



Human Papillomavirus Vaccination Trends, Barriers, and Promotion Methods Among American Indian/Alaska Native and Non-Hispanic White Adolescents in Michigan 2006–2015

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Published online: 19 January 2019

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Abstract

Human papillomavirus (HPV) infection, the most common sexually transmitted disease in the US, is a preventable cause of cancer. HPV vaccination has the potential to prevent 90% of HPV-related cancer cases but is underutilized, especially among American Indian/Alaska Native (AI/AN) adolescents. The objectives of this study were to (1) describe trends and identify predictors of HPV vaccination initiation and completion in Michigan's AI and Non-Hispanic White children age 9 through 18 years and (2) to identify barriers to HPV vaccination and promotion methods at the tribal, state, and local levels in Michigan. Data from Michigan's immunization information system from 2006 to 2015 were used for analysis. Additionally, semi-structured interviews were conducted with public health professionals across the state to identify barriers to and promoters of HPV vaccination. Predictors for vaccine initiation included being female, AI/AN, and living in high poverty zip code. Predictors of vaccine completion were female gender and younger age at vaccine initiation. Barriers to vaccination included misinformation and weak or inconsistent provider recommendations. Strategies used by health professionals to promote HPV vaccination included immunization summaries, vaccine information statements, the Vaccines for Children (VFC) program, and provider training. Findings suggested the need for education of parents to demystify HPV vaccine benefits and risks and provider training for more consistent recommendations.

Keywords Human papillomavirus · American Indian · Michigan · Cervical cancer · HPV vaccine · Vaccine promotion

Introduction

Human papillomavirus (HPV) refers to a family of more than 150 viruses that are spread through sexual activity [1, 2]. Most strains of HPV are asymptomatic and resolve without treatment, but approximately 10% of HPV strains lead to

issues such as genital warts and cancers of the anus, cervix, throat, penis, vagina, and vulva. Strains 6 and 11 cause the majority of genital warts, and 80% of HPV-related cancers are caused by strains 16 and 18. Given that 9 out of 10 people in the US will become infected with at least one strain of HPV, promoting effective prevention strategies is a pressing public health issue [3].

HPV vaccine is important in prevention and control of cervical cancer and other HPV-related conditions. According to the most current guidelines established by the Centers for Disease Prevention and Control (CDC), all children who are 11 or 12 years of age are recommended to get two shots of HPV vaccines 6 to 12 months apart [1]. The HPV vaccine series can be started at age 9 years, and individuals who did not get vaccinated when they were young may get HPV vaccine through age 26 for women and age 21 for men. Currently, three HPV vaccines are available in the U.S. Food and Drug Administration has approved Gardasil, a quadrivalent (Types 6, 11, 16, 18) vaccine in 2006, Cervarix, bivalent

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(Types 16, 18) in 2009, and Gardasil 9, a 9-valent (Types 16, 18, 31, 33, 45, 52, and 58) vaccine in 2014 [4].

Despite the effectiveness of HPV vaccines at preventing cancer, known barriers exist to vaccine initiation and completion. Since the CDC recommendations came out in 2006, HPV vaccination initiation and completion rates have increased consistently, but at a slower rate than other teen vaccines [5]. Further, persistent disparities exist in vaccination completion. In 2015, American Indian/Alaskan Native (AI/AN) adolescents had the lowest completion (39%) compared to other ethnic/racial groups (Non-Hispanic White, NHW 40%, Black 41%, Hispanic 46%, Asian 54%) [6]. The underutilization of HPV vaccine among AI/ANs is important because this population group has particularly high cervical cancer incidence and mortality rates, as well as elevated incidence and mortality rates for colorectal cancers in certain regions, including the Northern Plains [7]. In spite of these continuous disparities, few studies have examined barriers and promoters of HPV vaccination among AI/AN adolescents.

Michigan is home to 12 federally recognized AI tribes. This study was implemented in partnership with Michigan Department of Health and Human Services and Intertribal Council of Michigan to examine the HPV vaccine trends among AI/AN adolescents and make recommendations to improve the HPV vaccine coverage in this population. The objectives of the study were to: (1) compare the HPV vaccine coverage between AI/AN adolescents and NHW adolescents, (2) identify factors associated with the initiation and completion of HPV vaccine series, and (3) identify health professionals' perspectives regarding promoters and barriers to HPV vaccine initiation among AI/AN youths.

