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Short communication

Trends in HPV vaccine administration and HPV vaccine coverage in children by race/ethnicity and socioeconomic status during the COVID-19 pandemic in an integrated health care system in California

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ABSTRACT

Background: We sought to evaluate the trends of HPV vaccination between 03/2019–09/2021 and whether the impact of the COVID pandemic on HPV vaccination varied by race/ethnicity and neighborhood deprivation index (NDI).
Methods: Electronic medical records at Kaiser Permanente Southern California were used to assess monthly volume of HPV vaccine doses administered among children aged 9–12.9yrs, and up-to-date coverage (% vaccinated) by age 13 between 03/2019–09/2021. Modified Poisson models were used to evaluate the interactions between race/ethnicity, NDI and the pandemic periods on HPV vaccine coverage.
Results: HPV vaccine doses administered in 2020/2021 have returned to the 2019 level after the initial drop. The average up-to-date coverage in 05/2021–09/2021 (54.8%) remained lower than the pre-pandemic level (58.5%). The associations between race/ethnicity, NDI and HPV vaccine coverage did not vary due to the pandemic.
Conclusion: HPV vaccine promotion efforts are needed to address COVID-19 pandemic's lasting impact on HPV vaccination coverage.

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1. Introduction

The coverage of the human papillomavirus (HPV) vaccination in children and adolescents has been historically lower than the other childhood and adolescent vaccines [1]. That said, a steady increasing trend in HPV vaccine coverage in adolescents has been observed nationally since 2006 [2]. Starting in March 2020, the SARS-CoV-2 (COVID-19) pandemic has created substantial disruptions to preventive care services, including vaccination [3]. Few studies have focused on the uptake of HPV vaccine during the pandemic. One study estimated substantial reduction of HPV vaccine coverage by 24% in 2020 compared to 2019 [4]. Data from 10 US jurisdictions showed substantial decline in March -May 2020, and an increase in June-September 2020 which was not sufficient to offset the decline [5]. The NIS-Teen survey revealed reduced

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HPV vaccine initiation in March-October 2020, which resumed in November-December 2020 to a level that was comparable to 2019 [1]. The NIS-Teen surveys, however, do not include children younger than age 13. These few studies examined vaccine administration in the first year of the pandemic. Little is known about whether the HPV vaccine administration pattern persisted throughout the pandemic and how HPV vaccine coverage is affected.

The pandemic has widened racial and socioeconomic (SES) health inequities [6]. The impact of the pandemic by race/ethnicity and SES on "return-to-vaccination", however, has not been extensively reported. Such data will be critical to inform strategies to reduce potential disparities. In this study, we examined (1) the trends of HPV vaccine administration in 9–12 year-olds; (2) the trends of HPV vaccine coverage by age 13 [as per Advisory Committee on Immunization Practices (ACIP)'s routine HPV vaccine recommendations] [7]; and (3) whether the effect of the pandemic on HPV vaccine coverage varied by race/ethnicity and neighborhood SES status between 03/2019 and 09/2021 in an integrated health care system.

2. Methods

2.1. Study setting and population

This study was conducted at Kaiser Permanente Southern California (KPSC), a large integrated health care delivery system serving over 4.7 million members broadly representative of the racial/ethnic and socioeconomic diversity of the residents in southern California [8]. HPV vaccination is offered at KPSC without cost and can be obtained at primary care and pediatric clinics, nurse clinics, urgent care, or emergency rooms. To evaluate the trend of HPV vaccine administration, children who received any dose of the HPV vaccine between age 9–12.9 years while a KPSC member between 03/01/2019 and 09/30/2021 were included. We focused on children younger than age 13 since this age group is the target for adherence to ACIP's routine recommendation [7]. To evaluate the trend of coverage by age 13, those who met the following criteria were eligible: (1) turned age 13 between 03/01/2019 and 09/30/2021; (2) maintained continuous KPSC membership between age 9 and age 13, which allowed the complete capture of HPV vaccination history. This study was approved by the KPSC's Institutional Review Board (IRB). The requirement of informed consent was waived by the KPSC IRB.

