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Original article

Effect of universal varicella vaccination and behavioral changes against coronavirus disease 2019 pandemic on the incidence of herpes zoster

Kimiyasu Shiraki[a,*], Nozomu Toyama[b], Keiko Tanaka[a], Akiko Ito[a], Junko Yamamoto[a], The members of the Miyazaki Dermatologist Society[1]

[a] Senri Kinran University, Osaka, Japan
[b] Toyama Dermatologic Clinic, Miyazaki, Japan

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ABSTRACT

Background: Since 2014, universal varicella vaccination has reduced the varicella and herpes zoster (HZ) incidence in vaccine recipients and increased the incidence in the child-rearing generation until 2017.
Objective: This study aimed to understand the future epidemiologic trends of HZ after the disappearance of varicella epidemics and during the coronavirus disease 2019 (COVID-19) pandemic.
Methods: The Miyazaki Dermatologist Society has been monitoring and analyzing the incidence of HZ patients after universal vaccination since 1997.
Results: The HZ incidence in Oka varicella vaccine recipients aged 0–4 years decreased with the reduction in chickenpox incidence. The HZ incidence among those aged 5–9 years increased between 2015 and 2017 and decreased thereafter. From 2014–2020, the HZ incidence continued to increase to 36.6%, 51.3%, 70.2%, 56.7%, and 27.3% among those aged 10–19, 20–29, 30–39, 40–49, and 50–59 years, respectively. The HZ incidence in patients aged ≥ 60 years increased by 2.3% annually from 2014 to 2020, corresponding to an annual 2% increase since 1997, and was unaffected by varicella epidemics. COVID-19 infection control measures, lifestyle changes and the resulting stress did not affect the HZ incidence in 2020.
Conclusion: Universal varicella vaccination eliminated varicella epidemics, and HZ was reduced in vaccine recipients. The HZ incidence for those aged 10–59 years increased from 2014 to 2020, in contrast to those aged ≥ 60 years, which is attributable to booster immunity expiration due to varicella contact in this age group.

1. Introduction

Epidemiological studies on herpes zoster (HZ) in the Miyazaki Prefecture performed by the Miyazaki Dermatologist Society since 1977 have reported increasing HZ incidences of approximately 2% annually among all ages [1–3]. Universal varicella vaccination since October 2014 reduced the number of varicella patients. Accordingly, a reduction in varicella cases increased the HZ incidence in the child rearing adults aged 20–49 years due to the loss of the chance to boost immunity after contact with varicella patients, and the HZ incidence was reduced in Oka varicella vaccine recipients aged 0–4 as a short-term effect until 2017 [1,2].

Varicella-zoster virus (VZV) causes varicella in the first exposure to VZV and becomes latent in the sensory ganglia. VZV reactivation causes HZ in elderly or immunocompromised patients. Varicella exposure boosts immunity to VZV and reduces the incidence of HZ [4–7]. The Oka varicella vaccine boosts immunity to VZV and reduces the HZ incidence in elderly people [8–10]. The VZV gE vaccine reduces the incidence of HZ in elderly people [11]. Thus, boosting VZV immunity, which can be achieved by contact with varicella patients as an excellent natural booster, reduces the HZ incidence. Protective booster immunity against HZ by Oka varicella vaccine begins to decrease to 79.2% or 62.0% in 1 year, 44.4% or 46.8% in 3 years, and the significant difference in preventive effect disappears in 8 years [12,13]. Although the duration of the HZ preventive effect of varicella contact is not clear, the duration of the protective booster against HZ by Oka varicella vaccine for 8 years can be applied to estimate the expiratory period for patients with varicella infection in the HZ epidemiological study.

The HZ incidence has been increasing annually by 2% since 1997 [1,2]. We reported an increase in HZ incidence in patients aged

Abbreviations: HZ, herpes zoster; VZV, varicella-zoster virus; COVID-19, coronavirus disease 2019

* Correspondence to. Senri Kinran University, 5-25-1 Fujishiro-dai, Suita, Osaka 565-0873, Japan
E-mail address: k-shiraki@cs.kinran.ac.jp (K. Shiraki).

[1] The members of the Miyazaki Dermatologist Society are listed in the Appendix.

