Vaccine 37 (2019) 5509–5512

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Short communication

Ten years of experience with herpes zoster vaccine in primary care- how attitudes and practices have changed and what it may mean for a new zoster vaccine

Angela Guo [a,*], Megan C. Lindley [a], Laura P. Hurley [b,c], Jessica A. Allen [d], Mandy A. Allison [b,e], Sean T. O'Leary [e], Lori A. Crane [b,f], Michaela Brtnikova [b,e], Brenda L. Beaty [b], Allison Kempe [b,e], Kathleen L. Dooling [a]

[a] National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, 1600 Clifton Rd, Atlanta, GA 30333, United States
[b] Adult and Child Consortium for Health Outcomes Research and Delivery Science, University of Colorado Anschutz Medical Campus and Children's Hospital Colorado, 13001 E 17th Pl, Aurora, CO, United States
[c] Division of General Internal Medicine, 777 Bannock St, Denver, CO 80204, United States
[d] Office of the Associate Director for Communication, Centers for Disease Control and Prevention, 1600 Clifton Rd, Atlanta, GA 30333, United States
[e] Department of Pediatrics, Colorado School of Public Health, University of Colorado Anschutz Medical Campus, 13001 E 17th Pl, Aurora, CO, United States
[f] Department of Community and Behavioral Health, Colorado School of Public Health, University of Colorado Anschutz Medical Campus, 13001 E 17th Pl, Aurora, CO, United States

ARTICLE INFO

Article history:
Received 25 April 2019
Received in revised form 31 July 2019
Accepted 1 August 2019
Available online 7 August 2019

Keywords:
Herpes zoster
Vaccination
Primary care

ABSTRACT

Zoster vaccine live (ZVL [Zostavax]) has been recommended for the prevention of herpes zoster (HZ) among immunocompetent adults ≥60 years in the United States since 2008. To examine changes in healthcare providers' perceptions and practices related to HZ disease and vaccination, we administered surveys to national networks of primary care physicians in 2005, 2008, and 2016. Ten years after ZVL was first licensed, physicians were more likely to respond that they perceived HZ as a serious disease and more strongly recommended ZVL, and were less likely to report less likely to report several major barriers to HZ vaccination such as patient cost, vaccine effectiveness and competing medical concerns. Overall, physician attitudes appear to be more favorable towards zoster vaccination after a decade of availability of a HZ vaccine. The new recombinant zoster vaccine (RZV [Shingrix]) may benefit from physician's increased perception of the importance of HZ and HZ vaccination.

Published by Elsevier Ltd.

1. Introduction

In 2005, results from the Shingles Prevention Study established the efficacy of a vaccine for herpes zoster (HZ) [1]. Zoster vaccine live (ZVL [ZOSTAVAX™), a single dose, live attenuated vaccine, was licensed by the Food and Drug Administration in 2006 and recommended by the Advisory Committee on Immunization Practices (ACIP) in 2008 for the prevention of herpes zoster among immunocompetent adults ≥60 years [2]. Since 2008, ZVL coverage has slowly increased in United States, from 6.7% in 2008 to 33.4% in 2016, despite extensive public awareness campaigns and provider outreach [3].

In October 2017, a new recombinant zoster vaccine (RZV [Shingrix]) was licensed by FDA for adults ≥50 years and preferentially recommended by ACIP for prevention of herpes zoster in immunocompetent adults ≥50 years [4]. In clinical trials, RZV, a two dose, inactive adjuvanted vaccine, was found to be over 90% efficacious in preventing HZ in adults ≥50 years, compared to ZVL, which is approximately 50% effective in preventing HZ in adults ≥60 years [1,5,6]. Our objective was to examine changes in healthcare providers' perceptions and practices related to HZ disease and vaccination since the recommendation of ZVL and anticipate how those perceptions may impact provider practices for RZV.

