European Journal of Pediatrics (2024) 184:71
https://doi.org/10.1007/s00431-024-05910-y

RESEARCH

# Recovery from HPV vaccination deficits caused by the COVID-19 pandemic in Germany: a modeling study of catch-up HPV vaccination among adolescent girls

**Kunal Saxena[1] · Cornelia Wähner[2] · Agnes Luzak[3] · Thorsten Reuter[2] · Edith Morais[1] · Ya-Ting Chen[1]**

Received: 4 November 2024 / Revised: 27 November 2024 / Accepted: 30 November 2024 / Published online: 7 December 2024


## Abstract

Health care disruptions associated with the COVID-19 pandemic have caused persistent decreases in human papillomavirus (HPV) vaccination uptake in Germany. The objective of this study was to estimate the cumulative deficit in first doses of the HPV vaccine administered to girls in Germany since the beginning of the pandemic and the projected time to recover from this deficit at different catch-up vaccination uptake levels, focusing on girls 9–14 years of age. This study used a published HPV vaccination modeling tool. Retrospective vaccination data from 2019 were used to calculate the baseline vaccination rate, while data from 1 January 2020 to 31 December 2023 were used to estimate the size and duration of the HPV vaccination deficit accrued since the beginning of the COVID-19 pandemic. We modeled scenarios in which the rate of monthly vaccinations increased from the 2023 average to 5%, 10%, or 15% above the baseline 2019 level. The average monthly number of first doses of HPV vaccine administered to girls 9–14 years of age was 7.4% below the 2019 baseline level in 2020, 21.2% below baseline in 2021, 21.0% below baseline in 2022, and 19.5% below baseline in 2023. At a catch-up vaccination uptake of 5–15% above the 2019 baseline, there would be an estimated accumulated deficit of 267,052–285,798 first doses by 31 December 2024 that would clear between October 2029–April 2040. A catch-up vaccination uptake of 12.3% (11.9–12.7%) every month above baseline would be needed to clear the accumulated deficit by the end of 2030. *Conclusions*: Significant HPV vaccination deficits have accrued in Germany since the beginning of the COVID-19 pandemic. Sustained efforts to vaccinate the affected cohorts are now needed to mitigate the long-term impacts of the vaccination deficit.

**What is known:**

- *Health care disruptions associated with the COVID-19 pandemic have caused persistent decreases in human papillomavirus (HPV) vaccination uptake in Germany.*

**What is new:**

- *Our model projected that the HPV vaccination deficit would be cleared between October 2029 (15% above the 2019 baseline level) and April 2040 (5% above the 2019 baseline level).*
- *A catch-up rate of 12.3% (11.9–12.7%) above the 2019 baseline level would be needed to clear the HPV vaccination deficit by 31 December 2030.*
- *Sustained efforts to vaccinate the affected cohorts are now needed to mitigate the long-term impacts of the accrued vaccination deficit on mortality, morbidity, and health care costs from HPV-associated diseases.*

**Keywords** Human papillomavirus · HPV vaccination · HPV immunization · Girls · COVID-19 · Germany

Communicated by Gregorio Milani

✉ Kunal Saxena
kunal.saxena@merck.com

[1] Merck & Co., Inc., V&I Outcomes Research, Rahway, NJ, USA

[2] MSD Sharp & Dohme GmbH, Medical Affairs, Munich, Germany

[3] MSD Sharp & Dohme GmbH, Market Access, Munich, Germany

## Abbreviations

| | |
|---|---|
| EHR | Electronic health record |
| HPV | Human papillomavirus |
| STIKO | Standing Committee on Vaccination |

## Introduction

Human papillomavirus (HPV) can cause anogenital warts and certain cancers, including almost 100% of cervical cancers and substantial proportions of anal, oropharyngeal, penile, vaginal, and vulvar cancers [1, 2]. Effective and safe vaccines are available that protect against acute HPV infections and their long-term sequelae, including cancers [3–6]. In Germany, a bivalent vaccine that protects against oncogenic HPV genotypes 16 and 18 is currently approved and available for use, as is a nonavalent vaccine that protects against oncogenic or wart-associated genotypes 6, 11, 16, 18, 31, 33, 45, 52, and 58.

Routine HPV vaccination of girls in Germany has been recommended by the Standing Committee on Vaccination (STIKO) and fully reimbursed since 2007. Initially, vaccination with a 3-dose schedule was recommended and reimbursed for girls 12–17 years of age [7], but in 2014, STIKO's recommendations were updated to a 2-dose schedule for girls 9–14 years of age and a 3-dose catch-up vaccination schedule for girls 15–17 years of age [8]. In mid-2018, these primary and catch-up vaccination schedule recommendations were expanded to include boys with reimbursement for boys beginning in 2019 [9]. The number of first doses of HPV vaccine administered to German boys reached the same level as for girls within 3–4 months of the 2018 recommendation expansion [10]. By the end of 2019, the first HPV vaccine doses were administered to 6.5% of eligible boys who were 9 years of age and 20.9% of boys who were 14 years of age [10].

The introduction of HPV vaccination in Germany has been associated with a decreased incidence of HPV infections, anogenital warts, cervical lesions, and other anogenital diseases [11–14]. Modeling studies have consistently found that HPV vaccination is also a cost-effective strategy in Germany [15–18]. Despite these benefits, data from the Robert-Koch-Institute show that in 2020, just 51% of girls and 17% of boys 15 years of age had completed a full course of HPV vaccination [19]. Further, a national study found that the number of first doses of HPV vaccine administered in Germany decreased sharply at the onset of the COVID-19 pandemic in March 2020, falling to 42% below the March 2019 level for boys and 49% below the March 2019 level for girls [10]. Vaccination uptake gradually increased during the second half of 2020 but then fell again after the second lockdown and reached the minimum in August 2021, when the vaccination rate for boys was 72% lower than baseline [10]. These findings mirror global trends in the uptake of HPV and other routine vaccinations for all age groups during the COVID-19 pandemic; the resulting vaccination deficits have persisted, and there is evidence that greater deficits exist for HPV than for other routine vaccinations [6, 20–40].