Methods

A secondary data analysis of Michigan Care Improvement Registry (MCIR) 2005–2015 was conducted to examine the HPV vaccination coverage and to identify factors associated with the initiation and completion of HPV vaccination series. Also, semi-structured interviews of health care providers and public health professionals who work for tribal communities were conducted to identify promoters and barriers to HPV vaccine initiation.

MCIR Data Analysis

Data Source and Eligibility

Michigan requires all immunizations administered to children under the age of 20 born after 31 December 1993 to be reported to its immunization information system within the MCIR. We used MCIR data on HPV vaccine doses provided

between 8 June 2006 and 5 July 2015. The study sample consisted of AI/AN or NHW Michigan residents who were born in Michigan between 1 January 1997 and 5 July 2004.

Variables

Vaccine initiation and vaccine completion were the two outcome variables examined in this study. The individual who had at least one dose of HPV vaccine during the data period was considered to have “initiated” the HPV vaccine series. At the time of the data analysis, three doses were required for the series completion. Thus, for the “completion” the individual had to have at least three doses during the data period. The exposure variable was the race (AI/AN or NHW). The MCIR data had been linked with the Michigan birth certificate database, which provides the race/ethnicity information of mothers. For the purpose of this study, we identified an individual as AI/AN if the mother's race was recorded as AI/AN in the birth certificate. Similarly, we identified an individual as NHW if the mother's race was recorded as NHW in the birth certificate.

Other variables examined include the child's gender, vaccine initiation age, the percentage of individuals under federal poverty line in the zip code area the child was living, number of Vaccines for Children (VFC) providers in the zip code area where the child was living, the type of vaccine clinic (private, health department, school, tribal, other), and funding eligibility (private, VFC-eligible, other). The number of VFC sites (a federally funded program for free vaccination to children with no health insurance or who cannot afford its cost) in a given zip code area was used as a proxy for the accessibility of vaccination services [8]. Because the household income information was not available from the MCIR database, we used US Census data to calculate the percentage of individuals in each zip code who live below 100% of the federal poverty line.

Analysis

The vaccine initiation rate was calculated by dividing the number of individuals who received at least one dose of vaccine by the number of individuals who were age-eligible (11 to 21 years of age) to receive vaccine in a given year. The vaccine completion rate was calculated by dividing the number of individuals who received at least three doses by the number of individuals who had at least one dose (i.e., who initiated the vaccine series in a given year). In order to identify factors associated with vaccine initiation and completion, we first conducted univariate logistic regression. We also conducted to multivariable logistic regression analysis to examine whether the mother's race (AI/AN or NHW) has a significant association with vaccine initiation and completion after adjusting for

other potential confounders. All analyses were conducted using SAS statistical software, version 9.4.

Interviews of Providers and Public Health Professionals

In order to obtain a geographically representative sample, a total of 14 professionals from seven sites across Michigan were interviewed. Interviewees included three nurses, two mid-level providers, three office administrators, and six health promotion specialists from a variety of settings including federally qualified health centers, local health departments, the state immunization program, tribal health centers, and school-based health centers (SBHCs). An interview guide was developed to inquire about the HPV vaccination intervention programs and environmental, socio-cultural and personal barriers to HPV vaccination use among AI/AN adolescents. The interviews were audio recorded and transcribed verbatim. The first author (BMK) conducted a thematic analysis to identify codes. The first author and another author (SWG) reviewed the codes and grouped them into two themes (promoters and barriers) and selected quotes that are reflective of these themes. This study was approved by the University of Nebraska Medical Center and Michigan Department of Health and Human Services Institutional Review Boards and by the Inter-Tribal Council of Michigan.

Results

Trends and Predictors of Vaccination Initiation and Completion

Table 1 shows demographic characteristics and vaccine initiation status among 4722 AI/AN and 679,787 NHW adolescents who met the inclusion criteria. There were no significant differences in gender among AI/AN and NHW youths. Over half (51.3%) of AI/AN adolescents lived in the areas where the poverty rate is 17% or higher, compared to 31.4% of NHWs. Regarding the number of VFC sites in a given zip code area, it was found that 23.7% of AI/AN adolescents lived in areas with five or more sites, compared to 17.9% of NHWs. During the entire period, the percentage of adolescents who initiated HPV vaccine was significantly higher in the AI/AN sample compared to the NHW sample (47.5% vs. 36.4%).