2. Materials and methods

In 2005, 2008, and 2016, the University of Colorado Denver's Vaccine Policy Collaborative Initiative and the Centers for Disease Control and Prevention administered surveys related to HZ disease and vaccination to national networks of general internal medicine (GIM) and family medicine (FM) physicians.

Physicians were recruited from random samples of the American College of Physicians and the American Academy of Family Physicians membership. Survey instruments were pre-tested in

* Corresponding author at: Centers for Disease Control and Prevention, 1600 Clifton Rd NE, Mailstop H24.5 Building 24, Atlanta, GA 30333, United States.
E-mail address: ndv1@cdc.gov (A. Guo).

https://doi.org/10.1016/j.vaccine.2019.08.002
0264-410X/Published by Elsevier Ltd.

community advisory panels and pilot tested among a subset of GIM and FM physicians. Surveys were based on the Health Belief Model [7] and assessed physician's current attitudes, knowledge and practices regarding HZ vaccination. Respondents were presented information about current HZ vaccine policy, and then asked questions about their perceptions regarding the vaccine and barriers to HZ vaccination with closed ended, Likert-type responses ("strongly agree," "somewhat agree," "somewhat disagree," and "disagree"). Surveys were administered via mail and Internet, per the participant's preference. Additional methods and results for each survey have been previously published [8–10].

We compared responses to questions included in the 2016 survey to responses to those same questions in either the 2005 or 2008 survey, depending on when they were asked. We used chi-square tests to assess statistically significant differences in overall distribution of responses. Responses to most survey questions were similar between GIM and FM, so data were combined for this analysis.

3. Results

The combined response rates of eligible physicians to the surveys given in 2005, 2008, and 2016 were 68% (595/871), 72% (598/828), and 65% (603/923), respectively.

3.1. Provider attitudes towards HZ disease and vaccination (2016 vs 2005)

In 2016, compared to 2005, physicians were more likely to strongly agree that herpes zoster and post-herpetic neuralgia (PHN) caused significant burden of disease among their elderly patients (59.8% vs 35.1%) and that the burden was sufficient to make the vaccine important among adults aged 50–59 (28.6% vs 16.1%), 60–79 (68.0% vs 34.0%), and ≥80 years (58.0% vs 32.5%). Distribution of responses for these questions were significantly different in 2016 compared to 2005 (Table 1).

3.2. Provider practices and perceived barriers (2016 vs 2008)

In 2016, compared to 2008, more physicians reported strongly recommending the zoster vaccine to eligible patients aged ≥60 years (77.4% vs 41.4%) (Table 2). Similar proportions of physicians reported stocking and administering ZVL in their offices in 2016 and 2008 (55.1% vs. 51.2% p = 0.19). However, among those who reported ever administering HZ in their office, there was a significant increase in the number of physicians who reported that they had stopped administering it as result of cost and reimbursement issues (21.0% vs 12.2%, p = 0.0003).

Table 2
Physician practices and perceived barriers for administering herpes zoster vaccine, 2008 vs 2016.

	2008 (n = 598±)	2016 (n = 602±)	P-value*
What is the strength of your recommendation for zoster vaccine to eligible patients ≥60 years old and not immunocompromised?			
Strongly recommend	41.4%	77.4%	<0.0001
Recommend, but not strongly	47.0%	16.2%	
Don't recommend for or against	10.9%	2.7%	
Recommend against	0.9%	3.7%	
I stock and administer the vaccine in my office			
Yes	51.2%	55.1%	0.19
No	48.8%	44.9%	
I refer patients to a pharmacy to purchase vaccine and administer in my office†			
Yes	38.6%	31.1%	0.008
No	61.4%	68.9%	
I refer patients to a pharmacy to purchase vaccine and it is administered at the pharmacy			
Yes	32.6%	76.9%	<0.0001
No	67.4%	23.1%	
If ever administered the vaccine in your office, stopped administering the vaccine as a result of cost and reimbursement issues?			
	n = 444	n = 490	
Yes	12.2%	21.0%	0.0003
No	87.8%	79.0%	
Perceived barriers to administering herpes zoster vaccine			
Cost concerns for my patients			
Not a barrier	7.1%	11.6%	0.0003
Minor/Moderate barrier	39.6%	46.1%	
Major barrier	53.4%	42.3%	
My concerns about safety of the vaccine			
Not a barrier	62.8%	89.1%	<0.0001
Minor/Moderate barrier	35.0%	10.6%	
Major barrier	2.1%	0.3%	
My concerns about the effectiveness of the vaccine			
Not a barrier	51.2%	58.9%	0.03
Minor/Moderate barrier	44.1%	37.3%	
Major barrier	4.8%	3.8%	
More pressing medical issues taking precedence over this vaccine			
Not a barrier	34.9%	42.1%	<0.0001
Minor/Moderate barrier	52.8%	52.6%	
Major barrier	12.3%	5.3%	

