

# Parental intent to initiate and complete the human papillomavirus vaccine series in the USA: a nationwide, cross-sectional survey



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## Summary

**Background** Human papillomavirus (HPV) vaccine uptake among US adolescents is primarily dependent on the intent of their parents. To the best of our knowledge, an analysis quantifying parental intent to initiate and complete the HPV vaccine series in the USA at both the national and state level has not been done. We aim to estimate parental intent to initiate and complete the HPV vaccine series at the national-level and state-level and to identify reasons for lack of intent to initiate and complete the vaccine series.

**Methods** This cross-sectional study uses data from the adolescent component of the 2017–18 National Immunization Survey (NIS-Teen). Study participants were parents or caregivers of US adolescents aged 13–17 years, who were most knowledgeable about the immunisation status of the adolescents. The primary outcome was parental intent to vaccinate the adolescent in the next 12 months. The secondary outcomes were (1) the prevalence of reasons given for lack of intent to initiate and complete the HPV vaccine series, and (2) the relationship between receiving a recommendation from a health-care provider to vaccinate and intent to initiate the vaccination series. We computed national-level and state-level estimates for parental lack of intent to initiate and to complete the vaccine series; population-level estimates were derived using survey weights. A survey design-adjusted Wald *F* test was used for bivariate analysis. A multivariate logistic regression model was used to examine the association between health-care provider recommendation and parental intent to initiate the series. Analyses were stratified by history of health-care provider recommendation to initiate the HPV vaccine series.

**Findings** In 2017–18, the parent or caregiver of 82 297 US adolescents aged 13–17 years completed the NIS-Teen survey. 30 558 (37.1%) were unvaccinated and 9073 (10.8%) received only one HPV vaccine dose. Parents of 58.0% (17 171/29 086) of unvaccinated adolescents with data available on parental intent had no intention to initiate the HPV vaccine series. More than 65% of parents of unvaccinated adolescents in Idaho, Kansas, Michigan, Montana, Nebraska, North Dakota, Oklahoma, and Utah had no intention to initiate the HPV vaccine series. Parents of 23.5% (2166/9072) of initiators with data available on parental intent had no intention to complete the HPV vaccine series. More than 30% of parents in Arkansas, Florida, Georgia, Hawaii, Idaho, Utah, and West Virginia did not intend to complete the HPV vaccine series, whereas in the District of Columbia (11.2% [22/166]) and Rhode Island (20.4% [21/112]) parental lack of intent was relatively low (both regions have an HPV vaccine mandate). The most common reason for lack of intent among parents to initiate the vaccine for unvaccinated adolescents was safety concerns (22.8% [4182/16 455]); lack of a recommendation from a health-care provider (22.2% [440/1944]) was the most frequently cited reason for absence of intent to complete the series among parents of adolescents who received only one HPV vaccine dose. Receipt of a recommendation from a health-care provider was associated with greater odds of parental intent to initiate the HPV vaccine series (odds ratio 1.11, 95% CI 1.01–1.22). 45.5% (13 156/29 086) of parents of unvaccinated adolescents had reportedly received an HPV vaccine recommendation. Parents of 60.6% (7938/13 156) of unvaccinated adolescents with a recommendation from a health-care provider and data available on parental intent had no intention to initiate the series.

**Interpretation** Lack of parental intent to initiate and complete the HPV vaccine series for adolescents is a major public health concern in the USA. Combating vaccine safety concerns and strong recommendations from health-care providers could improve the currently suboptimal HPV vaccination coverage.

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## Introduction

An estimated 34 800 human papillomavirus (HPV)-associated cancers (ie, cervical, oropharyngeal, anal,

penile, vaginal, and vulvar cancers) were diagnosed annually in the USA during 2012–16.<sup>1</sup> Although cancer incidence in the USA in general is declining, the

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### Research in context

#### Evidence before this study

According to the 2019 US Centers for Disease Control and Prevention report, nearly half of the US adolescents who are eligible for the human papillomavirus (HPV) vaccine are not up to date on vaccination. Given the absence of mandates (ie, a legislative order to receive the HPV vaccine for school entry) in most states, HPV vaccination in US adolescents is mainly dependent on the intent of their parents. We searched PubMed for studies published in English from Jan 1, 2007, to March 15, 2020, with the search terms “human papillomavirus vaccine” or “HPV vaccine”, and “parental intent” or “lack of intent”, and “hesitancy”, and “reasons for hesitancy.” Our search found no previous studies that have examined national-level and state-level estimates of parental intent to initiate and complete the HPV vaccine series in the USA. Previous US studies have described parental reasons for lack of intent for their adolescents to receive the HPV vaccination. However, national estimates of reasons for lack of intent to initiate and complete the vaccine series are unavailable.

#### Added value of this study

Using data from a nationally representative survey of US adolescents (the adolescent component of the National Immunization Survey [NIS-Teen]), we estimated national-level and state-level parental intent to initiate and complete the HPV vaccine series and discerned reasons for parental lack of intent for

series initiation and completion. Nationally, more than half of the parents of unvaccinated adolescents had no intention to initiate the HPV vaccine series. In Idaho, Kansas, Michigan, Montana, Nebraska, North Dakota, Oklahoma, and Utah, more than 65% of parents of unvaccinated adolescents had no intention to initiate the HPV vaccine series. Moreover, 61.9% of the parents of unvaccinated adolescents in Wyoming and 57.1% in Mississippi (states with some of the lowest HPV vaccine coverage in the nation) did not intend to initiate the series. Nationally, almost a quarter of the parents of adolescents who received the first dose of the vaccine had no intention to complete the series. In Arkansas, Florida, Georgia, Hawaii, Idaho, Utah, and West Virginia, more than 30% of the parents had no intention to complete the HPV vaccine series. Lack of parental intent to complete the vaccine series was 11.2% in the District of Columbia and 20.4% in Rhode Island; HPV vaccination is mandated in both regions. Safety concerns were most commonly cited as the main reason for not intending to initiate the series. By comparison, a lack of provider recommendation was most commonly cited as the main reason for not intending to complete the HPV vaccine series.