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20–49 years and a decrease in HZ incidence in patients aged 0–4 years in 2017 since universal varicella vaccination began in 2014 [1,2]. We further analyzed the epidemiological changes in HZ in 2020, when contact with varicella patients and its booster effect is disappearing. The varicella vaccination rate for the target subjects for the first and second inoculation were 26.4% and 75% in 2014, and 90% and 105% in 2015, respectively, and vaccination coverage rates have been high since then, indicating the target children of varicella vaccine are taking Oka varicella vaccine [14,15]. The HZ incidence in Oka varicella vaccine recipients aged 0–4 years decreased with the reduction in the number of varicella patients. The HZ incidence among those aged 5–9 years increased between 2015 and 2017 and decreased thereafter.

This study showed that the HZ incidence decreased in Oka varicella vaccine recipients aged 0–9 years, increased in recipients aged 10–59 years because of the loss of varicella contact to booster immunity, and was not affected in recipients aged ≥ 60 years. The HZ incidence continued to increase by 27–70% among those aged 10–59 years from 2014 to 2020, possibly because of the expiration of boosting immunity by contact with varicella patients. Another important information is the impact of the coronavirus disease 2019 (COVID-19) pandemic on the epidemiology of HZ. A total of 757 and 5117 COVID-19 patients among the 1062,954 population in the Miyazaki Prefecture were recorded on December 31, 2020 and August 27, 2021 [16–18], but the COVID-19 pandemic has significantly changed daily living by thoroughly implementing prevention measures, including handwashing, mask wearing, and refraining from going out. So far, no significant effect of COVID-19 on HZ has been observed.

2. Materials and methods

2.1. Collection of patients and study population

Information on HZ patients in the Miyazaki Prefecture has been monitored based on patient care by the Miyazaki Dermatologist Society since 1997 [1–3,19,20]. Information on the number of varicella patients under infectious disease surveillance in the prefecture was obtained from the Miyazaki Prefectural Institute for Public Health and Environment. The distribution of age and sex groups between 1997 and 2020 was obtained from the Miyazaki prefectural government [17]. All new medically documented cases of HZ in 41 clinics, which included 34 dermatology clinics and the dermatology departments of seven flagship general hospitals associated with the Miyazaki Dermatologist Society, were evaluated. Dermatologists completed a questionnaire concerning the age and sex of HZ patients [1–3,19,20]. The surveillance by the Miyazaki Dermatologist Society covered 85% of HZ patients with a correct clinical HZ diagnosis rate of approximately 98% [19,20].

2.2. Statistical analysis

The incidence of varicella and HZ from the surveillance was expressed as the incidence per 1000 person-years in each age group or total population from the estimated population of the Miyazaki Prefecture households [17]. The HZ incidence and the variation in HZ incidence were compared between from 1997 to 2014 and from 2014 to 2020 using Student's *t*-test. The HZ and varicella incidences among those aged 0–9 years were compared using the chi-square test on the number and population of patients in each year based on the number and population of patients in 2014. Statistical significance was defined as a P-value of less than 0.05. This study was approved by the ethics committee of Senri Kinran University (UMIN Clinical Trials Registry Nos.: UMIN000008738 and UMIN000034029).

3. Results

3.1. Increase in patients with HZ from 1997 to 2020 in the Miyazaki Prefecture

Fig. 1 shows the transition of the population, number, and incidence of HZ in Miyazaki Prefecture from 1997 to 2020, and these trends from 2014 to 2017 have been extended from 2017 to 2020. The population decreased from 1.176 million to 1.063 million (90.4%), and the ratio of those aged > 60 years increased from 25.2% in 1997 to 39.4% in 2020. The proportion of adults aged 20–49 years decreased from 38.5% in 1997 to 30.0% in 2020. The number of total patients and those aged > 60 and 20–49 years increased from 4243 to 6853 (161.5%), 1833 to 4, 009 (218.7%), and 935–1412 (151.0%), respectively, from 1997 to 2020, as shown in Fig. 1b. While the HZ incidence increased with the increase in the total number of patients, the increasing tendency in the HZ incidence in those aged 20–49 years was more remarkable than that in all patients (Fig. 1c). This increase was even more pronounced than that in the overall incidence by comparing the transition from 2014 to 2020 based on 1997 (Fig. 1d). The HZ incidence rose sharper from 2018 to 2020 than its rise from 2014 to 2017. The HZ incidence increases of the total population among those aged < 60, > 60, and 20–49 years were 3.61–6.44 (178.7%), 2.74–4.48 (163.5%), 6.18–9.56 (154.6%), and 2.06–4.42 (214.5%), respectively, from 1997 to 2020 as shown in Fig. 1c and d. An increase in the HZ incidence was observed in four age groups until 2013 at approximately 2% annually, and the HZ incidence abruptly increased among those aged 20–49 years from 2014 to 2017 and further from 2017 to 2020, as shown in Fig. 1d. An abrupt increase in HZ incidence was noted after the introduction of universal varicella vaccination, especially in the population aged 20–49 years.