± Number of respondents that participated in the survey.
* P-value for comparison between survey years as calculated by chi-square test.

Table 1
Physician perceptions and practices on herpes zoster and herpes zoster vaccination, 2005 vs 2016.

	2005 (n = 595±)	2016 (n = 603±)	P-value*
Herpes zoster and post-herpetic neuralgia cause significant burden of disease in my older patients			
Strongly agree	35.1%	59.8%	<0.0001
Somewhat agree	46.2%	34.0%	
Somewhat/strongly disagree	18.7%	6.2%	
In my practice, the burden of herpes zoster and its complications in patients 50–59 years old is sufficient to make a vaccine important			
Strongly agree	16.1%	28.6%	<0.0001
Somewhat agree	44.6%	33.8%	
Somewhat/strongly disagree	39.3%	37.5%	
In my practice, the burden of herpes zoster and its complications in patients 60–79 years old is sufficient to make a vaccine important			
Strongly agree	34.0%	68.0%	<0.0001
Somewhat agree	45.6%	25.3%	
Somewhat/strongly disagree	20.4%	6.7%	
In my practice, the burden of herpes zoster and its complications in patients ≥ 80 years old is sufficient to make a vaccine important			
Strongly agree	32.5%	58.0%	<0.0001
Somewhat agree	40.9%	29.1%	
Somewhat/strongly disagree	26.6%	12.9%	

± Number of respondents that participated in the survey.
* P-value for comparison between survey years as calculated by chi-square test.

In 2016, compared to 2008, physicians were more likely to report referring patients to pharmacies to buy and receive the zoster vaccine (76.9% vs 32.6%, p < 0. 0001), and less likely to refer patients to pharmacies to buy the vaccine and administer the vaccine in their office (31.1% vs 38.6%, p = 0.008).

In 2016, compared to 2008, physicians were less likely to report the following as "major barriers" to administering or recommending HZ vaccine in their office: cost concerns for their patients, their concerns about the safety and effectiveness of the vaccine, and more pressing medical issues taking precedence over HZ vaccination (Table 2). While physicians were less likely to report cost concerns for patients as a major barrier for administering the vaccine in 2016, cost concerns for patients remained the biggest barrier identified by physicians, with 42.3% of physicians still reporting patient costs as a major barrier in 2016.

4. Discussion

Ten years after the first HZ vaccine was licensed in the United States, physicians were more likely to respond that zoster and PHN caused significant burden of disease among their older patients and that vaccination against zoster was important. Physicians' increased perception of the importance of zoster and PHN is likely influenced by extensive public awareness and provider outreach campaigns following the licensure of ZVL, increasing rates of zoster among adults in the United States, and over a decade of availability of a vaccine to prevent the disease [11].

Notably, this increased perception in the importance of zoster and PHN was least pronounced when physicians were asked about patients 50–59 years old. In 2016 only 29% of physicians responded that they strongly agreed that burden of zoster in patients 50–59 years old is sufficient to make a vaccine important, compared to 68% when asked the same question about patients 60–79 years old. With the new vaccine now licensed and recommended for adults aged 50 and older, additional education may be needed to promote vaccination in this younger age group which also has significant burden of disease.