#### Implications of all the available evidence

Given the absence of a mandate for the HPV vaccine in most US states, addressing reasons for parental lack of intent for HPV vaccine series initiation and completion is crucial to the improvement of HPV vaccine coverage in the USA.

collective burden of HPV-associated cancers is increasing in the USA, mainly attributable to a marked increase (nearly 3% annually) in oropharyngeal and anal cancer incidence from 2001 to 2015.<sup>1,2</sup> The HPV vaccine is an effective intervention for the prevention of anogenital HPV infections and associated cancers.<sup>3,4</sup> Observational studies suggest that the vaccine might also protect against oral HPV infection.<sup>5,6</sup>

The US Advisory Committee on Immunization Practices recommends a two-dose HPV vaccine regimen for girls and boys initiating the series before their 15th birthday and a three-dose regimen thereafter.<sup>7</sup> Timely initiation and completion of the series is crucial to optimise immune response to the HPV vaccine.<sup>8</sup> However, only half of US adolescents had completed the vaccine series and nearly 32% were unvaccinated in 2018.<sup>9</sup> The variation in HPV vaccine series completion across all states in the USA was also substantial (with the highest completion rate in Rhode Island [77.7%] and the lowest in Mississippi [28.8%]).<sup>10</sup>

Initiation and completion of the HPV vaccination series by adolescents is largely dependent on the intent of their parents. Theoretical models have identified intention as the most important construct for behavioural change, making parental vaccination behaviour a primary focus for vaccine-promoting interventions.<sup>11,12</sup> Parental attitudes towards the HPV vaccine might be driven by vaccine naivety in unvaccinated adolescents.<sup>13</sup>

However, once their adolescents receive the first HPV vaccine dose, factors that drive parents to decide to complete (or not to complete) the series might be different. We aim to estimate the intention of parents to have their adolescent children initiate and complete the HPV vaccine series, at the national and state level, using data from the adolescent component of the 2017–18 National Immunization Survey (NIS-Teen). We also aim to identify reasons for an absence of parental intent for series initiation and completion.

## Methods

### Study design and participants

In this cross-sectional study, we analysed data from the 2017–18 NIS-Teen, an annual random-digit-dial survey of adolescents aged 13–17 years living in the USA. The procedure for 2017–18 data consolidation is described in the appendix (p 1). Each year for the survey, households with adolescents are identified. An adult respondent (ie, parent or caregiver) most knowledgeable about the adolescent’s vaccination history is interviewed by phone after obtaining verbal informed consent. Subsequently, an extensive review of the data is done for completeness, and sampling weights are calculated after adjustment for subsampling and non-response to achieve an accurate representation of the adolescent population of the USA. A subset of participants in the NIS-Teen (approximately

See Online for appendix

51% in 2017–18) consented to contact their health-care providers, and immunisation history for these participants was subsequently verified by mailing requests for medical records. For the purpose of this study, we used the entire sample of adolescents with data on parental intent and reasons. Details regarding the sampling methodology, data processing, and estimation of the survey weights are available in the appendix (p 1) and on the NIS-Teen website.<sup>14</sup>

### Procedures

The NIS-Teen survey collects data regarding age, sex of the adolescent, race and ethnicity, and their relationship with the parent or caregiver. Data regarding the poverty status of the adolescents, insurance status, and state of residence are also reported. All respondents (ie, parents or caregivers) were asked whether they recalled the adolescent receiving the HPV vaccine (“Has teen ever received any human papillomavirus shots?”). Those who responded “yes” were asked to report the total number of HPV vaccine doses received. Respondents who responded “no” were assigned zero for the total number of doses received. We categorised adolescents as unvaccinated (adolescents who received zero HPV vaccine doses) or as initiators (adolescents who received only one HPV vaccine dose). Adolescents who received more than one dose were not included in the analyses. All results reported from the survey represent one parent responding on behalf of one adolescent from their household.

Parental intent to vaccinate was based on the question, “How likely it is that teen will receive HPV shots in the next 12 months?” Response options were “very likely”, “somewhat likely”, “not too likely”, “not likely at all”, and “not sure/don’t know”. This question was asked to all parents or caregivers regardless of whether the adolescent had received the HPV vaccine. Parents who responded “not too likely” or “not likely at all” were categorised as having an absence of intention to vaccinate their adolescents. If the adolescent received zero doses of the HPV vaccine, parents or caregivers were also asked, “What is the main reason teen will not receive any HPV shots in the next 12 months?” If the adolescent received at least one dose of the HPV vaccine, parents or caregivers were instead asked, “What is the main reason teen will not receive all HPV shots in the next 12 months?” Parents selected the main reason from a list of predefined reasons; if unlisted, the response was elicited in an open-ended manner. In the final dataset, all reasons were recorded into 28 unique yes or no questions by the NIS-Teen staff.

### Statistical analysis

We identified unvaccinated adolescents and adolescents who received only the first HPV vaccine series dose (ie, initiators) from the 2017–18 NIS-Teen survey data. Descriptive statistics were used to examine the socio-demographic characteristics of unvaccinated and vaccine-initiating adolescents; the Wald *F* test was used to

examine differences in categorical variables, and the *t* test was used to examine differences in continuous variables. The primary outcome was parental intent to vaccinate in the next 12 months. National-level and state-level estimates for parental absence of intent to initiate and to complete the vaccine series were computed using survey-weighted frequency procedures.

The first secondary outcome was the reason for absence of intent among parents to initiate and complete the HPV vaccine series. A survey design-adjusted Wald *F* test with Bonferroni correction for multiple comparisons was used for bivariate analysis that compared the proportion of parents of unvaccinated and vaccine-initiating adolescents selecting a given reason as the main reason for their lack of intent. Parental reasons for not initiating versus completing the HPV vaccine series were stratified by the sex of the adolescents. Analyses were restricted to adolescents with information on parental reasons for no intent to vaccinate. The subset of adolescents with information verified by a health-care provider was used for sensitivity analysis to examine the robustness of estimates.

A recommendation from a health-care provider is an important mediator for the initiation and completion of the HPV vaccine series.<sup>15</sup> Therefore, the analyses were stratified on the basis of the history of recommendation from a health-care provider to initiate the HPV vaccine. The second secondary outcome was the association between health-care provider recommendation and parental intent. A multivariable logistic regression model adjusted for sociodemographic variables was used to examine the characteristics associated with receiving a health-care provider recommendation and parental intent to initiate the vaccine series. Similarly, we used a multivariate logistic regression model to examine the factors associated with lack of intent among parents of unvaccinated adolescents who received a recommendation from a health-care provider to initiate the HPV vaccine, and those who did not receive such a recommendation.

