cervical cancer, two patients with ovarian tumors, and one patient with ovarian cancer, was affected by the results. Two asymptomatic RT-PCR-positive patients did not develop COVID-19, but their treatment was delayed until the confirmation of negative results. The other three patients were RT-PCR-negative, but abnormal CT findings suggested the possibility of COVID-19, which delayed treatment. The patients receiving first-line preoperative chemotherapy for ovarian cancer had clinically evident exacerbations because of the treatment delay. CONCLUSION: During the epidemic phase of an emerging infectious disease, we found that COVID-19 has several other effects besides its incidence. The postponing treatment was the most common, therefore, treatment of ovarian tumors and ovarian cancer was considered to be the most likely to be affected among gynecological diseases. Protocols that allow for easy over-diagnosis can be disadvantageous, mainly because of treatment delays, and therefore, the protocols must be developed in light of the local infection situation.

Snyder, A., S. Jang, I. S. Nazari, A. Som, E. J. Flores, M. D. Succi and B. P. Little (2021). "Google search volume trends for cancer screening terms during the COVID-19 pandemic" J Med Screen: 969141321999426.

The COVID-19 pandemic has led to delays in cancer diagnosis, in part due to postponement of cancer screening. We used Google Trends data to assess public attention to cancer screening during the first peak of the COVID-19 pandemic. Search volume for terms related to established cancer screening tests ("colonoscopy," "mammogram," "lung cancer screening," and "pap smear") showed a marked decrease of up to 76% compared to the pre-pandemic period, a significantly greater drop than for search volume for terms denoting common chronic diseases. Maintaining awareness of cancer screening during future public health crises may decrease delays in cancer diagnosis.

Sormani, J., A. M. Datchoua, P. Petignat, B. Kenfack and N. C. Schmidt (2021). "Effects of the COVID-19 pandemic on an urban cervical cancer screening program in West Cameroon." Int J Gynecol Cancer.

Woo, Y. L., P. Gravitt, S. K. Khor, C. W. Ng and M. Saville (2021). "Accelerating action on cervical screening in lower and middle-income countries (LMICs) post COVID-19 era" Prev Med 144: 106294.

Cervical cancer remains the fourth most common cancer in women, with 85% of deaths occurring in LMICs. Despite the existence of effective vaccine and screening tools, efforts to reduce the burden of cervical cancer must be considered in the context of the social structures within the health systems of LMICs. Compounding this existing challenge is the global COVID-19 pandemic, declared in March 2020. While it is too soon to tell how health systems priorities will change as a result of COVID-19 and its impact on the cervical cancer elimination agenda, there are opportunities to strengthen cervical screening by leveraging on several trends. Many LMICs maximized the strengths of their long established community-based primary care and public health systems with expansion of surveillance systems which incorporated mobile technologies. LMICs can harness the momentum of the measures taken against COVID-19 to consolidate the efforts against cervical cancer. Self-sampling, molecular human papillomavirus (HPV) testing and digital health will shift health systems towards stronger public health and primary care networks and away from expensive hospital-based care investments. While COVID-19 will change health systems priorities in LMICs in ways that may de-prioritize cervical cancer screening, there are significant opportunities for integration into longer-term trends towards universal health coverage, self-care and digital health.

Part 2: Related Ouput

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MEETING REPORT Open Access

Prevention and control of HPV infection and HPV-related cancers in Colombia- a meeting report

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From Prevention and control of HPV and HPV related cancers in Colombia: Lessons learnt and the way forward
Bogota, Colombia. 15-16 November 2018