Physicians were also more likely to strongly recommend zoster vaccination and less likely to report several major barriers to HZ vaccination, although cost to patients continues to be a major perceived barrier to HZ vaccination. More physicians in 2016 reported referring patients to pharmacies to purchase and receive the vaccine, reflecting the growing role pharmacists play in administering adult vaccines. As of 2015, all 50 states have passed legislation giving pharmacists authority to administer immunizations [12]. Furthermore, since zoster vaccines are covered under Medicare Part D, which is a pharmacy benefit program, pharmacists may have easier access to reimbursement for HZ vaccination compared to physicians. There was a statistically significant increase in the proportion of physicians who reported they stopped administering the vaccine due to cost and reimbursement issues, as provider-related cost and reimbursement issues remain a key barrier for physicians to administer zoster vaccine in their practice. However, increased availability of zoster vaccine at pharmacies will likely outweigh these factors and lead to overall increased accessibility of zoster vaccine to help improve vaccination coverage.

Some barriers to vaccination, such as patient cost, vaccine effectiveness and competing medical concerns, have diminished in importance. However, cost to patients remains the biggest barrier identified by physicians. Costs for ZVL have not declined over time and shingles vaccines are often covered under the most expensive tiers of Medicare Part D, requiring higher co-pays for patients. Since the newly licensed RZV is a two-dose vaccine, the overall cost for RZV vaccination will be higher than ZVL [13]. The higher cost of the new vaccine may be an additional barrier for providers recommending or administering the vaccine to their patients. The need to stock more doses to fully vaccinate patients may also represent a challenge, as up-front costs of vaccine purchase have been identified by physicians as a major barrier to administering HZ vaccine [9].

Concerns related to the safety of ZVL have diminished with use over the past 10 years. It is possible that physicians may need a similar "warming up" period to get comfortable with the safety profile of the new RZV vaccine. RZV is notably more reactogenic than ZVL, which may lead to additional concerns from physicians when administering the vaccine to their patients. However, RZV is an inactive vaccine, and will not carry some of the safety concerns of ZVL, a live attenuated vaccine, particularly when considering vaccination policy for immunocompromised patients.

Concerns related to efficacy of ZVL have also diminished. This follows the real-world performance of ZVL as evidenced by large post-licensure observational studies that found no serious adverse events associated with ZVL administration in immunocompetent adults and estimates of vaccine effectiveness similar to those reported in clinical trials within four years post-vaccination [14]. However, studies of long-term effectiveness of ZVL have found evidence of waning of protection. Interestingly physician's perceptions about concerns of the effectiveness of ZVL as a barrier diminished in 2016 even as studies were being published showing waning of protection from the vaccine over time.

There are several limitations to this study. We did not survey the same respondents across survey years, so our data does not reflect changes in attitudes or practices among individual physicians. Our results may have also been influenced by social desirability bias, with physicians overestimating the extent to which they recommend or administer the vaccine. However, our study is unique in its ability to analyze responses to the same questions regarding physician attitudes and practices from the beginning to nearly a decade post ZVL licensure in a nationally representative subset of GIM and FM physicians.

5. Conclusion

Overall, physician attitudes appear to be more favorable towards zoster vaccination after a decade of availability of a HZ vaccine. With a new, more effective vaccine in the market, there is potential to significantly reduce the burden of HZ among older adults. RZV may benefit from increased perception among physicians of the importance of HZ and its complications among their older adult patients, and physicians' increasingly favorable attitude towards HZ vaccination. Further research is needed to examine attitudes and practice regarding HZ vaccine of other healthcare providers, pharmacists in particular, that play an increasing role in the delivery of shingles vaccination. Provider acceptance and recommendation of RZV will be critical in order to increase the proportion of eligible adults protected against HZ and its complications.