Globally, around 1.6 million girls are thought to have missed an HPV vaccination in 2020 alone [40]. These deficits in the uptake of HPV vaccination that accrued during the COVID-19 pandemic are predicted to have severe long-term impacts on morbidity, mortality, and health care costs [37, 39, 41, 42]. To study this vaccination deficit, we developed a modeling tool that uses real-world country-specific HPV vaccination data to estimate the number of HPV vaccine doses missed during the COVID-19 pandemic, and the level of catch-up vaccination uptake needed to clear these deficits [36, 38]. The objective of the current study was to model the HPV vaccination deficit in Germany during the COVID-19 pandemic, as well as the projected time to recover from this deficit at different catch-up vaccination uptake levels. Because fully funded HPV vaccination of German boys began at the start of 2019 and vaccination uptake was not stable during the model's baseline period [10], we limited our analysis to the female population.

## Methods

### Study design

In this modeling study, the cumulative deficit of first doses of HPV vaccine administered to girls 9–14 and 15–17 years of age in Germany was estimated during different phases of the COVID-19 pandemic. We obtained empirical vaccination data for girls 9–17 years of age, but focused our deficit clearance modeling analyses on girls 9–14 years of age, as this age group will have more opportunities to catch up on missed doses before full reimbursement ends, one day prior to their 18th birthday. We analyzed data on first doses of HPV vaccine as a proxy for number of unique individuals affected. The study incorporated a retrospective analysis of anonymized electronic health record (EHR) data to estimate the impact of the COVID-19 pandemic on HPV vaccination among this group. The study database contains no identifying information and is compliant with all German data protection regulations. As such, no specific consent framework or independent ethics board review was required.

### Input data

Anonymized EHR data were obtained from two databases: the IQVIA™ Vaccine Analyzer and IQVIA™ PharmaScope Vaccine DocSplit. The IQVIA™ Vaccine Analyzer database contains information about patient demographic characteristics, diagnoses, and prescriptions (including exact date of administered vaccinations) drawn from a panel of 460 office-based physicians from 353 practices. The panel includes 0.5% of all German general practitioners, 0.6% of gynecologists, and 2.1% of pediatricians. Data are collected

directly from patient management software in the participating practices and extrapolated to a national level utilizing the IQVIA™ PharmaScope Vaccine DocSplit which provides information on the number of nationally prescribed doses within the statutory and private health insurance sector in Germany. IQVIA™ Vaccine Analyzer has been shown to have patient demographics and vaccine administration data that are representative for the national population, and to be suitable for use in studies of vaccination in Germany [43]. Detailed information on the methods of the two databases were published previously [10, 43].

Vaccination data from the previously mentioned databases were extracted for girls who were resident in Germany and 9–14 or 15–17 years of age at the time of vaccination. The year of birth, but not the exact date of birth, was known for each individual, and so age in years at the time of vaccination was inferred as the difference between the birth year and the date of vaccination. Data were extracted for all girls who were part of an included age group for the entirety of the respective year or who entered an included age group during the respective year. For example, the 2019 data for the 15–17 years of age group were derived from all girls with a 15th, 16th, or 17th birthday during 2019. All administrations of first doses of bivalent and nonavalent HPV vaccines were recorded. A first dose was defined as administration of an HPV vaccine to an individual (identified by a unique anonymous code) with no other dose of HPV vaccine recorded in the study database during the prior 18 months.

## Model structure and catch-up vaccination scenarios

The study used the COVID-19 Recovery Tool, a Microsoft Excel model that can use diverse types of country-specific input data to estimate the number of missed vaccine doses from the beginning of the COVID-19 pandemic to the current day and the expected time to clear the accumulated deficit at different levels of vaccination uptake [36, 38]. The model's temporal structure for this study comprised a baseline pre-COVID-19 period (1 January to 31 December 2019), a COVID-19 impact period (1 January 2020 to 31 December 2023), a transition period (1 January to 31 December 2024), and a catch-up period (1 January 2025 onward; Fig. 1). The year 2019 was chosen as baseline pre-COVID-19 period, and the post-pandemic monthly uptake rates were compared against the baseline uptake.

Empirical HPV vaccination data from EHRs were extracted for each month of the baseline and COVID-19 impact period. All recorded data on first doses of HPV vaccination for girls aged 9–17 years old were extracted from the available physician panel including general practitioners, gynecologists, and pediatricians for the period of 1 January 2019 to 31 December 2023. Patients of unknown sex as well as those outside of the desired age range were excluded from the analysis.

The HPV vaccination deficit during each month of the COVID-19 impact period was calculated by subtracting the number of first doses administered each month from the number of first doses administered during the corresponding month of the baseline period (Online Resource 1). During the transition period, the model gradually increased the number of first vaccine doses administered each month in a linear manner, from the level at the end of the COVID-19 impact period to a base-case catch-up level that was set to 10% higher than the baseline period vaccination uptake. This 10% catch-up vaccination rate was then applied to the imputed number of monthly vaccine doses administered during each month of the catch-up period. Finally, accumulated vaccination deficits and deficit recovery times were estimated. In addition to the base-case analysis (10% catch-up vaccination rate) described above, we also modeled optimistic and pessimistic scenarios with transition period and