2.2. Data collection

Data on demographics, HPV vaccination and membership history were collected using KPSC's electronic health records. Information on neighborhood deprivation index (NDI) was created from home address based, census-tract SES and demographic characteristics from the American Community Survey [9].

2.3. Statistical analysis

The number of HPV vaccine doses given to children aged 9 to 12.9 between 03/01/2019 and 09/30/2021 were plotted for each calendar month overall, by sex, and by race/ethnicity. Given that KPSC membership between age 9–12.9 years were stable during the study period, number of doses administered was directly used for ease of interpretation. Using 2019 as the reference year, the number of doses administrated in each month was transformed into a percentage relative to the volume of doses administered in that month in 2019. A sub-analysis restricting to those with continuous membership since age 9 examined the doses administered as first vs. second dose separately.

The distribution of demographic characteristics of children who turned age 13 were calculated overall and by the following calendar periods: pre-pandemic (03/01/2019–02/29/2020); pandemic period 1 (03/01/2020–04/30/2021, the start of the pandemic to the month when COVID-19 vaccines became available); and pandemic period 2 (05/01/2021–09/30/2021). Due to the large sample sizes (which can lead to significant p-values despite small differences), we used the standardized difference to compare the distribution of demographic characteristics across calendar periods [10]. An absolute value of < 0.1 is considered a negligible difference [10]. Next, the proportion of (1) any dose ($\geq$1 dose) coverage; and (2) up-to-date coverage (>=2 doses) was plotted for each calendar month (for children who turned 13 in that month) to provide a visual depiction of the trends, overall, by sex, and by race/ethnicity. The average coverage was calculated for each calendar period.

Bivariate and multivariable Poisson regression models with robust error variance (modified Poisson) with piecewise linear splines were used to evaluate the trend of HPV vaccine coverage by age 13 [11]. The location and the number of knots for the linear splines were determined based on visual inspection of the monthly trend figures as well as the P-values (<0.05) of the change of trend. For the outcome (1) any dose ($\geq$1 dose) coverage, one knot was placed at month 12 (02/2020); for the outcome (2) up-to-date coverage [defined as $\geq$ 2 dose (of these, 99.9% met the up-to-date definition used by HEDIS [1,12] and the NIS-TEEN national HPV vaccine coverage studies, i.e., 3+ doses or 5 months – 4 days between the first and second dose)] two knots were placed at month 12 (02/2020) and month 26 (04/2022) to model the change of coverage over time. The effect estimate for trend were then evaluated in multivariable models adjusting for sex, race/ethnicity, NDI (quartiles), prior membership length and member home service area.

The associations between race/ethnicity, NDI quartiles and HPV vaccine coverage by age 13 were also examined and compared using crude and adjusted modified Poisson regression models, overall and separately for each calendar period, adjusting for the covariates listed above. Two-way interaction terms were created between the race/ethnicity and the calendar periods, as well as between NDI quartiles and calendar periods and tested using score test. The final models did not include any interaction terms due to lack of statistically or clinically significant interactions. All analyses were conducted using SAS statistical software Version 9.4; Cary, North Carolina, USA.

3. Results

A large decline of HPV vaccine doses administered was observed in March-April 2020 (Fig. 1), which returned to the 2019 level by May 2020. Another decline was observed in January 2021, followed by a rapid reversal as of February 2021. Similar patterns were observed across sex and race/ethnicity. In the sub-analysis restricting to those with continuous membership since age 9, the doses administered in the pandemic period was more likely the first dose than the second dose, and this difference was larger compared to the pre-pandemic period (**Supplemental Fig. 1**).