Table 2 shows the results for vaccine initiation. Results of the univariate and multivariable analyses were similar. Multivariable analysis shows that males were less likely to initiate than females [adjusted odds ratio (aOR)=0.61; 95% confidence interval (CI) 0.61, 0.62], most likely due to a delayed recommendation (i.e., the recommendation for males had not been issued until 2010). AI/ANs had 1.55 times higher aOR of initiation than NHWs (95% CI 1.45, 1.64). Interestingly, compared to adolescents who lived in the lowest poverty areas, adolescents who lived in the highest poverty level had higher aOR of initiating

Table 1 Demographic characteristics and vaccine initiation status of the sample

Variables	American Indian/Alaska Native (n=4,722)	Non-Hispanic White (n=679,787)	P-values
Child's gender			0.1153
Female	49.9	48.7	
Male	50.1	51.3	
% Under poverty			<0.0001
< 8	12.5	28.9	
9–12	21.2	23.4	
13–16	15.3	16.3	
17–21	24.9	15.5	
≥ 22	26.1	15.9	
Number of Vaccines for Children providers in zip code area			<0.0001
0	20.9	22.2	
1	20.5	18.4	
2–4	34.9	41.5	
≥ 5	23.7	17.9	
Vaccine initiation			<0.0001
Yes (≥ 1 shots)	47.5	36.4	
No (0 shot)	52.5	63.6	

Table 2 Unadjusted and adjusted odds ratios for initiation 8 of HPV vaccination

Variables	Numbers	OR	95% CI	aOR	95% CI
Gender					
Female	333,571	Ref.		Ref.	
Male	350,938	0.63	0.62–0.64	0.61	0.61–0.62
Mother's race					
Non-Hispanic White	679,787	Ref.		Ref.	
American Indian/Alaska Native	4722	1.59	1.50–1.68	1.55	1.46–1.64
% Under poverty					
< 8	197,117	Ref.		Ref.	
9–12	159,817	1.04	1.03–1.05	1.04	1.02–1.05
13–16	111,314	1.18	1.17–1.2	1.19	1.17–1.21
17–21	106,832	1.20	1.18–1.22	1.22	1.20–1.24
≥ 22	109,430	1.32	1.30–1.34	1.36	1.34–1.38
Number of Vaccines for Children providers in zip code area					
0	151,997	0.98	0.96–0.99	1.01	0.99–1.03
1	125,851	Ref.		Ref.	
2–4	284,068	1.02	1.005–1.03	1.03	1.01–1.04
≥ 5	122,594	1.02	1.002–1.04	0.97	0.95–0.99

Logistic regression

Number of vaccine initiated 249,508 versus number of vaccine uninitiated 435,002

aOR adjusted odds ratio, CI confidence interval

the vaccine series (aOR = 1.36; 95% CI 1.34–1.38). Adolescents who lived in zip code areas with ≥ 5 VFC providers had a slightly lower aOR of initiation as compared to ones who lived in zip code areas with one VFC provider (aOR = 0.97, 0.05% CI 0.95, 0.99).

Table 3 shows results for vaccine completion. Results of the univariate and multivariable analyses were similar. Multivariable analysis shows that males were less likely to complete the vaccine series than females (aOR = 0.62; 95% CI 0.61, 0.63) but there was no statistically significant difference between AI/ANs and NHWs. Children who started the vaccine series before the recommended age (but after the minimum age) had 2.5 times higher odds to complete the series than those who started at recommended age (95% CI 2.38, 2.64). Although there was not a clear trend, adolescents living in communities with the highest poverty rate had lowest aOR of completing vaccines as compared to their counterparts with lowest poverty rate. Adolescents who received the vaccine at health departments and other facility types were less likely to complete the series (aOR = 0.71; 95% CI 0.69, 0.73).

The 3+ completion rates increased over time, regardless of gender and race (Fig. 1). AI/AN rates were higher than NHW rates regardless of gender. Rates for male adolescents, although increasing over time, did not catch up to females, as the vaccine recommendation for males was not issued until 2010.