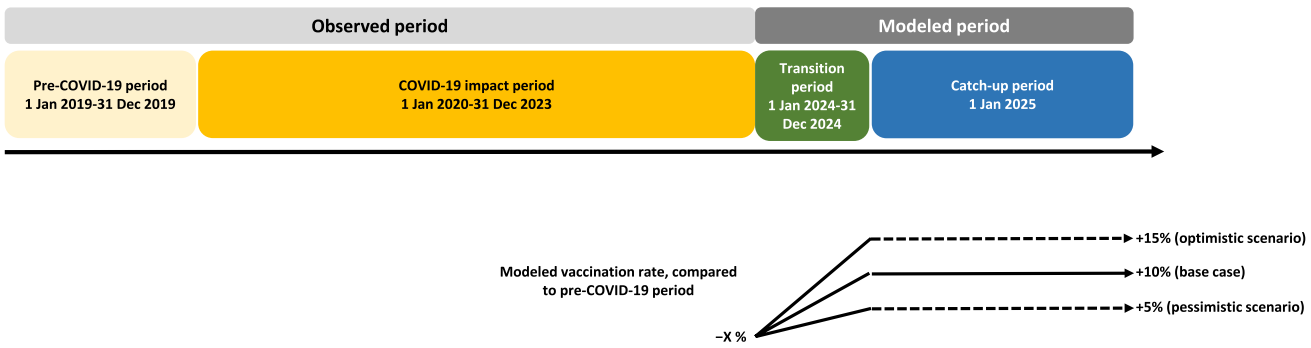
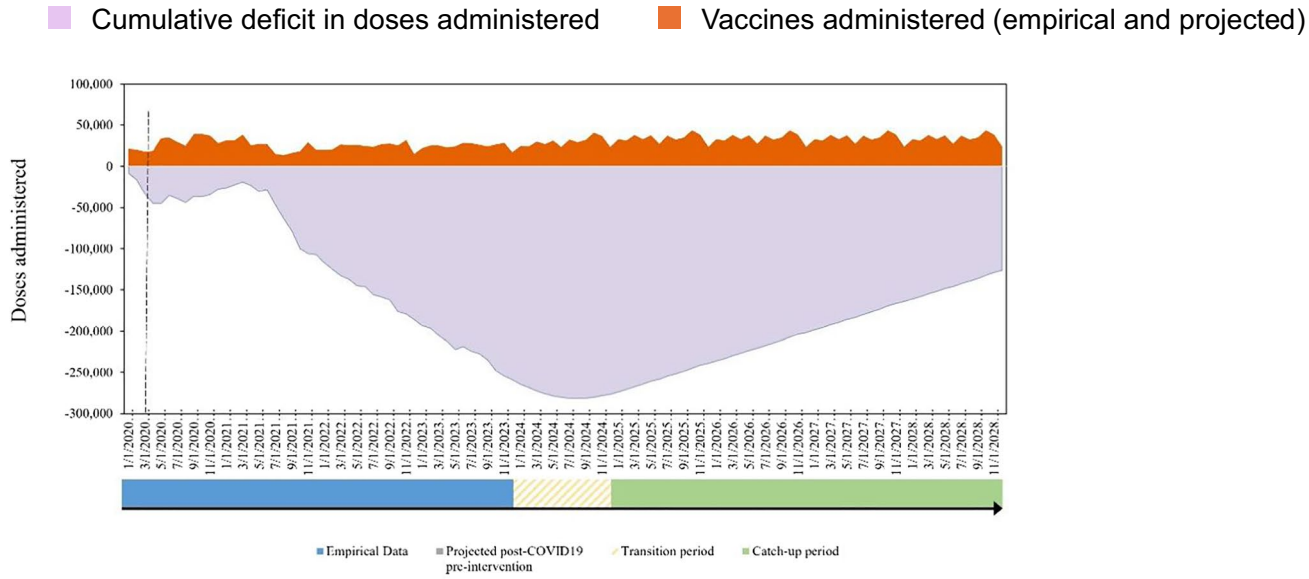
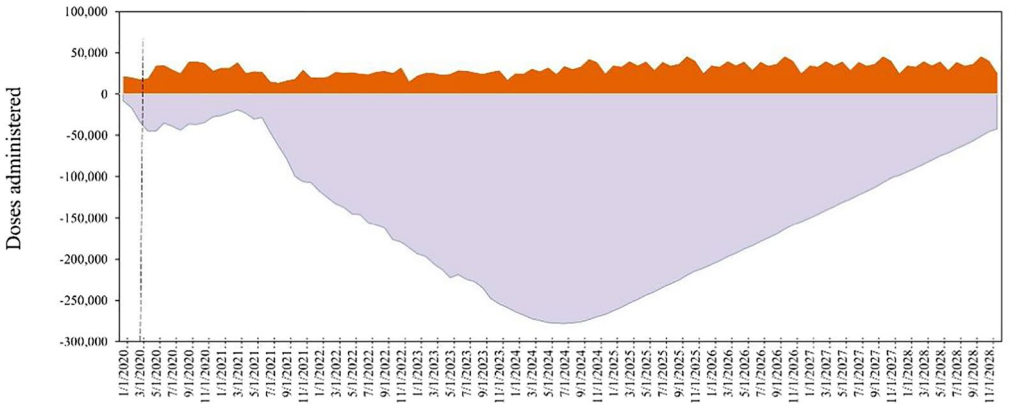



**Fig. 1** Temporal structure of the COVID-19 Recovery Tool model of human papillomavirus vaccination among adolescent girls in Germany. During the modeled period, the number of first vaccine doses administered each month was increased in a linear manner from the observed level at the end of the COVID-19 impact period (-X% compared to baseline) to a level set to 5–15% higher than the observed vaccination rate during the baseline pre-COVID-19 period. This catch-up vaccination rate was then maintained during the catch-up period

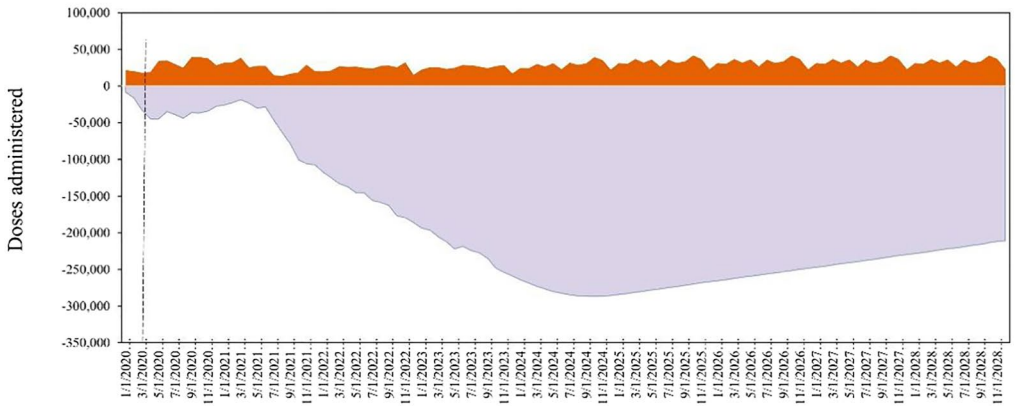
## A) Base-case: catch-up vaccination rate 10% higher than 2019 baseline




## B) Optimistic scenario: catch-up vaccination rate 15% higher than 2019 baseline




## C) Pessimistic scenario: catch-up vaccination rate 5% higher than 2019 baseline



◂**Fig. 2** Deficit in the number of first doses of human papillomavirus vaccine administered to adolescent girls 9–14 years of age in Germany. Administered doses are shown in orange and the cumulative deficit in administered doses in gray. Dashed line denotes the beginning of the COVID-19 pandemic in March 2020

catch-up vaccination rates of 15% and 5% above baseline, respectively.