All analyses were restricted to participants with non-missing data for the outcome of interest and were adjusted for strata and weights using the SAS survey procedures to account for the complex survey design. Statistical significance was tested at  $p < 0.05$ . All analyses were done according to the analytical guideline for the NIS-Teen data using the SAS statistical software (version 9.4).<sup>16</sup>

### Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

### Results

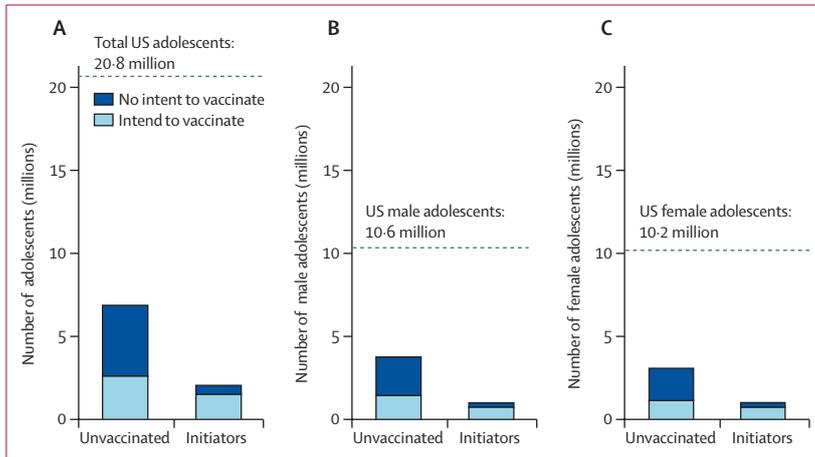
Between Jan 5, 2017, and Jan 31, 2019, the parent or caregiver of 82 297 US adolescents aged 13–17 years completed the NIS-Teen survey. 30 558 (37.1%) adolescents were

unvaccinated (ie, received zero doses), and 9073 (10·8%) adolescents had initiated (ie, received only one dose) the HPV vaccine series according to their parents or caregivers. The characteristics of unvaccinated adolescents and those who received one dose are shown in the appendix (p 3). Using the survey data, we estimated

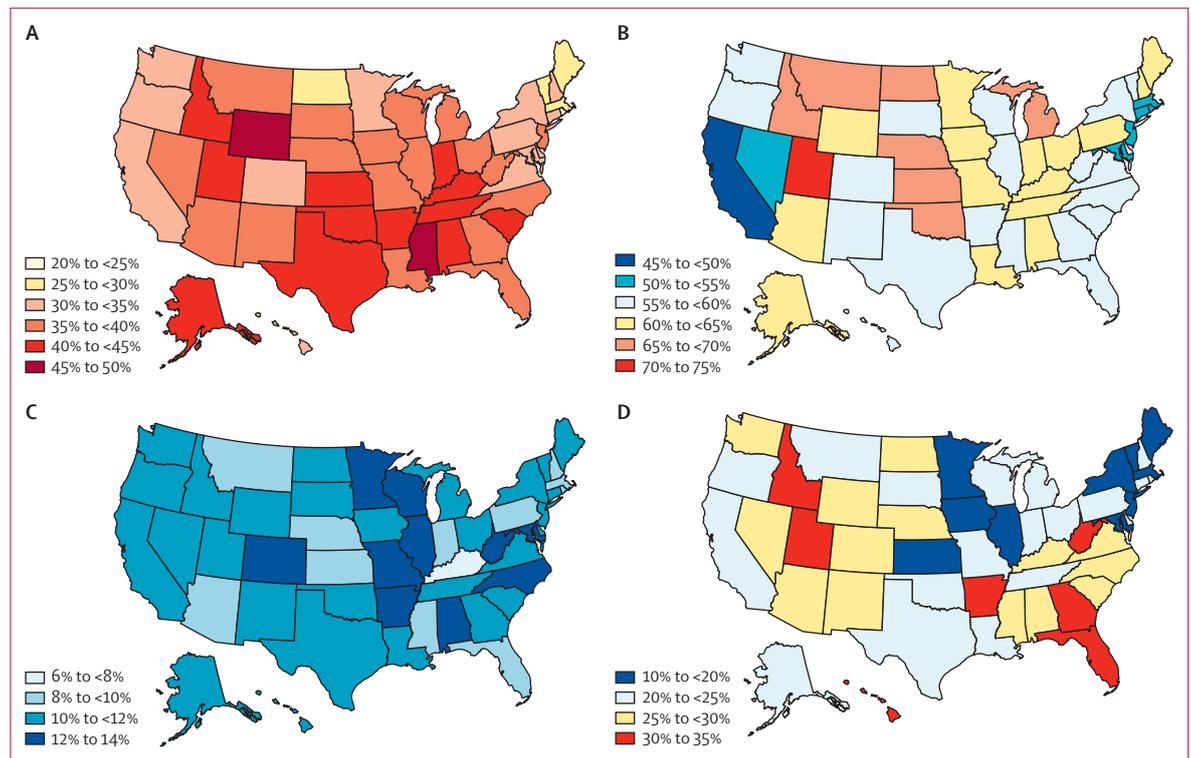
that 7·7 million of the US adolescent population aged 13–17 years during 2017–18 (20·8 million) were unvaccinated, and that 2·2 million were initiators of the HPV vaccination regimen.

Information on parental intent was available for 29086 (95·2%) unvaccinated adolescents and 9072 (99·9%) initiators. Overall, 17171 (58·0%) of the 29086 parents of unvaccinated adolescents did not intend to initiate the HPV vaccine series; we estimated that proportionally this would translate to parents of 4·3 million of 7·3 million unvaccinated US adolescents with no intention to initiate the vaccine series (figure 1A). The proportion of unvaccinated boys with parental lack of intent was 57·0% (9755/16650; estimated to equate to 2·3 million of 4·1 million US adolescent boys; figure 1B) and the proportion of unvaccinated girls with parental lack of intent was 59·4% (7416/12436; estimated to equate to 1·9 million of 3·3 million US adolescent girls; figure 1C).