Abstract

The Human Papillomavirus (HPV) Prevention and Control Board is an independent multidisciplinary board of international experts that disseminates relevant information on HPV to a broad array of stakeholders and provides guidance on strategic, technical and policy issues in the implementation of HPV control programs. In response to drastic drop of vaccine coverage following the adverse event crisis in Carmen del Bolivar, Colombia, the HPV Prevention and Control Board in collaboration with the Colombian National Cancer Institute and Colombian League Against Cancer convened a meeting in Bogota, Columbia (November 2018). The goal of the meeting was to bring together national and international group of experts to report the disease burden, epidemiology and surveillance of HPV and HPV-related cancers, to discuss the successes and especially the challenges of HPV vaccination and screening in Colombia, as well as the lessons learnt from neighbouring countries. The meeting provided a platform to confer various stakeholder's perspectives, including the role of the Colombian healthcare system and to catalyse various parts of the public health community in Colombia into effective action. The conclusion of the meeting included following suggestions to strengthen HPV prevention and control: 1) Re-introducing school-based vaccine programs, 2) Integrating primary and secondary prevention programs, 3) Developing an innovative crisis communication plan targeting healthcare workers, teachers and general population, 4) Building trust through efficient and timely communication, 5) Building strong relationship with media to ensure a stable vaccination campaign support, and 6) Promoting empathy among healthcare professionals towards patients to build trust and communicate effectively.

Keywords: Human papilloma virus, HPV, Vaccination, Cervical cancer prevention, Screening

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The newsletter on Human Papillomavirus because we can envisage cervical cancer elimination

nº 105

HPV vaccination in Colombia.

From a nightmare to a bright and promising dawn

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In August 2012 the HPV vaccine was introduced in the national immunization program. It was a school-based program directed to girls in 4th grade of primary school and aged 9 years and older. National coverage rates were over 80% until June 2014, when reports of adverse symptoms (headache, paresthesia, shortness of breath, chest pain and fainting) were reported from over 500 girls who have received the HPV vaccine months before and who were residing in Carmen de Bolivar. This is a small town in the north of Colombia suffering from socio-economic deprivation and severely affected by intrafamilial and political violence. An epidemiological study concluded that the symptoms did not have a biological relationship with the HPV vaccine and could be due to a mass stress reaction or mass psychogenic illness. The national media as well as social media, diffused videos of girls fainting, twitching, and arriving unconscious at emergency rooms; the response to the crisis was late and inappropriate and the public confidence on the vaccine dropped and national coverage rates fell to as low as 14% and 5% for the 1st and 2nd dose in 2016.

Figure 1 illustrates the tragic impact of this drop in the prevention of cervical cancer. In the cohort of girls born in 2003 and who received the HPV vaccine in 2012 (with a coverage rate of 88% for the 2nd dose), 4,300 new cases of cervical cancer and 1,900 deaths from this cancer will be avoided when these women have reached 75 years of age. On the other hand, in the cohort of girls born in 2007 and who received the vaccine in 2016 (with a coverage rate of 5% for the 2nd dose), only 220 new cases of cervical cancer will be avoided when these women have reached 75 years of age. In other words, it is estimated that 13 new cases of cervical cancer and 6 deaths from cervical cancer will be avoided in women reaching 75 years of age for every 1000 girls vaccinated against HPV.

Following the Carmen de Bolivar crisis, the school-based HPV vaccination was stopped and a "Mesa de Concertacion", a roundtable for the elimination of HPV-related cancer in Colombia, was organized by the Colombian League Against Cancer, Profamilia, scientific societies, parent associations, and the Ministry of Health.

The response to the HPV vaccination crisis was late and inappropriate and the public confidence on the vaccine dropped dramatically. National coverage rates fell to as low as 14% for the first dose and 5% for the second dose in 2016