## Results

### Estimated vaccination deficits

Empirical model input data extracted from EHRs showed that in 2020 the average monthly number of first doses administered to girls 9–14 years of age decreased by 7.4% compared to the 2019 baseline level, then fell to 21.2% below baseline in 2021, 21.0% below baseline in 2022, and 19.5% below baseline in 2023 (Online Resource 1). The largest decreases were observed in July 2021 (55.7% below baseline for girls 9–14 years of age). There was a small improvement in 2023, with an average monthly administration rate of − 19.5% compared to the corresponding months in 2019. The average monthly number of first dose administrations at the start of the transition period was set to 19.5% below baseline.

The first HPV vaccine doses administered in Germany and the accumulated vaccination deficit during the COVID-19 pandemic are shown in Fig. 2. At the end of the COVID-19 impact period/beginning of the transition period, there was an accumulated deficit of 258,761 first doses among girls 9–14 years of age. In the base-case scenario, when the monthly number of vaccinations during the 12-month transition period was gradually increased from 19.5% below baseline to 10% above baseline, the number of accumulated missed first doses at the end of the transition period / beginning of the catch-up period was estimated to have grown to 276,427 (73.8% of the annual first doses administered during the baseline period; Table 1). An optimistic scenario (catch-up rate 15% higher than baseline) and pessimistic scenario (catch-up rate 5% higher than baseline) were also modeled, resulting in an optimistic projected deficit of 267,052 doses (71.3%) and a pessimistic projected deficit of 285,798 doses (76.3%). For girls 15–17 years of age, the accumulated deficit of first doses at the end of the COVID-19 impact period / beginning of the transition period was 168,109. At the beginning of the catch-up period the deficit was estimated at 188,192 in the base-case, 185,304 in the optimistic scenario, and 191,077 in the pessimistic scenario.

### Vaccination deficit clearance scenarios

In the base-case analysis, the catch-up vaccination rate of 10% above baseline was estimated to result in the clearance of the accumulated deficit of first doses of HPV vaccine by 20 May 2032 among girls 9–14 years of age (Table 2). The higher catch-up rate used in the optimistic scenario was estimated to clear the deficit > 2.5 years sooner (clearance date of 3 October 2029), while the lower rate used in the pessimistic scenario delayed deficit clearance by nearly 8 years compared to the base-case (clearance date of 7 April 2040).

The projected dates of deficit clearance at catch-up vaccination levels of 10–50% are graphed in Fig. 3. Depending on the three scenarios, catch-up vaccination uptake of 12.3% (11.9–12.7%) above baseline would be needed to clear the deficit of first doses by 31 December 2030. These uptake levels would equate to an additional 3842 first doses administered each month between 1 January 2025 and 31 December 2030.

## Discussion

The COVID-19 pandemic has disrupted vaccination and other preventive health services. In the present study, we used data on the number of first doses of HPV vaccine administered to girls 9–14 years of age in Germany to estimate the number of missed doses since the onset of the pandemic. We also estimated the time that will be needed to clear this deficit under three catch-up vaccination scenarios with uptake 5%, 10%, and 15% above the 2019 baseline.

Our model identified a substantial deficit in the number of first doses of HPV vaccine administered to girls 9–14 years, taking at least 4.75 years to clear in even the most optimistic scenario. Clearing the deficit by the end of 2030 would require a catch-up rate of 11.9–12.7% above the 2019 baseline. This rate is higher than the catch-up rates previously estimated for Greece and Switzerland (8.2% and 8.4% above baseline, respectively, to clear each country's deficit by December 2024) [36]. While the prior analysis used the same model, it included a shorter observed period (up to 31 December 2021) and earlier transition and catch-up periods [36]. The later catch-up period (starting in January 2024) in the current analysis contributes to the higher catch-up rate that would be needed to clear the German vaccination deficit by the end of 2030. The 2021 average monthly first vaccine dose deficit of − 21.2% observed in the current study was also greater than that observed in Greece (− 12.3%) or Switzerland (− 7.9%), which may also have contributed to the differences in the required catch-up vaccination rates estimated for these countries. Of note, Switzerland has a school-based HPV vaccination program, while Greece and

**Table 1** Estimated number of missed first doses of human papillomavirus vaccine at the beginning of the catch-up period

| Scenario | Catch-up rate [a] | Girls 9–14 years of age | | Girls 15–17 years of age | |
|---|---|---|---|---|---|
| | | Missed doses | %[b] | Missed doses | %[b] |
| Base-case | 10% | 276,427 | 73.8 | 188,192 | 148.9 |
| Optimistic | 15% | 267,052 | 71.3 | 185,304 | 146.6 |
| Pessimistic | 5% | 285,798 | 76.3 | 191,077 | 151.1 |

[a]The number of first doses of HPV vaccine administered during the transition period (1 January to 31 December 2024) was increased linearly from the estimated level at the end of the COVID-19 impact period (girls 9–14 years of age, 19.5% lower than the 2019 baseline period vaccination level; girls 15–17 years of age, 37.7% lower than baseline) to a catch-up vaccination uptake of 5%, 10%, or 15% higher than baseline

[b]The number of missed first doses was divided by the annual number of first doses administered during the baseline period

**Table 2** Estimated first dose human papillomavirus vaccination deficit clearance dates for girls 9–14 years of age

| Scenario | Catch-up rate[a] | Estimated time to clear deficit (months) | Date of deficit clearance |
|---|---|---|---|
| Base-case | 10% | 88.6 | 20 May 2032 |
| Optimistic | 15% | 57.1 | 3 October 2029 |
| Pessimistic | 5% | 183.2 | 7 April 2040 |

[a]The number of first doses of HPV vaccine administered during the transition period (1 January to 31 December 2024) was increased linearly from the estimated level at the end of the COVID-19 impact period (19.5% lower than the 2019 baseline period vaccination level) to a catch-up vaccination uptake of 5%, 10%, or 15% higher than baseline

Germany do not, which may partially explain the smaller vaccine dose deficit estimated in the Swiss analysis.