In the state-specific analysis of unvaccinated adolescents, parental lack of intent was 50% or more in the District of Columbia and across all states (except California [49·9%]), regardless of whether they have a legislative order to receive the HPV vaccine for school entry. Notably, lack of intent in Idaho (69·9% [328/472; estimated to equate to 33835 of 48402 adolescents in Idaho]) and Utah (72·6% [377/524; estimated to equate to 75477 of



**Figure 1: Estimated number of US adolescents by HPV vaccination status (unvaccinated or initiators) and parental intent to vaccinate**  
 (A) All adolescents. (B) Male adolescents. (C) Female adolescents. Unvaccinated adolescents received no doses of the HPV vaccine series, initiators received one dose of the HPV vaccine series. HPV=human papillomavirus.



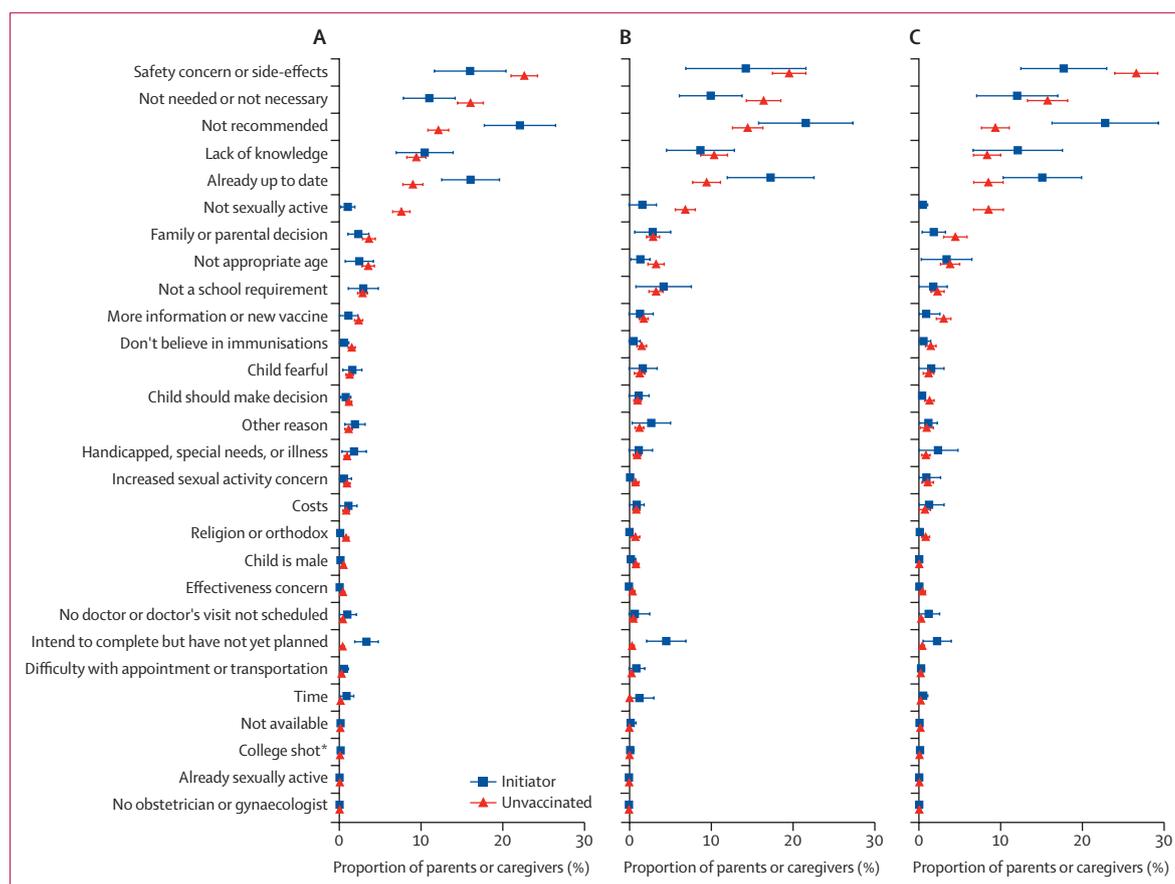
**Figure 2: Parental lack of intent to initiate and complete the HPV vaccine series by state in the USA**  
 Data are from the National Immunization Survey-Teen 2017–18. (A) Proportion of unvaccinated adolescents. (B) Proportion of unvaccinated adolescents with no parental intent to initiate the HPV vaccine series. (C) Proportion of adolescents who have initiated the HPV vaccine series, and received only one dose. (D) Proportion of adolescents who initiated the HPV vaccine series with no parental intent to complete the series. HPV=human papillomavirus.

103 988 adolescents in Utah) was higher compared with other states (figure 2; appendix p 4–6). More than 65% of parents of unvaccinated adolescents in Kansas, Michigan, Montana, Nebraska, North Dakota, and Oklahoma had no intention to initiate the HPV vaccine series. In Wyoming, 61·9% (368/597; estimated to equate to 10 609 of 17 143 adolescents in Wyoming) of parents of unvaccinated adolescents did not intend to initiate the series, and in Mississippi, that proportion was 57·1% (404/654; estimated to equate to 51 119 of 89 549 adolescents in Mississippi); Wyoming and Mississippi are the states with the lowest vaccination coverage in the USA.