For the examination of HPV vaccine coverage by age 13, a total of 280,853 children who turned age 13 during the study time window were identified. After excluding those without continuous membership since age 9, 96,387 were included in the evaluation (36,385 pre-pandemic, 43,615 pandemic period 1, and 16,387 in pandemic period 2). The distributions of sex, race/ethnicity and

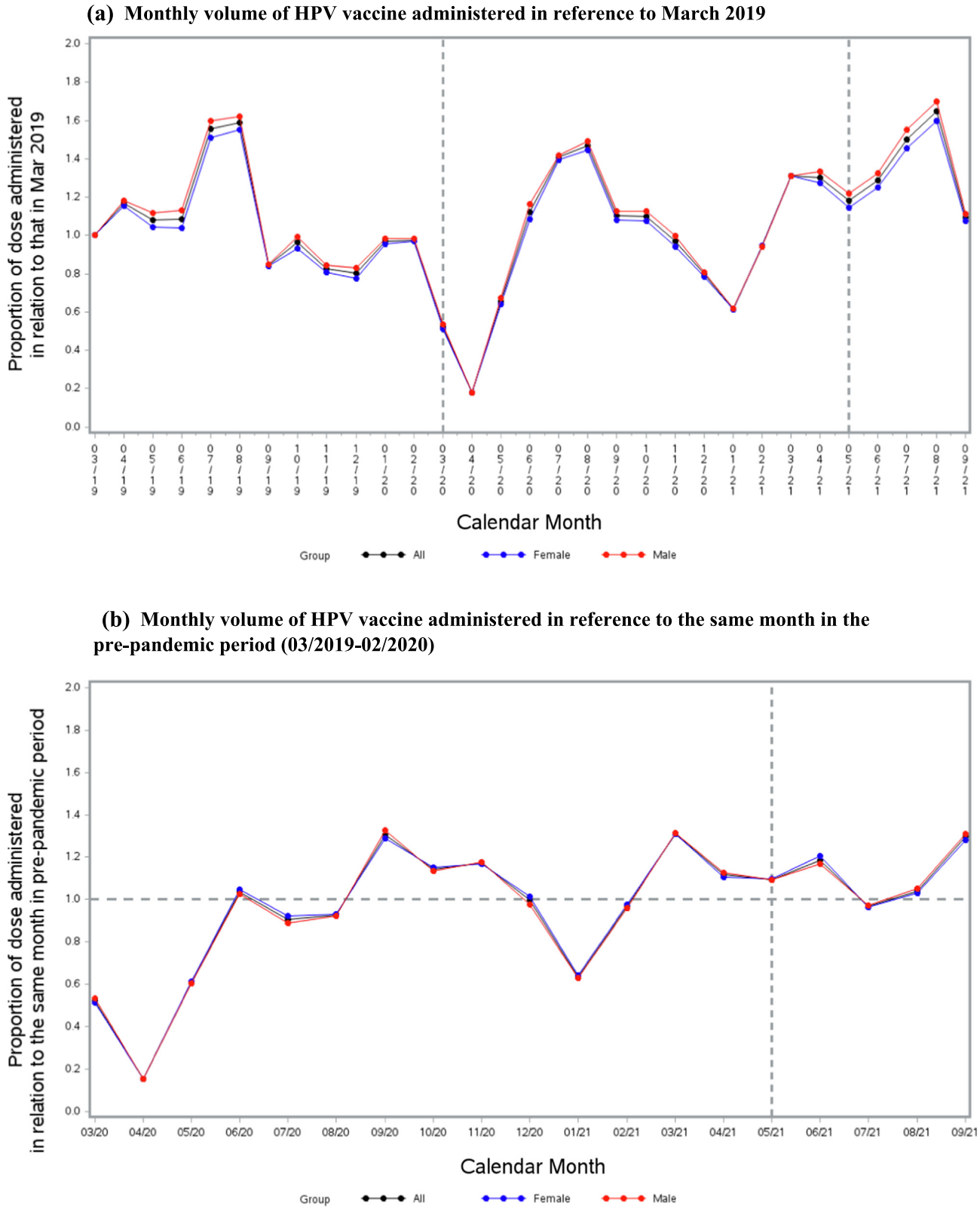

Fig. 1. Volume of HPV vaccine administrated between March 2019 - September 2021 in relation to March 2019 (the reference month) at KPSC. 1(a): Monthly volume of HPV vaccine administered in reference to March 2019. 1(b): Monthly volume of HPV vaccine administered in reference to the same month in the pre-pandemic period (03/2019–02/2020).