We estimated that 258,761 first doses had been missed by 1 January 2024 among girls 9–14 years of age and that the deficit grew to between 267,052 (15% catch-up vaccination scenario) and 285,798 (5% scenario) doses by 1 January 2025. The accumulated vaccination deficit for girls 15–17 years of age was estimated to be somewhat smaller overall than that accrued for girls 9–14 years of age (185,304–191,077 versus 267,052–285,798 by 1 January 2025). It is important to note that even though the absolute number of dose deficit may be lower in the 15–17 year cohort, proportionally the deficit is much larger (~ 149% vs. ~ 73%) compared to 9–14 year cohort. Part of the reason for these results is that the size of the eligible cohort in girls 15–17 years of age is about one-third of the size of the 9–14-year-old cohort. This was also reflected in the baseline (2019) uptake differences in the two age groups, where overall the dose uptake during pre-COVID timeframe is smaller in the catch-up cohort than the primary cohort. Rapidly clearing the deficit among this older age group is particularly urgent as in Germany the recommendation for HPV vaccination with mandatory reimbursement ends 1 day before their 18th birthday, so when girls age out (≥ 18 years) they will either (1) not receive their complete HPV series or (2) potentially have to pay out-of-pocket for their HPV vaccination as health insurance companies are no longer obliged to pay for the vaccination for patients aged 18 years and older.

Urgent measures will be needed to clear the COVID-19-related HPV vaccination deficit in Germany. This will be a significant challenge, since Germany's pre-COVID-19 female HPV vaccine coverage rate was well below the World Health Organization's and the European Commission's target of 90% [19, 44, 45]. Our findings suggest that the pandemic has further slowed progress toward achieving this target.

HPV vaccine uptake is influenced by several factors, including knowledge and awareness, trust in healthcare providers, and cultural, social, and policy-related factors. A 2022 survey of 1,095 German adults found low awareness of HPV and the vaccine, with nearly two-thirds (63.8%) of respondents having never have heard of HPV and only 44.9% of respondents aware that a preventive vaccine against HPV existed [46].

One of the logistical barriers to improving HPV vaccination uptake in Germany is that vaccinations are administered by physicians at their offices, with no formal invitation or reminder system in place and no school-based programs in the country. A previous study found a positive association between HPV vaccination and voluntary attendance at the J1 health check [47]. More proactive promotion of the J1 visit, such as through an organized universal reminder system, has thus been suggested as a means to improve HPV vaccination uptake [47–49]. Further, the implementation of school-based HPV vaccination in Germany has also been suggested, as have improved education on the importance of HPV vaccination for disease prevention, organized vaccination invitation and reminder systems, increased political support and cooperation [48, 49]. Stronger recommendations from health care providers have also been shown to improve HPV vaccine uptake in other countries [50].

Efforts to improve HPV vaccination will need to account for vaccine hesitancy and other patient concerns, including the impacts of the politicization of COVID-19 vaccination campaigns on overall attitudes to vaccination. Germany generally has relatively high levels of vaccine acceptance and is at roughly the Western European median level on many measures of extreme anti-vaccination attitudes [51, 52]. However, in a pooled analysis of survey respondents from Germany and eight other Western European countries, vaccine safety concerns and lack of information on HPV

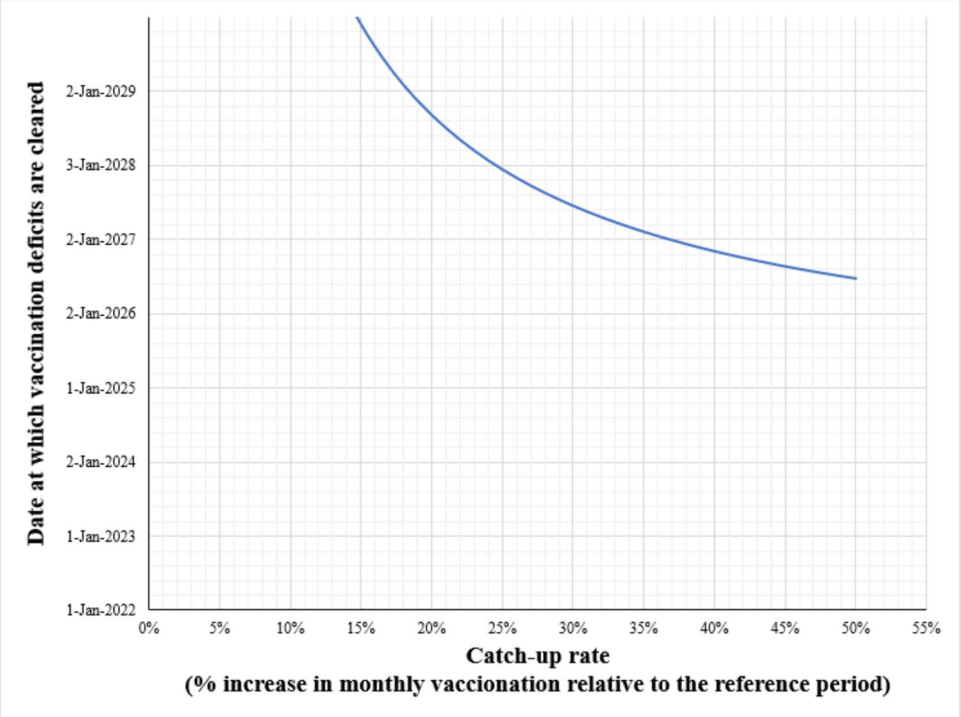



**Fig. 3** Projected date at which the number of cumulative missed first doses of human papillomavirus vaccine would reach zero with a catch-up period beginning 1 January 2025 and different catch-up vaccination rates

vaccinations were frequently cited as reasons for not being vaccinated against HPV [53]. Responses to these common concerns will need to be incorporated into educational initiatives designed to address the deficit in HPV vaccination that has accumulated during the COVID-19 pandemic.