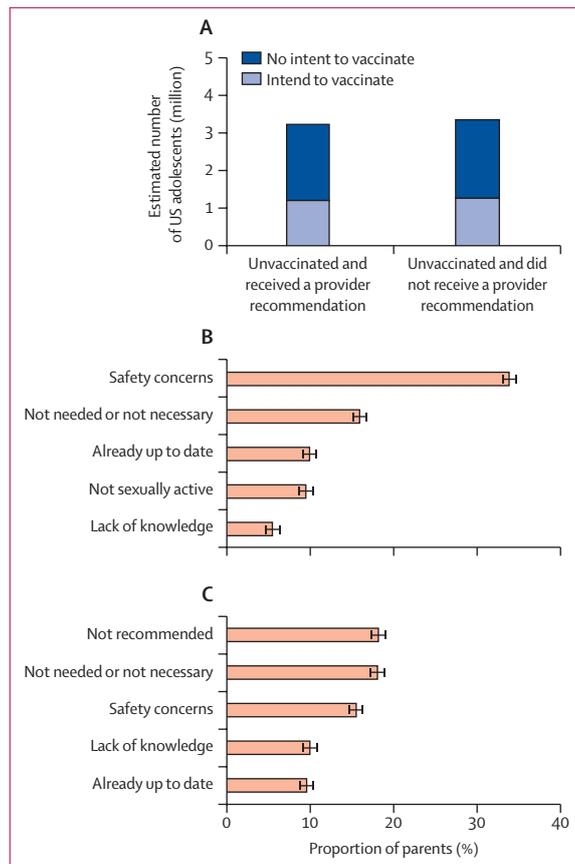
Parents of 23·5% (2116/9072) of adolescents who initiated the vaccine series did not intend to complete the series, which we estimated to equate to 0·5 million of 2·2 million adolescents (figure 1A). The proportion of boys with parental lack of intent to complete the series was 22·9% (1092/4717; estimated to equate to 0·2 million of 1·1 million boys who initiated the series in the USA; figure 1B) and for girls, that proportion was

24·1% (1024/4355; estimated to equate to 0·3 million of 1·1 million girls; figure 1C). In the state-specific analysis, parental lack of intent to complete the HPV vaccine series was high for initiators in Idaho (33·7% [48/139; estimated to equate to 4829 of 14 342 initiators in Idaho] figure 2; appendix p 4) compared with other states. Lack of intent to complete the HPV vaccine series was more than 30% in Arkansas, Florida, Georgia, Hawaii, Idaho, Utah, and West Virginia. In the District of Columbia (11·2% [22/166; estimated to equate to 319 of 2843 initiators in the District of Columbia]) and Rhode Island (20·4% [21/112; estimated to equate to 1061 of 5191 initiators in Rhode Island]), where the HPV vaccine is mandated, lack of intent to complete the series was low compared with other states.

The five most common reasons for parental lack of intent to initiate the HPV vaccine series in unvaccinated adolescents were “safety concerns” (22·8% [4182/16 455]), “not needed or not necessary” (16·1% [2807]), “not recommended” (12·2% [2099]), “lack of knowledge” (9·5% [1687]), and “already up-to-date” (9·0% [1530]);



**Figure 3: Parental reasons for lack of intent to vaccinate by HPV vaccination status of the adolescent**  
 Data are from the National Immunization Survey-Teen 2017–18. The 28 reasons for lack of intent included in the survey and the proportion of parents who responded yes for each listed reason are illustrated. Unvaccinated adolescents received zero doses of the HPV vaccine series, initiators received only one dose of the HPV vaccine series. Parents were asked to identify the main reason; therefore, responses are mutually exclusive. (A) The most common reasons for parents of the overall adolescent population. (B) The most common reasons for parents of boys. (C) The most common reasons for parents of girls. Error bars represent the 99·8% CIs. HPV=human papillomavirus. \*Those who answered “college shot” believe the vaccination is needed when the adolescent enters university (ie, at age 18 years).



**Figure 4: Intent and reasons for lack of intent among parents of unvaccinated adolescents stratified by history of a recommendation from a health-care provider to initiate the HPV vaccine series** (A) The estimated number of unvaccinated US adolescents with and without a recommendation from a health-care provider to vaccinate, and whether their parents intend to get them vaccinated. (B) The five most common reasons for no parental intent to vaccinate among parents with a recommendation from a health-care provider to vaccinate. (C) The five most common reasons for no parental intent to vaccinate among parents with no recommendation from a health-care provider to vaccinate. Error bars represent 99.8% CIs.

figure 3A). “Safety concerns” was the most common reason for lack of intent to initiate the series for both male (19.6% [2037/9311]; figure 3B) and female (26.6% [2145/7144]; figure 3C) adolescents. For the total population of initiators who completed the survey, “not recommended” (22.2% [440/1944]) was the most common reason for the lack of intent to complete the vaccine series (figure 3A). “Safety concerns” (16.1% [320/1944]), “already up-to-date” (16.1% [312]), “not needed or not necessary” (11.1% [237]), and “lack of knowledge” (10.5% [216]) were also among the five most common reasons for the lack of intent to complete the vaccine series. In both boys (21.6% [218/998]) and girls (22.8% [222/946]), “not recommended” was cited by most parents as the main reason for lack of intent to complete the HPV vaccine series (figure 3B, 3C).

“Safety concerns” and “not needed or not necessary” were more frequently cited as main reasons by parents for

their lack of intent to initiate the HPV vaccine than for a lack of intent to complete the vaccine series by initiators. By comparison, “not recommended” and “already up-to-date” were more frequently reported by parents of initiators as the reason for lack of intent to complete the vaccine series than by parents of unvaccinated adolescents as reasons for lack of intent to start the series (appendix p 7). Statistically significant differences in the reasons behind parental intent between unvaccinated adolescents and initiators by sex are shown in appendix p 8 (boys) and appendix p 9 (girls). In sensitivity analysis restricted to the sample verified by a health-care provider, the five most common reasons for parental lack of intent among unvaccinated adolescents and initiators were the same as those in the main analysis (appendix p 10).

Results for the unvaccinated group were further stratified by recommendation from a health-care provider. Nationally, 45.5% [13 156/29 090] of unvaccinated adolescents and 90.5% [8291/9073] of those who received the first dose had reported receiving a recommendation to initiate the HPV vaccine series from a health-care professional. Despite a recommendation, 60.6% of parents of unvaccinated adolescents (7938/13 156; estimated to equate to 2.0 million of 3.3 million adolescents) had no intention to initiate the HPV vaccine series (figure 4A), and “safety concerns” was most commonly cited (33.7% [2680/7706]) as their primary reason for lack of intent (figure 4B). Similarly, 56.5% of parents of unvaccinated adolescents (8564/14656; estimated to equate to 2.1 million of 3.7 million adolescents) who did not receive a recommendation from a health-care provider had no intention for series initiation (figure 4A); among these parents, “not recommended” was the main reason (18.2% [1410/8119]) for not initiating the series (figure 4C). In the multivariate analysis, parents who had reportedly received a recommendation from a health-care provider to initiate the HPV vaccine were more likely to intend to vaccinate their adolescent than those who had not received a recommendation (odds ratio [OR] 1.11, 95% CI 1.01–1.22; appendix p 11).