NDI were similar across calendar periods with the absolute standardized differences less than 0.1 for all variables (Table 1).

Supplemental Fig. 2 shows the monthly data on any-dose coverage by age 13. In both crude and adjusted multivariable models, an increasing trend was found between 03/2019–02/2020 (ad-

Table 1
Demographic characteristics of children turning age 13 between March 2019-September 2021 at KPSC.

	Pre-Covid Period* **(03/2019–02/2020)** (N = 36385)	**Pandemic Period 1*** **(03/2020–04/2021)** (N = 43615)	**Pandemic Period 2*** **(05/2021–09/2021)** (N = 16387)
Gender, n (%)			
Female	17,677 (48.6%)	21,258 (48.7%)	7968 (48.6%)
Male	18,708 (51.4%)	22,357 (51.3%)	8419 (51.4%)
Race/Ethnicity, n (%)			
Non-Hispanic White	8766 (24.1%)	10,363 (23.8%)	3884 (23.7%)
Non-Hispanic Black	3020 (8.3%)	3621 (8.3%)	1360 (8.3%)
Hispanic	19,208 (52.8%)	22,779 (52.2%)	8574 (52.3%)
Asian/Pacific Islander	3716 (10.2%)	4634 (10.6%)	1641 (10.0%)
Others	771 (2.1%)	1095 (2.5%)	432 (2.6%)
Unknown	904 (2.5%)	1123 (2.6%)	496 (3.0%)
Neighborhood Deprivation Index (NDI)			
Mean (SD)	0.2 (0.8)	0.2 (0.9)	0.2 (0.9)
Median (IQR)	0.1 (-0.5, 0.8)	0.1 (-0.5, 0.8)	0.1 (-0.5, 0.8)
Prior membership			
Mean (SD)	9.7 (3.3)	9.7 (3.2)	9.7 (3.2)

* The absolute standardized differences comparing any two periods for all variables are < 0.1, which are considered neglectable differences.

justed trend: 0.24% increase in coverage per month, $p < 0.01$), while a decreasing trend was found for 03/2020 – 09/2021 (adjusted trend: 0.13% decrease per month, $p < 0.01$). For up-to-date coverage by age 13, three trends were used to describe the change over time. In both crude and adjusted multivariable models, there was a small increasing trend between 03/2019–02/2020 (adjusted trend: 0.38% increase per month, $p < 0.01$), a small decreasing trend between 03/2020–04/2021 (adjusted trend: 0.69% decrease per month, $p < 0.01$), and a small but statistically insignificant increasing trend in the second year of the pandemic (adjusted trend: 0.28% increase per month, $p = 0.32$, **Supplemental Table**). Data on the average coverage in each calendar period suggested that the coverage level in pandemic period 2 had not returned to the pre-pandemic period (Fig. 2).

The associations between race/ethnicity and HPV vaccine coverage were highly consistent across all three calendar periods (Table 2). Overall and within each calendar period, Asian/Pacific islanders, Hispanics and non-Hispanic blacks have a higher likelihood of having any dose or 2-dose coverage compared to non-Hispanic whites. In pandemic period 2, compared to non-Hispanic whites, the adjusted relative risks (RRs) were 1.22 (95% confidence interval 1.19, 1.26) and 1.37 (1.30, 1.44) for Asian/Pacific islanders; 1.21 (1.18, 1.24) and 1.30 (1.24, 1.35) for Hispanics; 1.08 (1.03, 1.12) and 0.98 (0.92, 1.06) for non-Hispanic blacks compared to non-Hispanic whites for any dose and up-to-date coverage, respectively. Test for interaction terms between race/ethnicity and the pandemic periods were not statistically significant ($p = 0.14$ and 0.10).