Barriers to and Promoters of Vaccination

Interview respondents identified several barriers to HPV vaccination, as well as strategies that are utilized to promote vaccination among AI/AN adolescents. Barriers and promoters relevant to parents' and adolescents' knowledge and beliefs are presented first, followed by barriers and promoters relevant to clinical providers.

Parent and Patient Knowledge and Beliefs

The most commonly mentioned barrier to HPV vaccination was parent and adolescent misinformation, which led to misunderstandings about who should get the vaccine, side effects, and safety.

The biggest barrier is the information on the internet, the inaccurate information. It says all kinds of bad things can happen from the [HPV vaccine] that aren't true... we're constantly trying to battle that.

Additionally, some respondents reported encountering concerns from parents about the potential side effects of the vaccine.

Parents are always saying 'Oh it's too new,' 'you haven't used it long enough,' 'you don't know all the

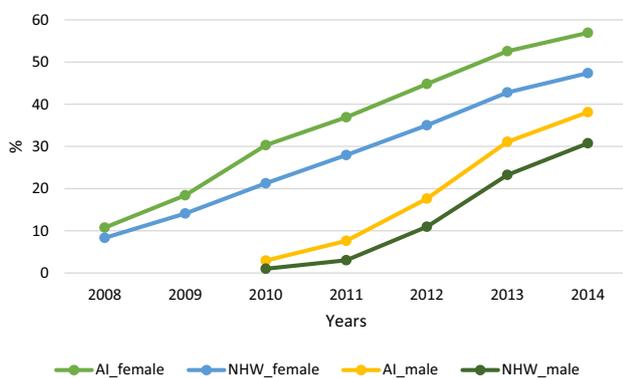
Table 3 Unadjusted and adjusted odds ratios for HPV vaccine completion

Variables	Numbers	OR	95% CI	aOR	95% CI
Gender					
Female	132,840	Ref.		Ref.	
Male	105,231	0.57	0.56–0.58	0.62	0.61–0.63
Vaccine initiation age (years)					
Before recommended age (9 and 10)	8866	2.62	2.49–2.75	2.50	2.38–2.64
Recommended age (11 and 12)	131,195	Ref.		Ref.	
Catch-up age (13+)	98,010	0.72	0.71–0.73	0.76	0.74–0.77
Mother's race					
Non-Hispanic White	235,851	Ref.		Ref.	
American Indian/Alaska Native	2220	1.05	0.97–1.15	1.05	0.95–1.15
% Under poverty					
< 8	61,444	Ref.		Ref.	
9–12	52,936	0.98	0.96–1.00	0.98	0.96–1.00
13–16	40,534	0.99	0.97–1.02	1.01	0.98–1.03
17–21	39,937	1.03	1.00–1.05	1.03	1.00–1.06
≥ 22	43,220	0.94	0.92–0.96	0.94	0.91–0.96
Number of Vaccines for Children providers in zip code area					
0	51,236	1.02	0.99–1.04	1.02	0.99–1.04
1	43,363	Ref.		Ref.	
2–4	99,968	1.06	1.03–1.08	1.05	1.02–1.07
≥ 5	43,504	1.07	1.04–1.10	1.07	1.04–1.10
Vaccine clinic facility type					
Private	205,870	Ref.		Ref.	
Health department	26,860	0.71	0.69–0.73	0.71	0.69–0.73
School	3649	0.99	0.92–1.05	1.10	1.03–1.18
Tribal	1386	1.04	0.94–1.16	1.06	0.95–1.20
Other	306	0.46	0.37–0.59	0.57	0.45–0.72
Funding eligibility					
Private	135,835	Ref.		Ref.	
Vaccines for Children-Eligible	5323	0.90	0.88–0.91	0.90	0.88–0.91
Other	96,916	1.1	1.09–1.22	1.11	1.05–1.17

Logistic regression

Number of vaccine completed 127,945 versus number of vaccine uncompleted 110,126)

aOR adjusted odds ratio, CI confidence interval

**Fig. 1** Time trend of completion rates of HPV vaccination among American Indians/Alaska Natives (AI/AN) and Non-Hispanic Whites (NHW) 2008–2014

side effects yet,' and 'how do you know what's going to happen in 20 years?'