The study has limitations. Our analyses combined empirical vaccination data with an established modeling tool to estimate the HPV vaccination deficits in Germany under three different scenarios, covering a range of possible catch-up vaccination rates. The accuracy of the model is limited by quality of the input data used, which were extracted from a panel of office-based physicians. However, a previous analysis found that the study databases are representative of the demographics of Germany and are suitable for vaccination-related analyses [43]. Exact dates of birth were not available, so inclusion in the age groups of interest was inferred based on year of birth; some vaccines administered to individuals outside the stated age range of each group may therefore have been included in our analyses, while some vaccines administered to individuals within the age range of interest may have been missed. However, we would expect the proportions of these categories of vaccinations to remain stable during the study period. In addition, traceability was only possible for individuals receiving their entire HPV vaccination series at the same participating practice; inaccuracies in dose classification (i.e., first versus subsequent dose) may occur if individuals transition from one practice to another. It is possible that such misclassifications may occur more frequently for older adolescents transitioning from a pediatrician to a general practitioner. Overall, however, we would expect dose misclassification to be a rare event with a stable frequency over time. Our analyses also made a number of assumptions about changes in vaccination rates during the modeled periods; inaccuracies in these assumptions would be expected to affect the accuracy of the estimated vaccine dose deficits and catch-up times. Finally, our model assumes that providers will be able to administer vaccines at the required catch-up rate of 5–15% above the pre-pandemic 2019 baseline vaccination rate. Sustaining these catch-up rates of 5–15% over a number of years may not be realistic, thus, the actual time to clear the deficit may be longer than modeled here.

## Conclusions

In conclusion, our analysis confirms that the COVID-19 pandemic caused a substantial deficit in HPV vaccination in Germany. Our model's projections highlight the urgency of implementing vaccination promotion interventions to address this deficit and prevent a future surge in the incidence of HPV-related cancers and other diseases.

**Supplementary Information** The online version contains supplementary material available at https://doi.org/10.1007/s00431-024-05910-y.

**Acknowledgements** The authors thank Cath Ennis, PhD, in collaboration with ScribCo for medical writing assistance.

**Authors' contributions** KS, CW, AL, TR, EM, and YC contributed to the study conception and design. Material preparation, data collection and analysis were performed by KS, CW, and AL. The first draft of the manuscript was written by KS, CW, and AL and all authors commented on previous versions of the manuscript. All authors read and approve the final manuscript.

**Funding** This study was funded by Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

**Data availability** That data that supported the findings of this study are available from the IQVIA Vaccine Analyzer and IQVIA PharmaScope Vaccine DocSplit, but restrictions apply to the availability of these data, which were used under license for the current study so are not publicly available. However, the data analyzed during this study are included in this published article.

## Declarations

**Ethics approval** This study used anonymized EHR retrospective vaccination data from two databases: the IQVIA™ Vaccine Analyzer and IQVIA™ PharmaScope Vaccine DocSplit. The study database contains no identifying information and is compliant with all German data protection regulations. As such, no specific consent framework or independent ethics board review was required.

**Consent to participate** Consent to participate is not applicable. The study database contains no identifying information and is compliant with all German data protection regulations.

**Consent for publication** Consent for publication is not applicable. The study database contains no identifying information and is compliant with all German data protection regulations.

**Competing interests** KS, EM, and YC are employees of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Rahway, NJ, USA, and may hold equity interest in Merck & Co., Inc., Rahway, NJ, USA.

CW, AL, and TR are employees of MSD Sharp & Dohme GmbH, Munich, Germany and may hold equity interest in Merck & Co., Inc., Rahway, NJ, USA.



## References

1. de Martel C, Georges D, Bray F, Ferlay J, Clifford GM (2020) Global burden of cancer attributable to infections in 2018: a worldwide incidence analysis. Lancet Glob Health 8(2). https://doi.org/10.1016/S2214-109X(19)30488-7
2. de Martel C, Plummer M, Vignat J, Franceschi S (2017) Worldwide burden of cancer attributable to HPV by site, country and HPV type. Int J Cancer 141(4). https://doi.org/10.1002/ijc.30716
3. Garland SM, Hernandez-Avila M, Wheeler CM, Perez G, Harper DM, Leodolter S et al (2007) Quadrivalent vaccine against human papillomavirus to prevent anogenital diseases. N Engl J Med 356(19). https://doi.org/10.1056/NEJMoa061760
4. Joura EA, Giuliano AR, Iversen OE, Bouchard C, Mao C, Mehlsen J et al (2015) A 9-valent HPV vaccine against infection and intraepithelial neoplasia in women. N Engl J Med 372(8). https://doi.org/10.1056/NEJMoa1405044
5. Paavonen J, Naud P, Salmeron J, Wheeler CM, Chow SN, Apter D et al (2009) Efficacy of human papillomavirus (HPV)-16/18 AS04-adjuvanted vaccine against cervical infection and precancer caused by oncogenic HPV types (PATRICIA): final analysis of a double-blind, randomised study in young women. Lancet 374(9686). https://doi.org/10.1016/S0140-6736(09)61248-4
6. World Health Organization (2022) Strategic Advisory Group of Experts (SAGE) Working Group on potential contribution of HPV vaccines and immunization towards cervical cancer elimination: Background Document and Report to SAGE, March 2022, https://cdn.who.int/media/docs/default-source/immunization/position_paper_documents/human-papillomavirus-(hpv)/hpv-background-document--report-march-2022.pdf. Accessed February 13, 2023
7. Robert Koch Institut. Mitteilung der Ständigen Impfkommission (STIKO) am Robert Koch-Institut (2007) Impfung gegen humane Papillomaviren (HPV) für Mädchen von 12 bis 17 Jahren – Empfehlung und Begründung. Epidemiologisches Bull 12. https://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2007/Ausgabenlinks/12_07.pdf?__blob=publicationFile
8. Robert Koch Institut. Mitteilung der Ständigen Impfkommission am Robert Koch-Institut (RKI) (2014) Empfehlungen der Ständigen Impfkommission (STIKO) am Robert Koch-Institut/Stand: August 2014. Epidemiologisches Bull 34. https://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2014/Ausgaben/34_14.pdf?__blob=publicationFile
9. Robert Koch Institut (2018) Wissenschaftliche Begründung für die Empfehlung der HPV-Impfung für Jungen im Alter von 9 bis 14 Jahren. Epidemiologisches Bull 26. https://doi.org/10.17886/EpiBull-2018-032.1
10. Wähner C, Hübner J, Meisel D, Schelling J, Zingel R, Mihm S et al (2023) Uptake of HPV vaccination among boys after the introduction of gender-neutral HPV vaccination in Germany before and during the COVID-19 pandemic. Infection 51(5). https://doi.org/10.1007/s15010-023-01978-0
11. Osmani V, Fett S, Tauscher M, Donnachie E, Schneider A, Klug SJ (2022) HPV vaccination leads to decrease of anogenital warts and precancerous lesions of the cervix uteri in young women with low vaccination rates: a retrospective cohort analysis. BMC Cancer 22(1). https://doi.org/10.1186/s12885-022-10214-1
12. Mikolajczyk RT, Kraut AA, Horn J, Schulze-Rath R, Garbe E (2013) Changes in incidence of anogenital warts diagnoses after the introduction of human papillomavirus vaccination in Germany-an ecologic study. Sex Transm Dis 40(1). https://doi.org/10.1097/OLQ.0b013e3182756efd
13. Reuschenbach M, Mihm S, Wolle R, Schneider KM, Jacob C, Braun S et al (2020) Burden of HPV related anogenital diseases in young women in Germany - an analysis of German statutory health insurance claims data from 2012 to 2017. BMC Infect Dis 20(1). https://doi.org/10.1186/s12879-020-05002-w
14. Denecke A, Iftner T, Iftner A, Riedle S, Ocak M, Luyten A et al (2021) Significant decline of HPV 6 infection and genital warts despite low HPV vaccination coverage in young women in Germany: a long-term prospective, cohort data analysis. BMC Infect Dis 21(1). https://doi.org/10.1186/s12879-021-06139-y