The associations between NDI subgroups and HPV vaccine coverage were also consistent across all three calendar periods (Table 2). The adjusted RR of the most deprived neighborhood for 2-dose coverage by age 13 in the pre-pandemic period was 1.09 (1.06–1.12) compared to the least deprived neighborhoods and was 1.04 (1.01–1.07) and 1.04 (0.99–1.08) in pandemic periods 1 and 2, respectively (Table 2). Interaction term between NDI and the pandemic periods was statistically significant ($p < 0.01$) for 2 dose coverage but not for 1 dose coverage ($p = 0.40$).

4. Discussion

We found that although HPV vaccine administration plummeted during March – May 2020 and during the 2020–2021 winter COVID surge, the monthly level of doses given was similar to the pre-pandemic year during most of the pandemic period. That said, the first dose and the second dose administrations had different rates of return from initial drop, with a greater return of the first dose administration. Impact of the pandemic on HPV vaccine up-to-date coverage by age 13 was mild and the decreasing trend appeared to cease starting in May 2021. The mild impact was likely due to the fact that vaccination coverage depends on uptake in the prior years before turning age 13, and due in part to the fact that disruption in HPV vaccine administration was of short duration during the pandemic at KPSC. However, the level of coverage had not returned to the pre-pandemic level, and the increasing trend observed before the pandemic had not been resumed. These data suggest that enhanced efforts to facilitate HPV vaccine uptake and series completion are needed to overcome the disruptive effect of the pandemic.

Our findings on the differential HPV vaccine coverage by race/ethnicity are consistent across the pre-pandemic and pandemic periods and we did not find evidence of a differential impact of the pandemic on minority races/ethnicities. We observed a "reverse disparity" (i.e., Whites and/or higher SES groups experienced a greater gap in care) in our study for HPV vaccine coverage. A prior systematic review and meta-analysis by Spencer et al concluded reverse racial disparity for HPV vaccine initiation. For series completion the authors concluded that minorities were at a disadvantage compared to whites, although this disparity appeared to decrease over time [13]. Prior studies suggested that physician bias, differential deference to medical authority, social norm and vaccine hesitancy may be potential reasons behind these findings [14–16]. In our study we observed reverse disparity in an integrated system for both any dose and up-to-date coverage, adding to the evidence of this relatively unique phenomenon in preventive care uptake. The difference between NDI quartiles was less pronounced compared to those seen between race/ethnicity groups. These findings are, however, qualitatively consistent with prior literature which showed a higher HPV vaccination coverage among adolescents with low income and/or living in neighborhoods of high poverty [17,18] compared with more affluent adolescents.

There are several limitations that should be considered when interpreting these data. First, we did not have individual level SES data and relied on NDI to assess SES. Thus, our findings should be interpreted at the neighborhood SES level rather than the individual SES level. Second, we acknowledge that the HPV vaccine uptake pattern during the pandemic may have varied by state and health care systems, and our results may not generalize to those outside of California, who are uninsured, or not in an integrated health care system. Unpublished data from the CDC suggested a 18% drop in HPV vaccinations in the Vaccines for Children program comparing 2020 through 05/2021 to 2019 [19]. A study based on Louisiana Medicaid data reported a 35% drop in HPV vaccination in 2020 compared to 2017–2019 [20]. These findings support the notion that HPV vaccination pattern during the pandemic may vary between settings. Of note, KPSC took several measures to increase uptake of recommended childhood vaccination since May 2020 [3]. These include strategies to minimize risk of COVID-exposure (including screening for symptoms, limiting and monitoring points of entry, requiring face covering, employment of standard precautions, spatial separation, etc), outreach efforts for children needing vaccination (e.g., nurse outreach, parent reminder about the threat of vaccine preventable diseases, re-assurance of COVID safety), simultaneous vaccination to mini-