3.2. Comparison of age-dependent herpes zoster (HZ) incidence between 2014 and 2020

The increase in the HZ incidence in the total population was observed from 2014 to 2020; therefore, the age-dependent HZ incidence was compared between 2014 and 2017 and 2017 and 2020 in Fig. 2a and b, respectively. The HZ incidence increased in every generation, except for those aged 0–4 years. The HZ incidence increased the most in those aged 30–39 years among the age 10–59 years and reduced in the population aged 0–9 years from 2017 to 2020. Since the transition of the HZ incidence in each generation is rather complicated, we analyzed the changes in HZ incidence in each generation separately.

3.3. Three transition patterns in the HZ incidence in age groups from 2014 to 2020

Table 1 shows the HZ incidence in the total population, males, and females of each age group in 1997, 2014, and 2020, and the HZ incidence change from 1997 to 2014 and from 2014 to 2020, respectively. The mean HZ incidence was significantly higher in every generation from 2014 to 2020 than from 1997 to 2014. This increase in the mean HZ incidence before and after 2014 indicates the accumulation effect of the annual 2% increase in HZ incidence, resulting in a higher HZ incidence after 2014 than before 2014. Since it is necessary to eliminate the effects of this increase to assess real variations in the HZ incidence between 1997 and 2014 and from