Respondents mentioned focusing on delivering high-quality information to overcome these barriers and promote vaccination initiation and completion. Most respondents noted that reviewing the MCIR immunization summary sheet that explains which vaccines are due or overdue, at every visit can increase vaccination initiation and completion.

The best way we promote [the HPV vaccine] is by doing an immunization review at every visit, and reminding the [patient] that they're still eligible for it, and that we recommend it.

Many providers utilize vaccine information statements (VISs) in order to encourage vaccination. VISs are information sheets produced by the CDC that explain the risks and benefits of a vaccine to potential vaccine recipients [9]. Federal law requires that healthcare staff provide a VIS to a patient, parent, or legal representative before each dose of certain vaccines [9].

We offer vaccines at every visit, that's our goal. And if someone refuses, we give them the [Vaccine Information Statement].

Other promotion strategies focused on educating potential patients, including contests to win prizes for those who complete the vaccination series, advertising in school newsletters, and distributing information at health fairs.

[Educating the patient] does make a difference. We've had children say 'no, we want this shot,' especially in schools where they do different education that the nurses do with the student. It definitely makes a difference when they understand it's more than a poke in the arm.

I find a lot of times when we educate about HPV, the child goes home and comes back to get the shot. I find empowering the child really helps them because they do go home and talk to their parents.

Clinical Provider Practices

Respondents also mentioned barriers relevant to clinical provider practices, and strategies for overcoming these barriers. Some respondents reported weak or inconsistent provider recommendations as important barriers to vaccination.

I think a lot of [the barrier] is the recommendation that they're getting from physicians... whether it's a strong recommendation or an 'Oh, by the way...' I think that's a big part of starting the series.

A lot of the problem is the physicians. They're not 100% on board with administering the vaccine.

Perception is reality. If [providers] present it a certain way, that's how the patient is going to think about it. We definitely try to work with the providers to give them strategies [to talk about the vaccine with parents].

Additionally, clinic staff turnover and providers having insufficient time to discuss the vaccine in detail with the patient during the appointment were mentioned as barriers.

There are so many other things [providers] are doing... And it takes a lot of time to sit with a parent and talk with them if they're not absolutely wanting to do this... There's a whole waiting room full of kids [and]

you only have so many minutes. So what do you pick as your primary focus if you have 3-5 minutes? Sometimes you have a change of staff... and that person doesn't have enough information or maybe they don't know as much, as far as educating the patient.

Respondents described two statewide programs aimed at overcoming provider barriers in order to promote HPV vaccination initiation and completion. The adolescent Immunization grant from the CDC provided training to enrolled providers about how to use reminder/recall systems to send automated notices to patients who have not completed the series. Michigan also utilizes AFIX, an evidence-based quality improvement strategy promoted by the CDC (consisting of four components: Assessment, Feedback, Incentives, and eXchange), that assigns a coordinator, usually from the Local Health Department, to go to provider offices, determine vaccine coverage levels, and educate the staff on different strategies to increase coverage [10].

Additionally, the VFC program was touted as making a big difference in expanding vaccination access to underserved populations and equipping providers with knowledge about recommended vaccines.

With the VFC program, all children can get vaccinated. There's no reason we can't give the vaccines. Because whatever, even if they couldn't pay, even if they just had to pay \$5, they could still get the vaccines. And the state... with the VFC program... all Native Americans qualify, automatically.

We work with [VFC providers] to make sure they're following the guidelines... we work with them on storage and handling, and to understanding the recommendations for the vaccine so that they're giving the right vaccines to the right kids.

Discussion

The study examined socio-demographic determinants of initiation and completion of HPV vaccination and trends of completion rates among AI/AN adolescents compared to the NHW population in Michigan, and the results can be generalized to other similar populations. The perspective of health care and public health staff on barriers and promoters of vaccination were also presented. We found that adolescents whose mothers identified themselves as AI/AN were 1.5 times more likely to initiate the HPV vaccine series than adolescents whose mothers identified themselves as NHWs. Also, regardless of the race of mother, adolescents who were living in communities with higher poverty levels were more likely to start the HPV vaccination series than those living in communities with lower poverty levels. From the interviews, it appears that the

VFC program helped to increase the access to HPV vaccination among AI/AN adolescents and communities of lower socioeconomic status.