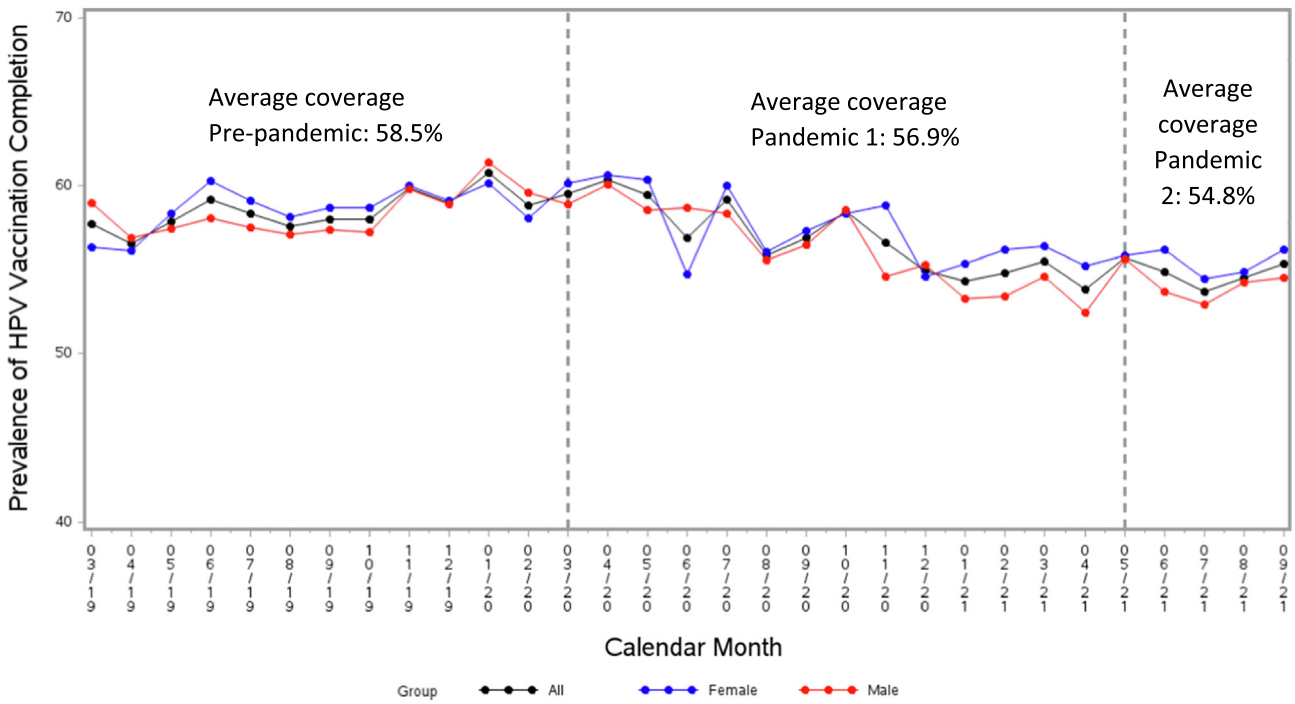

Fig. 2. Up-to-date coverage by age 13 for HPV vaccination between March 2019-September 2021 at KPSC.

Table 2
Adjusted modified Poisson regression for evaluating race/ethnicity and neighborhood deprivation index on HPV vaccine coverage by age 13.