Previous meetings

Information in this paper partially presented at the 48th National Immunization Conference, Atlanta, Georgia, May 15–17, 2018.

All authors attest they meet the ICMJE criteria for authorship.

Funding

This publication was supported by Cooperative Agreement Number 1 U01 IP000849-02, funded by the Centers for Disease Control and Prevention. Its contents are solely the responsibility

of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention or the Department of Health and Human Services.

Declaration of Competing Interest

None of the authors has a conflicts of interest.

References

[1] Oxman MN, Levin MJ, Johnson GR, Schmader KE, Straus SE, Gelb LD, et al. A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. N Engl J Med 2005;352(22):2271–84.

[2] Harpaz R, Ortega-Sanchez IR, Seward JF. Prevention of herpes zoster: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep 2008;57(5):1–30.

[3] Hung MC, Williams WW, Lu PJ, et al. Vaccination coverage among adults in the United States, National Health Interview Survey, 2016. Atlanta, GA: US Department of Health and Human Services, CDC; 2018. Available at: https://www.cdc.gov/vaccines/imz-managers/coverage/adultvaxview/pubs-resources/NHIS-2016.html. Accessed 23 January 2019.

[4] Dooling KL, Guo A, Patel M, et al. Recommendations of the advisory committee on immunization practices for use of herpes zoster vaccines. MMWR Morb Mortal Wkly Rep 2018;67:103–8.

[5] Lal H, Cunningham AL, Godeaux O, Chlibek R, Diez-Domingo J, Hwang S-J, et al. Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults. N Engl J Med 2015;372(22):2087–96.

[6] Cunningham AL, Lal H, Kovac M, Chlibek R, Hwang S-J, Díez-Domingo J, et al. Efficacy of the herpes zoster subunit vaccine in adults 70 years of age or older. N Engl J Med 2016;375(11):1019–32.

[7] Glanz K, Rimer BK, Viswanath K. Health behavior and health education: theory, research, and practice. John Wiley & Sons; 2008.

[8] Hurley LP, Harpaz R, Daley MF, Crane LA, Beaty BL, Barrow J, et al. National survey of primary care physicians regarding herpes zoster and the herpes zoster vaccine. J Infect Dis 2008;197(Suppl 2):S216–23.

[9] Hurley LP, Lindley MC, Harpaz R, et al. Barriers to the use of herpes zoster vaccine. Ann Int Med 2010;152(9):555–60.

[10] Hurley LP, Allison MA, Dooling KL, O'Leary ST, Crane LA, Brtnikova M, et al. Primary care physicians' experience with zoster vaccine live (ZVL) and awareness and attitudes regarding the new recombinant zoster vaccine (RZV). Vaccine 2018;36(48):7408–14.

[11] Harpaz R, Leung J, Gambhir M. Incidence of Pediatric and Adult Herpes Zoster in an Era of Varicella and Herpes Zoster Vaccines. Open Forum. Infect Dis 2015;2(suppl_1):1052.

[12] Weaver KK. Pharmacist-administered immunizations: What does your state allow?. Available at: https://www.pharmacist.com/article/pharmacist-administered-immunizations-what-does-your-state-allow. Accessed 3 January 2018.

[13] Umansky, D. The New Shingles Vaccine: What You Should Know About Shingrix. Consumer Reports. https://www.consumerreports.org/shingles-vaccine/new-shingles-vaccine-shingrix-what-you-should-know/. Accessed 24 January 2019.

[14] Advisory Committee on Immunization Practices. Grading of recommendations, assessment, development, and evaluation (GRADE): recombinant zoster vaccine (RZV) and herpes zoster live-attenuated vaccine (ZVL). Atlanta, GA: US Department of Health and Human Services, CDC, Advisory Committee on Immunization Practices; 2017. Available at: https://www.cdc.gov/vaccines/acip/recs/grade/herpes-zoster.html Accessed on 23 January 2019.