Among those who reportedly had received a recommendation to initiate the HPV vaccine series from a health-care provider, female sex and older age of the adolescent, non-Hispanic white race, and higher household income (>US\$75 000) were associated with lower odds of parental intent to vaccinate (appendix p 12). Similarly, among those who did not receive a recommendation from a health-care provider to initiate the HPV vaccine series, older age of the adolescent, non-Hispanic white race, and household income of more than \$75 000 were associated with lower odds of parental intent. Having the survey respondent be a mother caregiver (versus father) was associated with lower odds of parental intent to vaccinate among those who received a recommendation from a health-care provider, whereas a father caregiver was associated with lower intent among those who did not receive a recommendation.

## Discussion

To our knowledge, our study is the first to comprehensively describe parental intent to initiate and complete the HPV vaccine series as well as reasons for parental lack of intent in the USA. Nationally, more than half of the parents of unvaccinated adolescents did not intend to initiate the HPV vaccine series. Additionally, parents of nearly a quarter of the adolescents who had received the first HPV vaccine dose had no intention to complete the series. These findings are troubling given that parental intent is an important determinant of HPV vaccine initiation and completion in adolescents.

In our state-specific analysis, we found that in Mississippi and Wyoming (where HPV vaccine series completion rates are the lowest in the nation: Mississippi 28·8% and Wyoming 30·9%),<sup>10</sup> nearly 60% of the parents of unvaccinated adolescents had no intention to initiate the vaccine series. These findings have important public health implications. If the parental lack of intent persists in these states, the triad of low initiation rates, low series completion rates, and a history of poor HPV vaccine coverage might compromise herd immunity. As a result, these states could face a disproportionately higher burden of HPV-associated cancers in future decades, compared with states with greater HPV vaccine coverage. Our state-specific findings also highlight the importance of HPV vaccination mandates. In the District of Columbia and Rhode Island where the HPV vaccine is mandated, the proportions of unvaccinated adolescents were the lowest in the nation, and parental lack of intent for series completion was also lower than the national average. These findings suggest that such mandates have been effective in overcoming HPV vaccine hesitancy and improving HPV vaccination coverage.

Safety concern was the most common reason for parental lack of intent to initiate the HPV vaccine series. Substantial declines in HPV vaccine uptake have occurred due to safety scares in several countries, including Japan in 2013, Ireland in 2014, Denmark in 2015, and Colombia in 2015.<sup>17–20</sup> A literature review of determinants of HPV vaccine hesitancy in Europe identified vaccine safety concerns as one of the most important reasons (48% in the UK and Italy, 69% in the Netherlands, 60% in Romania, and 54% in Greece) for parental lack of intent.<sup>21</sup> Our findings suggest that HPV vaccination coverage in the USA is also affected by high parental refusal or deferral largely driven by safety concerns. Social media has been recognised as a major source of unsubstantiated content related to vaccine safety in the USA.<sup>22,23</sup> In a recent survey of 1263 American parents, nearly a third had heard stories about HPV vaccine harms from social media. Notably, these parents were more likely to refuse (OR 8·9, 95% CI 4·1–19·3) the HPV vaccine than the parents who had never heard such stories.<sup>24</sup> A systematic literature review also identified safety concerns as a major barrier to HPV vaccination in the USA.<sup>15</sup> To counter misinformation and tackle safety

concerns in the USA, national informational campaigns (similar to those launched in Ireland and Denmark) are urgently needed.<sup>18,25</sup> Health-care providers can also have a vital role in combatting misinformation by educating parents about HPV vaccine safety and benefits, thereby reducing vaccine hesitancy among parents.

The main reason for not intending to complete the HPV vaccine series once initiated was a lack of a recommendation from a health-care provider for subsequent doses. This finding might be partly explained by knowledge gaps regarding the HPV vaccination dosing schedule among US physicians. A recent national survey of US paediatricians and family physicians showed that at least a third of health-care professionals had incorrect knowledge or reported not knowing about the number of doses recommended by the Advisory Committee on Immunization Practices.<sup>26</sup> The use of reminder systems at the point of care might help mitigate this issue. However, in the same national survey, less than 50% of US physicians were reportedly using evidence-based methods (eg, standing orders and alerts in the medical record), prompting the need for vaccination at the point of care.<sup>27</sup> Our findings, along with these data, highlight the need for increased use of these reminder systems to improve HPV vaccine series completion.

A lack of knowledge and believing that the vaccines were not needed or not necessary were other major reasons for parental lack of intent to initiate and complete the series. Many US adults have knowledge gaps regarding HPV: 45% of men and women in a national study from 2017–18 had never heard about HPV and the HPV vaccine, and less than 25% of adults knew that HPV causes anal, penile, and head and neck cancers.<sup>28</sup> Parents' beliefs might be a combined effect of individuals' knowledge of HPV, attitude, personal beliefs, social influences, and lack of a recommendation from a health-care provider.<sup>29</sup> A strong recommendation from a health-care provider can substantiate the need for the HPV vaccine. In particular, a high-quality recommendation (one that is strongly endorsed, has a cancer prevention message, and emphasises urgency) can help improve HPV vaccine initiation and completion rates.<sup>30</sup>

Our findings regarding lack of knowledge and parental vaccine hesitancy are consistent with data from Europe. Insufficient knowledge has been reported as a major barrier to vaccination among parents in Romania (81% in 2015), the Netherlands (67% in 2009–11), and Denmark (70% in 2010).<sup>21</sup> Similar to in the USA, absence of a provider recommendation is also an issue contributing towards parental vaccine hesitancy in Europe. Studies from Spain, Italy, France, and Denmark reported that nearly a third of hesitant parents never received any HPV vaccine recommendations.<sup>21</sup> In studies from Spain and Italy, an average of 26% of hesitant parents reported having been advised against HPV vaccine by their health-care providers, and 19% of parents in a study from Germany reported receiving similar advice.<sup>21</sup>