Any dose coverage		Pre-pandemic				Pandemic Period 1				Pandemic Period 2			
Race/ethnicity	Reference	RR	LL	UL	P-value	RR	LL	UL	P-value	RR	LL	UL	P-value
Asian/Pacific Islander	Non-Hispanic White	1.23	1.20	1.25	0.00	1.24	1.22	1.26	0.00	1.22	1.19	1.26	0.00
Non-Hispanic Black		1.08	1.05	1.11	0.00	1.05	1.02	1.08	0.00	1.08	1.03	1.12	0.00
Hispanic		1.19	1.17	1.21	0.00	1.19	1.17	1.21	0.00	1.21	1.18	1.24	0.00
Others		1.14	1.09	1.18	0.00	1.11	1.07	1.15	0.00	1.13	1.07	1.20	0.00
Neighborhood deprivation index quartiles													
Quartile 3	Quartile 4	1.01	0.99	1.03	0.23	1.00	0.98	1.01	0.62	1.02	0.99	1.04	0.24
Quartile 2	(least deprived)	1.04	1.03	1.06	0.00	1.03	1.02	1.05	0.00	1.03	1.01	1.06	0.02
Quartile 1 (most deprived)		1.07	1.05	1.09	0.00	1.05	1.04	1.07	0.00	1.07	1.04	1.09	0.00
Up-to-date coverage		Pre-pandemic				Pandemic Period 1				Pandemic Period 2			
Race/ethnicity	Reference	RR	LL	UL	P-value	RR	LL	UL	P-value	RR	LL	UL	P-value
Asian/Pacific Islander	Non-Hispanic White	1.34	1.30	1.38	0.00	1.36	1.32	1.40	0.00	1.37	1.30	1.44	0.00
Non-Hispanic Black		1.02	0.98	1.06	0.34	0.99	0.95	1.03	0.54	0.98	0.92	1.06	0.66
Hispanic		1.24	1.21	1.27	0.00	1.26	1.23	1.29	0.00	1.30	1.24	1.35	0.00
Others		1.20	1.13	1.28	0.00	1.17	1.11	1.24	0.00	1.19	1.08	1.30	0.00
Neighborhood deprivation index quartiles													
Quartile 3	Quartile 4	0.99	0.97	1.02	0.67	0.98	0.95	1.00	0.08	0.99	0.95	1.03	0.72
Quartile 2	(least deprived)	1.03	1.01	1.06	0.01	1.01	0.99	1.04	0.43	0.99	0.95	1.03	0.58
Quartile 1 (most deprived)		1.09	1.06	1.12	0.00	1.04	1.01	1.07	0.00	1.04	0.99	1.08	0.12

RR: Rate ratio; LL: lower limit of 95% confidential interval; UL: upper limit of 95% confidence interval.
Model adjusted for sex, race/ethnicity, neighborhood deprivation index quartiles, medical service area, and prior length of KPSC membership.

mize number of visits needed, as well as drive-up vaccine clinics where feasible. These measures may have contributed to the quick rebound of the HPV vaccine administration. Our data indirectly support the positive impact of these timely and innovative vaccination efforts which may inform decision making for other health systems in future pandemics.

5. Conclusion

Our data suggest that HPV vaccine dose administration at KPSC had resumed to the pre-pandemic level, and the decreasing trend in up-to-date coverage by age 13 appeared to have ceased. However, complete HPV vaccine coverage had not returned to the pre-pandemic level and the trend has not increased as of September 2021. System efforts for promoting childhood and adolescent vaccination during a pandemic are likely necessary to ensure adequate vaccination rates. Enhanced efforts are needed to bring back the HPV vaccination coverage level in children.

Data statement

Anonymized data that support the findings of this study may be made available from the corresponding author on reasonable request from qualified researchers with documented evidence of training for human subjects protections.

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CRediT authorship contribution statement

Chun R. Chao: Conceptualization, Methodology, Investigation, Funding acquisition, Writing – original draft, Writing – review & editing. **Lanfang Xu:** Methodology, Investigation, Writing – review & editing. **Nancy Cannizzaro:** Project administration, Resources, Writing – original draft, Writing – review & editing. **David Bronstein:** Methodology, Investigation, Writing – review & editing. **Yunsun Choi:** Methodology, Investigation, Writing – review & editing. **Robert Riewerts:** Methodology, Investigation, Writing – review & editing. **Brian Mittman:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Richard K. Zimmerman:** Writing – review & editing. **Melissa Gilkey:** Writing – review & editing. **Beth Glenn:** Writing – review & editing. **Ernest Shen:** Methodology, Writing – review & editing. **Chunyi Hsu:** Project administration, Resources, Writing – review & editing. **Erin E. Hahn:** Conceptualization, Methodology, Investigation, Writing – review & editing.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Chao CR received research funding from Merck for an unrelated project.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2022.09.073.

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