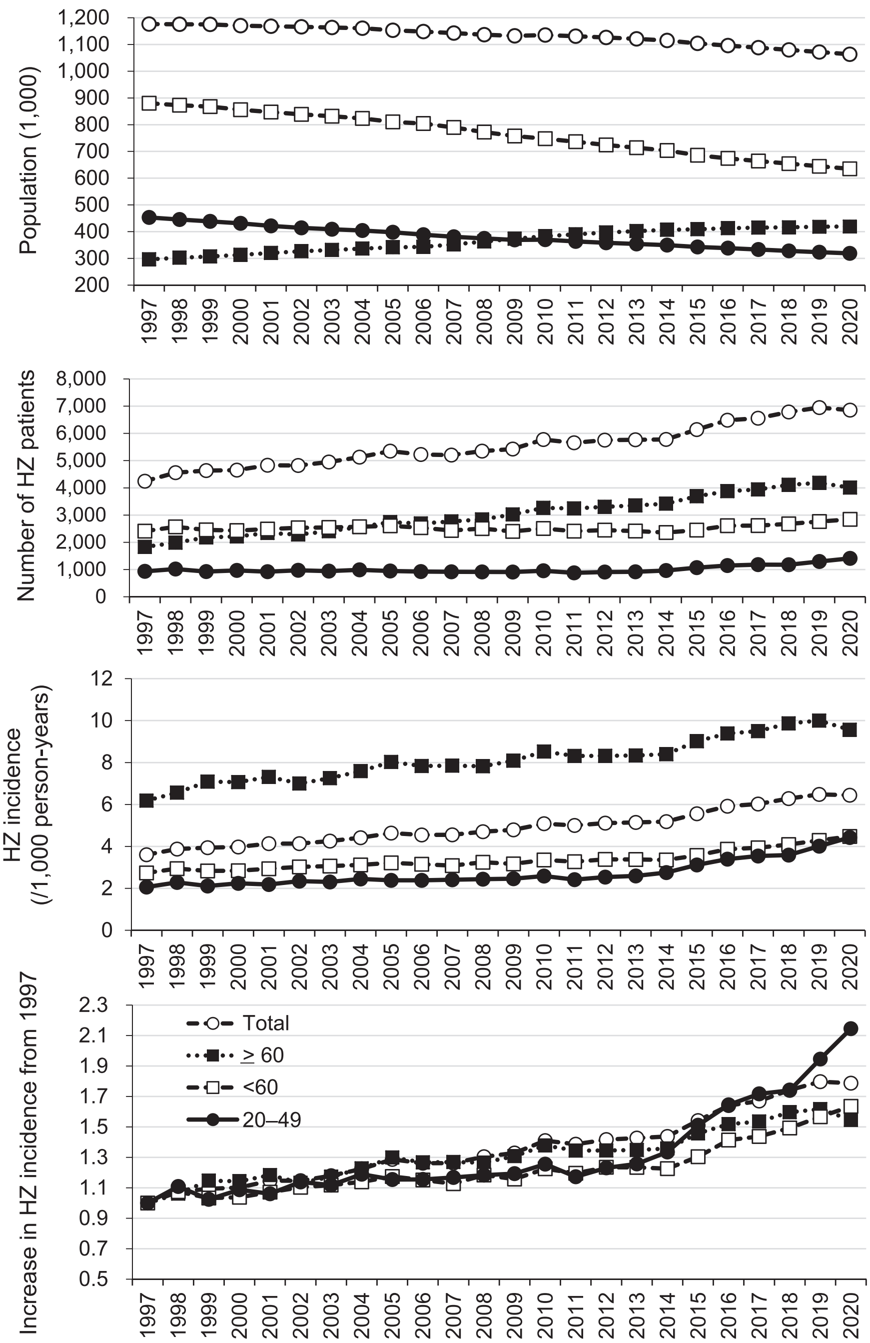

Fig. 1. Population and incidence of herpes zoster (HZ) patients in the Miyazaki Prefecture from 1997 to 2020. (a) Transition of total population (open circles), population aged 20–49 (closed circles), > 60 (closed squares), and < 60 (open squares) years from 1997 to 2020. (b) Transition of the number of HZ patients in the total population, population aged 20–49 years (closed circles), > 60 (closed squares), and < 60 (open squares) years from 1997 to 2020. (c) The HZ incidence in the total population, population aged 20–49 (closed circles), > 60 (closed squares), and < 60 (open squares) from 1997 to 2020. (d) The comparison of the HZ incidence in the total population, population aged 20–49 (closed circles), > 60 (closed squares), and < 60 (open squares) years from 1997 to 2020, aged > 60 years of those in 1997 as a standard (1.0). The HZ incidence gradually and linearly increased in all age groups, except for an abrupt increase in the population aged 20–49 years from 2014 to 2020.

2014 to 2020, the mean variation in the HZ incidence was compared between the two periods with the HZ incidence in 1997 and 2014 as zero in the first year of both periods. For those aged 0–9 and ≥ 60 years old, the variation before 2014 was larger, whereas for those aged 10–59 years, the variation after 2014 was greater. In the total population, the mean variation in HZ incidence tended to be larger before the universal varicella vaccination period from 1997 to 2014 than after the universal varicella vaccination period from 2014 to 2020. Universal varicella vaccination significantly reduced the mean annual variations in HZ incidence aged 0–4 years and increased them aged 10–59 years. In contrast, the mean annual variation in the HZ incidence among those aged ≥ 60 years before 2014 was larger than that after 2014, indicating that the HZ incidence was not affected by universal varicella vaccination, which is attributable to the

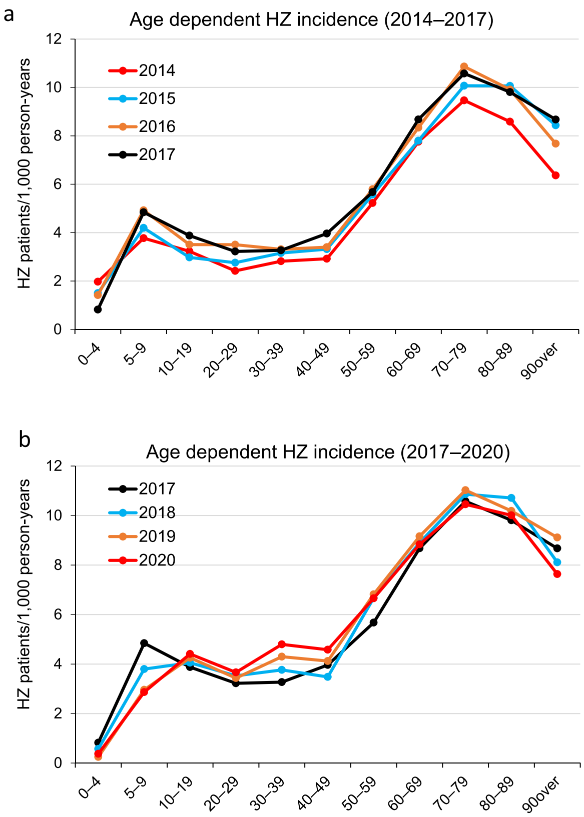

Fig. 2. Comparison of age-dependent herpes zoster (HZ) incidences (a) from 2014 to 2017 and (b) from 2017 to 2020. The HZ incidence reduced in those aged 0–4 years and increased in every generation especially in adults aged 20–49 years from 2014 to 2017 (Fig. 2a). The HZ incidence reduced in those aged 0–9 years and increased in those aged 10–59 years, especially in those aged 30–39 years from 2017 to 2020 (Fig. 2b).