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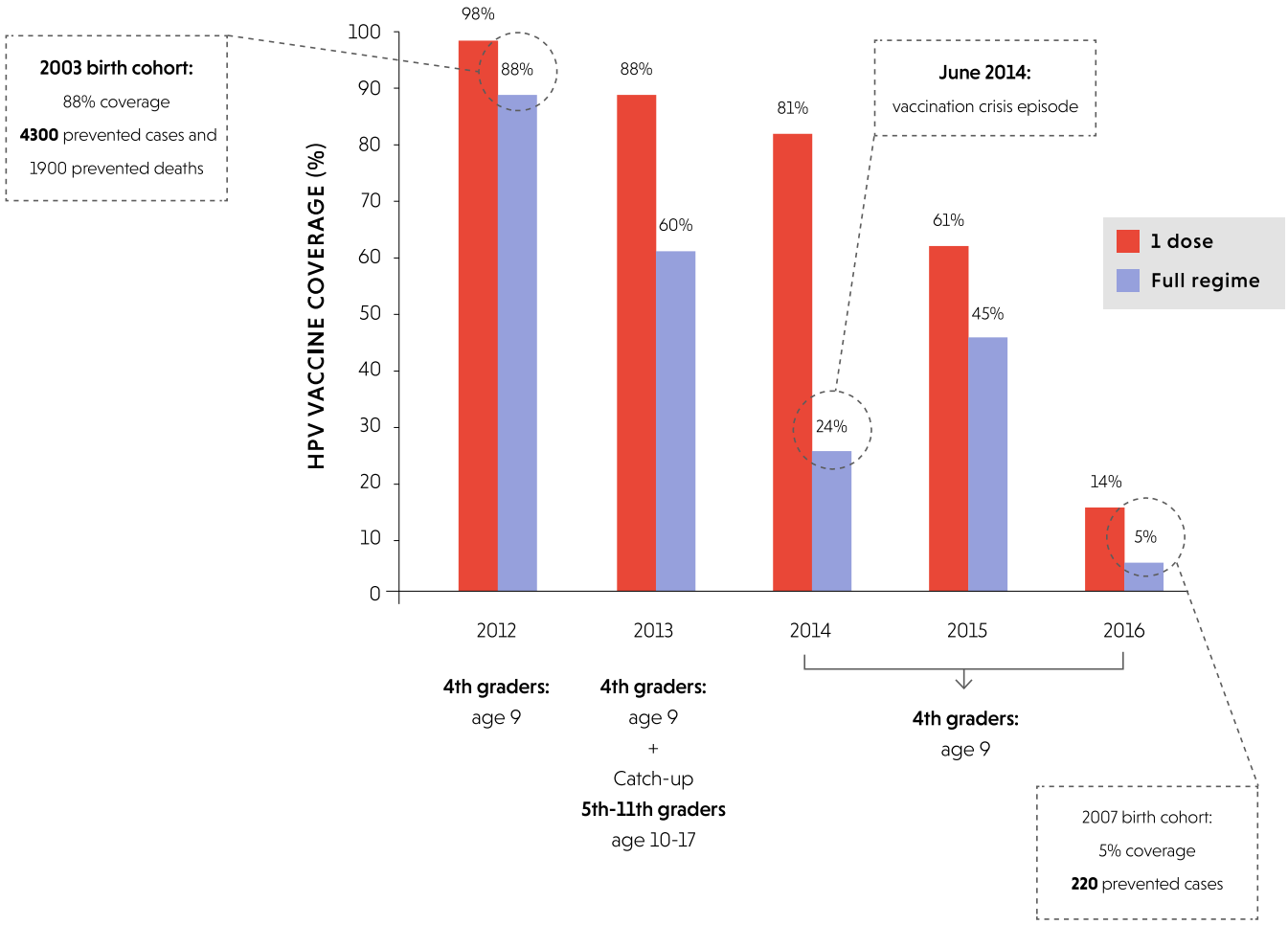
Figure 1

HPV vaccine coverage rates and expected number of cases of cervical cancer and of deaths prevented. Ages in legends are official age groups targeted by the public vaccination program.



Courtesy of Laia Bruni

In addition, an e-course on efficacy and safety of the HPV vaccine was developed by the Catalan Institute of Oncology (ICO) and the Colombian Cancer Institute to educate medical and para-medical personnel. So far, over 5,000 participants have completed the course. International collaboration has also been established with the HPV Prevention and Control Board that convened a meeting in Bogota, Colombia in November 2018 to help regaining confidence on the HPV vaccine.