Interestingly, although the rate of completion was higher among AI/ANs than NHWs, there was no statistically significant difference in likelihood that AI/AN and NHW adolescents complete the HPV vaccine series. One notable finding is that children who initiated the HPV vaccine series at age 9 or 10 were 2.5 times more likely to complete the series compared to those who started at the recommended age of 11 or 12. Perhaps children who initiated the HPV vaccine series before the recommended age had parents who were more proactive about preventive care. Nevertheless, this finding has an important clinical implication as far as the timing for providers to communicate about HPV vaccine with parents. As for the setting, our findings suggest that compared to the private clinics, adolescents who received the first dose of HPV vaccine at a health department were about 30% less likely to complete the vaccine series and those who received the first dose at a school-based clinic were 10% more likely to complete the series. These results may indicate the private clinics and schools may do better follow-up or are more convenient for the patients to receive the second and third doses. These findings align with the literature, which states that private insurances and school health centers are associated with increased vaccination rates [11, 12].

Nationally, the HPV vaccine completion rate has been lower among males than females. In 2014, in the US nearly 70% of female adolescents ages 13–17 who initiated the series went on to complete the series, compared to 58% of males [6]. This was not surprising given that the recommendation for boys to receive this vaccine came later than for girls, and there are gaps in knowledge about the benefits of HPV vaccine for conditions other than cervical cancer [13, 14]. Our study found that in Michigan, the HPV vaccine completion rate among males was much lower than the national average. In 2014, AI/AN and NHW males ages 13–17 had only 40% and 30% completion rate, respectively; the national rate could be higher compared to the Michigan rate due to the different age ranges examined [6]. These findings clearly indicate the need for increased efforts to promote HPV vaccine among male adolescents in Michigan. There needs to be more consistent education and messaging to encourage parents and adolescents to view it as a crucial male vaccine by increasing awareness of the other health risks posed by HPV infections, such as genital warts and anal cancer. This includes the training and materials targeted at providers, who do not recommend the vaccine to male patients as consistently as female patients [9, 13, 15]. Emphasizing the importance of the vaccine for both genders through awareness campaigns and promotional materials has the potential to increase initiation and completion for males [9, 16].

The interviews offered additional context about the barriers that clinical providers and public health professionals in Michigan face to encouraging HPV vaccination initiation and completion, as well as strategies used to overcome these barriers. The most commonly mentioned barriers were parent misinformation and weak provider recommendations. Similar barriers have been found in previous studies across diverse populations, and support the idea that the provider is the most important influence on whether or not a patient receives the HPV vaccine [17]. The most potent promotion methods cited by the interviewees included the use of the MCIR immunization summary, the VIS, educating adolescents themselves, and utilizing the tools and support made available by state programs to educate providers.

Better completion rates at SBHCs and positive feedback from SBHC staff reflect the literature and the importance of empowering and educating the adolescent, not just their parent, on the importance of the vaccine so that they can advocate for themselves [18, 19]. Educational materials should be developed that target adolescents and are accessible at middle and high schools, where they can discuss health information with their peers and become motivated to learn more about their own health [20]. Working to expand access to education about HPV and other STIs at school-sponsored sexual education classes would also go far to further understanding among adolescents about HPV and its impact, and increase adolescents' confidence to discuss these issues with their parent or provider [9, 20, 21].

Limitations

First, the MCIR contains immunization data for all children in Michigan, but does not always have record of children who may have left the state. Additionally, race data were not collected until 1997, and the only source of race data is the mother's race pulled from the birth certificate. This means that not only are the race data for mixed-race children not recorded, but children who live in Michigan but were not born in the state have no race data entered in MCIR. Therefore, the number of AI/AN children included in the study is an underestimate. Further, the views of the professionals interviewed for this study may not be representative of all clinical providers and public health professionals attending the AI/AN population in Michigan.

Conclusions

This study offers further insight into HPV vaccination among AI/AN youth. The findings suggest the need for continued education about HPV vaccination for parents, patients, and providers, as well as state-level supports that facilitate data monitoring and sharing in order to improve

vaccination initiation and completion among AI/AN adolescents. Implementing these strategies in communities throughout the United States could play a significant role in reducing the incidence of cancer.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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