Collectively, these reasons, in addition to safety concerns, might be contributing to the growing sentiment of vaccine hesitancy that WHO has identified as one of the ten most substantial threats to global health.<sup>31</sup>

An important finding of our stratified analysis was that despite having received a recommendation from a health-care provider to initiate the HPV vaccine series, a substantial proportion (>60%) of parents had no intention to do so in 2017–18, with the majority reporting safety as their primary concern. This finding is troubling when compared with data from a 2010 NIS-Teen study; the proportion of parents with no intent to initiate the vaccine series despite recommendation from a health-care provider in 2010 was 43%. The increasing proportion of parents who are reluctant to vaccinate their adolescents despite recommendation from a health-care provider reflects a strong and growing sentiment of hesitancy towards the HPV vaccine in the USA. The same study showed that in 2010 parental hesitancy towards other adolescent vaccines was relatively low compared with the HPV vaccine—16.1% for the tetanus, diphtheria, pertussis vaccine, 9.7% for meningococcal conjugate vaccines.<sup>32</sup>

Our study has some limitations. First, respondents to the NIS-Teen survey are parents or caregivers of adolescents. Although the survey protocol seeks to identify the parent who is most knowledgeable regarding the immunisation status of the adolescent, it is possible that some respondents did not comply with this protocol. Second, a small proportion of parents of adolescents with HPV vaccine contraindication might have cited “not recommended” as a reason for not intending to vaccinate. Information regarding vaccine contraindication is unavailable in the data from NIS-Teen; therefore, estimates pertaining to “not recommended” as a reason for lack of intent to vaccinate should be interpreted within the context of this caveat. Third, it is possible that some parents (because of fear of judgment or because they do not believe in vaccines) might have chosen not to respond to the entire survey, or to skip specific questions in the survey. The non-random nature of such missing data might have led to an underestimation or overestimation of parameters in our study. Fourth, survey responses are prone to social desirability and recall bias. However, at least two previous studies have reported high concordance between parent-reported and provider-reported HPV vaccine series initiation (84–92%) in the NIS-Teen survey, concluding that the responses from parents are reasonably accurate.<sup>33,34</sup> Finally, the survey asks parents to report only the main reason for their lack of intent to vaccinate; parents of some adolescents might have had more than one reason for this lack of intent. Nevertheless, capturing the primary reason allowed us to identify the most heavily weighted concern of parents for their hesitancy towards the HPV vaccine. Despite these limitations, the principal strength of our study is that it is generalisable to the US adolescent population and, to the

best of our knowledge, provides the most comprehensive information on parental intent for HPV vaccination in the USA.

Our findings show that HPV vaccine hesitancy is prevalent in the USA. Safety concerns are a substantial contributing factor to parental lack of intent to initiate the HPV vaccine series, and a lack of recommendations from health-care providers contributes substantially to parental lack of intent to complete the series. Although progress has been made in boosting HPV vaccination rates, coverage in 2018 did not improve among female adolescents aged 13–17 years (53.1% in 2017 and 53.7% in 2018) or in adults aged 18–26 years (21.6% in 2017 and 21.5% in 2018).<sup>7,35</sup> Our findings suggest that parental reluctance for their adolescents to receive the HPV vaccine might be a major impediment to achieving optimal vaccination coverage in the USA. If these trajectories continue, the Healthy People 2020 goal of achieving 80% HPV vaccination coverage among US adolescents will be far beyond reachable, particularly in states with low vaccination coverage and high parental hesitancy. Aggressive and coordinated efforts among health-care providers, parents, media, policy makers, and state health agencies are urgently needed to combat HPV vaccine hesitancy.

#### Contributors

KS and AAD designed the study. Data was analysed by KS, YZ, and AAD. KS and AAD drafted the manuscript with input from all authors. All authors approved the final version of the report.

#### Declaration of interests

ARG has received financial support from Merck, outside the submitted work, for her role as a member of several advisory boards and as a speaker at conference symposia. AAD has received consulting fees from Merck on unrelated projects, outside of the submitted work. All other authors declare no competing interests.

#### Data sharing

The National Immunization Survey Teen data, documentation, and codebook are available for download at <https://www.cdc.gov/vaccines/imz-managers/nis/datasets-teen.html>. Statistical code is available on request from KS ([kalyani.b.sonawane@uth.tmc.edu](mailto:kalyani.b.sonawane@uth.tmc.edu)).

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#### References

- 1 Van Dyne EA, Henley SJ, Saraiya M, Thomas CC, Markowitz LE, Benard VB. Trends in human papillomavirus-associated cancers—United States, 1999–2015. *MMWR Morb Mortal Wkly Rep* 2018; **67**: 918–24.
- 2 Deshmukh AA, Suk R, Shiels MS, et al. Recent trends in squamous cell carcinoma of the anus incidence and mortality in the United States, 2001–2015. *J Natl Cancer Inst* 2019; published online Nov 19. <https://doi.org/10.1093/jnci/djz219>.
- 3 Sonawane K, Nyitray AG, Nemutlu GS, Swartz MD, Chhatwal J, Deshmukh AA. Prevalence of human papillomavirus infection by number of vaccine doses among US women. *JAMA Netw Open* 2019; **2**: e1918571.