The following activities have been performed in the last two years:

1. The Arauca project

The Colombian League Against Cancer started a project in Arauca in June 2018 in collaboration with the Colombian Ministry of Health, the local health authorities, and the American Cancer Society and Johns Hopkins University to regain confidence on the HPV vaccine. Arauca is one of the Colombian departments with the highest political instability and violence and a very high mortality rate from cervical cancer (11.4 per 100,000) and one of the lowest HPV vaccination rates (4.7% in 2017). Girls to be vaccinated, parents of the girls, the teachers, the health care providers, and the local mass media

were interviewed regarding the attitudes and beliefs towards the vaccine. Based on the information collected a new communication strategy was developed from a bio-psycho-social perspective to educate and sensitize all these groups on the benefits and safety of the HPV vaccine. Tailored leaflets and videos were developed, basic lectures were delivered and the ICO/NCI online course on the efficacy and safety of the HPV vaccine was taken by the health care providers. The target population, girls of 9 years of age, is 2,340 in 2019.

Eighteen months after starting the project to regain confidence on the HPV vaccine, the coverage rate for the 1st vaccine dose increased significantly from 4,7% in 2017 to 41% in 2018 and to 83% in 2019

Eighteen months after starting the project, the coverage rate for the 1st vaccine dose increased significantly from 4,7% in 2017 to 41% in 2018 and to 83% in 2019. Since most of the increase in the 1st dose occurred in the last 6 months of 2019, coverage for the 2nd dose will be best assessed in the first 6 months of 2020.

2.Regional health services

In addition to the Arauca project, the health secretaries from a few departments (Antioquia and Nariño, Valle del Cauca) and from the city of Cali, have reinforced the strategies to increase the coverage rates using local and social media to educate adolescents, their parents, teachers and general community on the benefits and safety of the HPV vaccine. In 2019, the target population (girls of 9 years of age) in these departments were: Antioquia: 46,110, Nariño: 13,201 and Valle del Cauca: 27,948.

Table 1 summarizes the changes in the coverage rates from 2018 to 2019 in the departments of Arauca, Antioquia, Nariño and Valle del Cauca and their respective capital cities, Arauca, Medellin, Pasto, and Cali. In 2019, the HPV vaccine coverage rates in these departments are higher than the rates for the whole country (33% for the first dose and 11% for the second dose). To increase coverage of the 2nd dose a delayed second dose strategy is being discussed; currently the 2nd dose is being administered 6 months after the 1st dose.

These data show that when there is political will, it is possible to recover the HPV vaccination program. These strategies should be repeated in all regions of the country. ■

DISCLOSURE
The authors declare nothing to disclose.

HPVWorld is a project endorsed by

Table 1

Coverage rates for the HPV vaccine in Colombia (last updated: March 3, 2020)

		1st dose 2018	1st dose 2019	2nd dose 2018	2nd dose 2019
Selected departments	**Arauca**	**41%**	**83%**	**11%**	**24%**
	Antioquia	39%	48%	12%	19%
	Nariño	57%	53%	33%	32%
	Valle del Cauca	48%	54%	35%	21%
Selected cities	Arauca	32%	70%	5%	8%
	Medellin	20%	40%	8%	10%
	Pasto	39%	51%	14%	19%
	Cali	68%	75%	60%	31%
Total - Colombia		**29%**	**34%**	**9%**	**11%**

Information provided by the PAI, MSPS- Ministry of health of Colombia

▼ *A colombian girl who received her vaccine shot is being interviewed by the media, during one of the social activities to regain confidence in HPV vaccine among people in Arauca.*

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Impact of the COVID-19 pandemic on human papillomavirus–based testing services to support cervical cancer screening

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Abstract

Introduction: The World Health Organization elimination goal for cervical cancer relies on screening 70% of women at ages 35 and 45, preferentially through molecular HPV testing. The SARS-CoV-2 pandemic has led to an unprecedented demand for molecular tests and platforms. Our objective was to gain insight into the impact of SARS-CoV-2 on the actual or anticipated shortage of tests, equipment, consumables, and staff required to deliver molecular HPV laboratory services and to consider the implications for the sustainability and development of cervical screening programs.