15. Schobert D, Remy V, Schoeffski O (2012) Cost-effectiveness of vaccination with a quadrivalent HPV vaccine in Germany using a dynamic transmission model. Health Econ Rev 2(1). https://doi.org/10.1186/2191-1991-2-19
16. Kotsopoulos N, Connolly MP, Remy V (2015) Quantifying the broader economic consequences of quadrivalent human papillomavirus (HPV) vaccination in Germany applying a government perspective framework. Health Econ Rev 5(1). https://doi.org/10.1186/s13561-015-0054-6
17. Largeron N, Petry KU, Jacob J, Bianic F, Anger D, Uhart M (2017) An estimate of the public health impact and cost-effectiveness of universal vaccination with a 9-valent HPV vaccine in Germany. Expert Rev Pharmacoecon Outcome Res 17(1). https://doi.org/10.1080/14737167.2016.1208087
18. Damm O, Horn J, Mikolajczyk RT, Kretzschmar MEE, Kaufmann AM, Delere Y et al (2017) Cost-effectiveness of human papillomavirus vaccination in Germany. Cost Eff Resour Alloc 15. https://doi.org/10.1186/s12962-017-0080-9
19. Rieck T, Feig M, Siedler A (2022) Impfquoten von Kinderschutzimpfungen in Deutschland - aktuelle Ergebnisse aus der RKI-Impfsurveillance. Epidemiologisches Bull 48. https://doi.org/10.25646/10838
20. Gaythorpe KA, Abbas K, Huber J, Karachaliou A, Thakkar N, Woodruff K et al (2021) Impact of COVID-19-related disruptions to measles, meningococcal A, and yellow fever vaccination in 10 countries. Elife 10. https://doi.org/10.7554/eLife.67023
21. Hill HA, Chen M, Elam-Evans LD, Yankey D, Singleton JA (2023) Vaccination coverage by age 24 months among children born during 2018–2019 - National Immunization Survey-Child, United States, 2019–2021. MMWR Morb Mortal Wkly Rep 72(2). https://doi.org/10.15585/mmwr.mm7202a3
22. Hong K, Zhou F, Tsai Y, Jatlaoui TC, Acosta AM, Dooling KL et al (2021) Decline in receipt of vaccines by medicare beneficiaries during the COVID-19 pandemic - United States, 2020. MMWR Morb Mortal Wkly Rep 70(7). https://doi.org/10.15585/mmwr.mm7007a4
23. Kujawski SA, Yao L, Wang HE, Carias C, Chen YT (2022) Impact of the COVID-19 pandemic on pediatric and adolescent vaccinations and well child visits in the United States: A database analysis. Vaccine 40(5). https://doi.org/10.1016/j.vaccine.2021.12.064
24. Langdon-Embry M, Papadouka V, Cheng I, Almashhadani M, Ternier A, Zucker JR (2020) Notes from the field: rebound in routine childhood vaccine administration following decline during the COVID-19 pandemic - New York City, March 1-June 27, 2020. MMWR Morb Mortal Wkly Rep 69(30). https://doi.org/10.15585/mmwr.mm6930a3
25. Lassi ZS, Naseem R, Salam RA, Siddiqui F, Das JK (2021) The impact of the COVID-19 Pandemic on immunization campaigns and programs: a systematic review. Int J Environ Res Public Health 18(3). https://doi.org/10.3390/ijerph18030988
26. Liow C, Payne H, Gillen EM, Donthi S (2022) Declines in routine adult and teen vaccinations continued in 2021. https://avalere.com/insights/declines-in-routine-adult-and-teen-vaccinations-continued-in-2021
27. McDonald HI, Tessier E, White JM, Woodruff M, Knowles C, Bates C et al (2020) Early impact of the coronavirus disease (COVID-19) pandemic and physical distancing measures on routine childhood vaccinations in England, January to April 2020. Euro Surveill 25(19). https://doi.org/10.2807/1560-7917.ES.2020.25.19.2000848
28. Nuzhath T, Ajayi KV, Fan Q, Hotez P, Colwell B, Callaghan T et al (2021) Childhood immunization during the COVID-19 pandemic in Texas. Vaccine 39(25). https://doi.org/10.1016/j.vaccine.2021.04.050
29. Patel Murthy B, Zell E, Kirtland K, Jones-Jack N, Harris L, Sprague C et al (2021) Impact of the COVID-19 pandemic on administration of selected routine childhood and adolescent vaccinations - 10 U.S. Jurisdictions, March-September 2020. MMWR Morb Mortal Wkly Rep 70(23). https://doi.org/10.15585/mmwr.mm7023a2
30. Rao SR, Kampan N, Chew KT, Shafiee MN (2022) The impact of the COVID-19 pandemic on the national HPV immunization program in Malaysia. Front Public Health 10. https://doi.org/10.3389/fpubh.2022.907720
31. Sato APS (2020) Pandemic and vaccine coverage: challenges of returning to schools. Rev Saude Publica 54. https://doi.org/10.11606/s1518-8787.2020054003142
32. Seither R, Laury J, Mugerwa-Kasujja A, Knighton CL, Black CL (2022) Vaccination coverage with selected vaccines and exemption rates among children in kindergarten - United States, 2020–21 School Year. MMWR Morb Mortal Wkly Rep 71(16). https://doi.org/10.15585/mmwr.mm7116a1.
33. SeyedAlinaghi S, Karimi A, Mojdeganlou H, Alilou S, Mirghaderi SP, Noori T et al (2022) Impact of COVID-19 pandemic on routine vaccination coverage of children and adolescents: a systematic review. Health Sci Rep 5(2). https://doi.org/10.1002/hsr2.516
34. Shet A, Carr K, Danovaro-Holliday MC, Sodha SV, Prosperi C, Wunderlich J et al (2022) Impact of the SARS-CoV-2 pandemic on routine immunisation services: evidence of disruption and recovery from 170 countries and territories. Lancet Glob Health 10(2). https://doi.org/10.1016/S2214-109X(21)00512-X
35. World Health Organization (2021) Varied impact of COVID-19 on routine immunization in the European Region, https://www.who.int/europe/news/item/16-07-2021-varied-impact-of-covid-19-on-routine-immunization-in-the-european-region. Accessed January 31, 2023
36. Gountas I, Favre-Bulle A, Saxena K, Wilcock J, Collings H, Salomonsson S et al (2023) Impact of the COVID-19 pandemic on HPV vaccinations in Switzerland and Greece: Road to recovery. Vaccines (Basel) 11(2). https://doi.org/10.3390/vaccines11020258
37. Mennini FS, Silenzi A, Marcellusi A, Conversano M, Siddu A, Rezza G (2022) HPV vaccination during the COVID-19 pandemic in Italy: opportunity loss or incremental cost. Vaccines (Basel) 10(7). https://doi.org/10.3390/vaccines10071133
38. Saxena K, Marden JR, Carias C, Bhatti A, Patterson-Lomba O, Gomez-Lievano A et al (2021) Impact of the COVID-19 pandemic on adolescent vaccinations: projected time to reverse deficits in routine adolescent vaccination in the United States. Curr Med Res Opin 37(12). https://doi.org/10.1080/03007995.2021.1981842
39. Daniels V, Saxena K, Roberts C, Kothari S, Corman S, Yao L et al (2021) Impact of reduced human papillomavirus vaccination coverage rates due to COVID-19 in the United States: a model based analysis. Vaccine 39(20). https://doi.org/10.1016/j.vaccine.2021.04.003
40. UNICEF (2021) COVID-19 pandemic leads to major backsliding on childhood vaccinations, new WHO, UNICEF data shows. https://www.unicef.org/press-releases/covid-19-pandemic-leads-major-backsliding-childhood-vaccinations-new-who-unicef-data. Accessed January 31, 2023
41. Maulbecker-Armstrong C, Moser K, Ouedraogo N (2022) Lost cohorts in the HPV vaccination due to the covid-19 pandemic and potential effects on future HPV associated cancers. Deutscher Krebskongress, Krebsmedizin: Schnittstellen zwischen Innovation und Versorgung; Berlin, Germany: Oncology Research and Treatment, Paper No. 941
42. Velentzis LS, Smith MA, Killen J, Brotherton JML, Guy R, Canfell K (2023) A modelled analysis of the impact of COVID-19-related disruptions to HPV vaccination. Elife 12. https://doi.org/10.7554/eLife.85720