- 4 Villa A, Patton LL, Giuliano AR, et al. Summary of the evidence on the safety, efficacy, and effectiveness of human papillomavirus vaccines: umbrella review of systematic reviews. *J Am Dent Assoc* 2020; **151**: 245–54.
- 5 Sonawane K, Suk R, Chiao EY, et al. Oral human papillomavirus infection: differences in prevalence between sexes and concordance with genital human papillomavirus infection, NHANES 2011 to 2014. *Ann Intern Med* 2017; **167**: 714–24.
- 6 Chaturvedi AK, Graubard BI, Broutian T, et al. Effect of prophylactic human papillomavirus (HPV) vaccination on oral HPV infections among young adults in the United States. *J Clin Oncol* 2018; **36**: 262–67.
- 7 Meites E, Szilagyi PG, Chesson HW, Unger ER, Romero JR, Markowitz LE. Human papillomavirus vaccination for adults: updated recommendations of the advisory committee on immunization practices. *MMWR Morb Mortal Wkly Rep* 2019; **68**: 698–702.
- 8 Iversen OE, Miranda MJ, Ulied A, et al. Immunogenicity of the 9-valent HPV vaccine using 2-dose regimens in girls and boys vs a 3-dose regimen in women. *JAMA* 2016; **316**: 2411–21.
- 9 Walker TY, Elam-Evans LD, Yankey D, et al. National, regional, state, and selected local area vaccination coverage among adolescents aged 13–17 years—United States, 2018. *MMWR Morb Mortal Wkly Rep* 2019; **68**: 718–23.
- 10 Walker TY, Elam-Evans LD, Yankey D, et al. National, regional, state, and selected local area vaccination coverage among adolescents aged 13–17 years—United States, 2017. *MMWR Morb Mortal Wkly Rep* 2018; **67**: 909–17.
- 11 Dempsey AF, Zimet GD, Davis RL, Koutsky L. Factors that are associated with parental acceptance of human papillomavirus vaccines: a randomized intervention study of written information about HPV. *Pediatrics* 2006; **117**: 1486–93.
- 12 Kahn JA, Ding L, Huang B, Zimet GD, Rosenthal SL, Frazier AL. Mothers' intention for their daughters and themselves to receive the human papillomavirus vaccine: a national study of nurses. *Pediatrics* 2009; **123**: 1439–45.
- 13 Downs JS, de Bruin WB, Fischhoff B. Parents' vaccination comprehension and decisions. *Vaccine* 2008; **26**: 1595–607.
- 14 National Center for Immunization and Respiratory Diseases. National immunization survey-teen. A user's guide for the 2017 public-use data file. Centers for Disease Control and Prevention. <https://www.cdc.gov/vaccines/imz-managers/nis/downloads/NIS-TEEN-PUF17-DUG.pdf> (accessed Feb 10, 2020).
- 15 Holman DM, Benard V, Roland KB, Watson M, Liddon N, Stokley S. Barriers to human papillomavirus vaccination among US adolescents: a systematic review of the literature. *JAMA Pediatr* 2014; **168**: 76–82.
- 16 National Center for Health Statistics. Statistical methodology of the national immunization survey, 2005–2014. Centers for Disease Control and Prevention. 2017. <https://www.cdc.gov/vaccines/imz-managers/nis/methods.html> (accessed March 16, 2020).
- 17 Hanley SJ, Yoshioka E, Ito Y, Kishi R. HPV vaccination crisis in Japan. *Lancet* 2015; **385**: 2571.
- 18 Corcoran B, Clarke A, Barrett T. Rapid response to HPV vaccination crisis in Ireland. *Lancet* 2018; **391**: 2103.
- 19 Suppli CH, Hansen ND, Rasmussen M, Valentiner-Branth P, Krause TG, Mølbak K. Decline in HPV-vaccination uptake in Denmark—the association between HPV-related media coverage and HPV-vaccination. *BMC Public Health* 2018; **18**: 1360.
- 20 Castro CJ. The unbelievable story of the HPV vaccination program in Colombia...from a beautiful dream to a nightmare! *Proc Am Soc Clin Oncol* 2018; **4** (suppl 2): 169s.
- 21 Karafillakis E, Simas C, Jarrett C, et al. HPV vaccination in a context of public mistrust and uncertainty: a systematic literature review of determinants of HPV vaccine hesitancy in Europe. *Hum Vaccin Immunother* 2019; **15**: 1615–27.
- 22 Briones R, Nan X, Madden K, Waks L. When vaccines go viral: an analysis of HPV vaccine coverage on YouTube. *Health Commun* 2012; **27**: 478–85.
- 23 Keelan J, Pavri V, Balakrishnan R, Wilson K. An analysis of the human papilloma virus vaccine debate on MySpace blogs. *Vaccine* 2010; **28**: 1535–40.
- 24 Margolis MA, Brewer NT, Shah PD, Calo WA, Gilkey MB. Stories about HPV vaccine in social media, traditional media, and conversations. *Prev Med* 2019; **118**: 251–56.
- 25 Hansen PR, Schmidtlaicher M, Brewer NT. Resilience of HPV vaccine uptake in Denmark: decline and recovery. *Vaccine* 2020; **38**: 1842–48.
- 26 Kempe A, O'Leary ST, Markowitz LE, et al. HPV vaccine delivery practices by primary care physicians. *Pediatrics* 2019; **144**: e20191475.
- 27 The Community Guide. Vaccination programs: provider reminders. <https://www.thecommunityguide.org/findings/vaccination-programs-provider-reminders> (accessed April 4, 2020).
- 28 Suk R, Montealegre JR, Nemutlu GS, et al. Public knowledge of human papillomavirus and receipt of vaccination recommendations. *JAMA Pediatr* 2019; **173**: 1099.
- 29 Allen JD, Othus MK, Shelton RC, et al. Parental decision making about the HPV vaccine. *Cancer Epidemiol Biomarkers Prev* 2010; **19**: 2187–98.
- 30 Gilkey MB, McRee AL. Provider communication about HPV vaccination: a systematic review. *Hum Vaccin Immunother* 2016; **12**: 1454–68.
- 31 WHO. Ten threats to global health in 2019. <https://www.who.int/emergencies/ten-threats-to-global-health-in-2019> (accessed April 8, 2020).
- 32 Darden PM, Thompson DM, Roberts JR, et al. Reasons for not vaccinating adolescents: national immunization survey of teens, 2008–2010. *Pediatrics* 2013; **131**: 645–51.
- 33 Dorell CG, Jain N, Yankey D. Validity of parent-reported vaccination status for adolescents aged 13–17 years: national immunization survey-teen, 2008. *Public Health Rep* 2011; **126** (suppl 2): 60–69.
- 34 Hirth J, Kuo YF, Laz TH, et al. Concordance of adolescent human papillomavirus vaccination parental report with provider report in the national immunization survey-teen (2008–2013). *Vaccine* 2016; **34**: 4415–21.
- 35 Boersma P, Black LI. NCHS data brief: human papillomavirus vaccination among adults aged 18–26, 2013–2018. <https://www.cdc.gov/nchs/data/databriefs/db354-h.pdf> (accessed March 18, 2020).