Methods: A 19-item online questionnaire was created and made available online between December 2020 and February 2021. Five companies with clinically validated HPV and SARS-CoV-2 tests in their portfolios were invited to provide a statement on the volumes of molecular COVID-19 tests produced, relevant changes to manufacturing capacity, and their current and post-pandemic strategy for HPV tests.

Results: We received responses from 57 laboratories representing 30 countries and six continents. Among these, 74% reported experiencing a supply shortage, 54% reported a shortage of personnel, and 33% reported delays in ordering equipment. Three companies described expansion of manufacturing lines, investment in diagnostic infrastructure, and scale-up of manufacturing capacity. Two companies specifically referred to opportunities for the use of platforms for COVID-19 testing to support HPV testing in time.

Conclusions: The demand for SARS-CoV-2 testing is competing with HPV testing, compounded by a shortage of staff. This represents a challenge for existing laboratory services and for settings keen to implement HPV-based screening. However, supply challenges may be addressed in time, given the significant investment in manufacturing capacity. In addition, innovation around molecular COVID-19 testing systems may result in solutions that address the shortage of rapid low-cost HPV testing systems for low-resource settings. Finally, because the demand for COVID-19 testing is likely to decrease, this may release both workforce and platform capacity for high-throughput HPV testing. The global health community should be alert to the opportunities around innovation and capacity if cervical cancer elimination goals are to be reached.

Keywords: molecular testing, COVID-19, human papillomavirus, HPV, cervical cancer screening

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Introduction

In 2018, the World Health Organization's (WHO) director-general called for action to eliminate cervical cancer, with elimination defined as an incidence of less than four cases per 100,000 (1). Three key pillars are required and available to reach this goal: primary prevention through human papillomavirus (HPV) vaccination, ideally before onset of sexual activity; secondary prevention through screening, with relevant follow-up of screen-positive women; and, finally, timely treatment of precancerous lesions and invasive cancer. Although the goal of elimination could ultimately be reached with intensive HPV vaccination alone, it can be achieved earlier by a combination of pragmatic but effective screening and vaccination. Therefore, the targets are to fully vaccinate 90% of girls before age 15, to screen 70% of women with a high-performance test at ages 35 and 45, and to provide treatment and care to 90% of women with a diagnosed cervical disease. If 95% of countries manage to rapidly adopt the 90-70-90 targets, the goal of cervical cancer elimination may become a reality as early as 2030 (2, 3).

These goals are ambitious, and optimal cervical cancer screening demands large-scale testing using molecular HPV tests. In a recent survey, 254 distinct HPV tests were identified on the global market (4). Unfortunately, 60% of these tests are without a single peer-reviewed publication, and over 90% are not evaluated in line with accepted international performance metrics that ensure accuracy in screening settings (4). To promote and facilitate access to safe, reliable, and appropriate *in vitro* diagnostic technologies, the WHO performs prequalification of *in vitro* diagnostics for high-burden diseases. Currently, only three tests for HPV-based screening have been WHO prequalified (5). To summarize, there is still a relatively small pool of HPV tests that fulfill the operational and performance characteristics required to meet the global screening challenge.

Clearly the COVID-19 pandemic has had a major impact on global health. As of March 2021, nearly 115 million people have been infected with SARS-CoV-2, and more than 2.6 million have died from COVID-19 (6). The restrictions (e.g., social distancing, lockdown, and suspension of non-essential clinical services) imposed to reduce the spread of SARS-CoV-2 have led to reductions in the overall number of cancers diagnosed, with an increased proportion of cancer diagnoses at advanced stages. According to a study conducted by the WHO, 54% of countries reported disrupted cancer-treatment services during the first COVID-19 pandemic

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