43. Ohl N, Zingel R, Kostev K (2022) Investigation of the representativeness of the German IQVIA Vaccine Analyzer database. Int J Clin Pharmacol Ther 60(2). https://doi.org/10.5414/CP204098
44. European Commission (2022) Europe's Beating Cancer Plan. https://health.ec.europa.eu/system/files/2022-02/eu_cancer-plan_en_0.pdf
45. World Health Organization (2024) Immunization coverage. https://www.who.int/news-room/fact-sheets/detail/immunization-coverage. Accessed August 18, 2024
46. Sharma SJ, Schartinger VH, Wuerdemann N, Langer C, Mollenhoff K, Collin L et al (2022) Awareness of human papillomavirus (HPV) and HPV vaccination amongst the general population in germany: lack of awareness and need for action. Oncol Res Treat 45(10). https://doi.org/10.1159/000525697
47. Rieck T, Feig M, Delere Y, Wichmann O (2014) Utilization of administrative data to assess the association of an adolescent health check-up with human papillomavirus vaccine uptake in Germany. Vaccine 32(43). https://doi.org/10.1016/j.vaccine.2014.07.105
48. Schott E, Schaller K, Mons U, Ouedraogo N (2022) Approaches to increase HPV vaccination rate in Germany - challenges and opportunities. A qualitative study. Z Evid Fortbild Qual Gesundhwes 170. https://doi.org/10.1016/j.zefq.2022.02.002
49. Sternjakob-Marthaler A, Berko-Gottel B, Rissland J, Schope J, Taurian E, Muller H et al (2022) Human papillomavirus vaccination of girls in the German model region Saarland: Insurance data-based analysis and identification of starting points for improving vaccination rates. PLoS One 17(9). https://doi.org/10.1371/journal.pone.0273332
50. Constable C, Ferguson K, Nicholson J, Quinn GP (2022) Clinician communication strategies associated with increased uptake of the human papillomavirus (HPV) vaccine: A systematic review. CA Cancer J Clin 72(6). https://doi.org/10.3322/caac.21753
51. Hadjipanayis A, van Esso D, Del Torso S, Dornbusch HJ, Michailidou K, Minicuci N et al (2020) Vaccine confidence among parents: large scale study in eighteen European countries. Vaccine 38(6). https://doi.org/10.1016/j.vaccine.2019.11.068
52. Kennedy J (2019) Populist politics and vaccine hesitancy in Western Europe: an analysis of national-level data. Eur J Public Health 29(3). https://doi.org/10.1093/eurpub/ckz004
53. Robles C, Bruni L, Acera A, Riera JC, Prats L, Poljak M et al (2021) Determinants of human papillomavirus vaccine uptake by adult women attending cervical cancer screening in 9 European countries. Am J Prev Med 60(4). https://doi.org/10.1016/j.amepre.2020.08.032