high proportion of people in that age group, regardless of significant variations in HZ incidence among those aged ≤ 59 years. Although there was no significant variation before and after 2014 among those aged 30–39 years, or the core age group of the child-rearing generation, significant variations were observed before and after 2012 when universal varicella vaccination was started partially [2].

3.4. Annual transition of HZ incidence from 1997 to 2020

Figs. 3 and 4 show the annual transition patterns of HZ incidence in males and females in each generation from 1997 to 2020. The HZ incidence in the total population, the male population, and the female population gradually increased from 1997 to 2020, and increased significantly by 1.46%, 1.31%, and 1.58% per year from 1997 to 2014, and 4.9%, 0.87%, and 8.5% per year from 2014 to 2020, respectively. The HZ incidence in the total population increased from 2015, while that in females and males increased from 2015 and 2016, respectively, with a one-year delay. The incidence of HZ in patients aged 0–4 years decreased in 2014. The total, male, and female HZ incidences were reduced to 18.9%, 16.6%, and 21.8%, respectively, in patients aged 0–4 years and 75.4%, 78.2%, and 73.3%, respectively, in the 5–9 years from 2014 to 2020. The incidence of HZ in patients aged 5–9 years increased from 2016 to 2017 and began to decline from 2018 as vaccine recipients were aged 5–9 years. HZ incidence increased in age groups at 10–29 and 40–49 years from 2014 and at 30–39 years from 2012, as observed in Table 1. The HZ incidence at age 20–49 years increased in females from 2015 and in males from 2016. The incidence of HZ in patients aged 50–59 years increased gradually from 2014 to 2017 and remarkably from 2018. The HZ incidences increased by 36.6%, 51.3%, 70.2%, 56.7%, and 27.3% for those aged 10–19, 20–29, 30–39, 40–49, and 50–59 years, respectively, from 2014 to 2020. The HZ incidence in patients aged 60–69 years significantly increased, but the mean variations did not show a significant increase before and after 2014. The incidence of HZ in patients aged 70 years significantly increased, and the mean variations tended to be larger before 2014 than after 2014. An annual increase in HZ incidence of 2.3% was observed at age 60 years and older from 2014 to 2020, but an additional increase by universal varicella vaccination was not observed in contrast to that at the age of 10–59 years.

The HZ incidence was approximately 2.7 and 1.7 person-years higher in female than in male in age 50–59 and 60–69 years, respectively, since 1997. The 1.1-person-year difference in HZ incidence between males and females in total populations reflects the difference between the populations aged 50–69 years.

3.5. Reduction of the HZ incidence in Oka varicella vaccine recipients

Fig. 5 shows the varicella and HZ incidences in ages 0–4 and 5–9 years, and the varicella incidence decreased first, followed by the HZ incidence at 0–4 years of age. The HZ incidence in patients aged 5–9 years increased from 2015 to 2017 and began to decrease from 2018 to 2020. In addition to the reduction in the number of varicella patients by universal varicella vaccination since 2014, infection prevention measures against COVID-19 might have contributed to the reduction of varicella patients in 2020. The low HZ incidence in Oka varicella vaccine recipients aged 0–4 years and reduction in varicella epidemic increased the HZ incidence in patients aged 5–9 years as a short period, as reported previously [1,2]. The HZ incidence at ages 5–9 decreased since 2018 as vaccine recipients increased in age and joined ages 5–9 years.

3.6. Impact of lifestyle and behavioral changes due to the COVID-19 pandemic on HZ epidemiology

Since the COVID-19 pandemic began in Japan in 2020, a total of 757 COVID-19 patients in the Miyazaki Prefecture were recorded on December 31, 2020 [18]. Although the number of patients is limited, the pandemic has changed Japanese lifestyle and behavior by thoroughly implementing infection prevention measures, such as handwashing, mask wearing, and refraining from going out. The effect and associated stress of these behavioral and lifestyle changes on HZ incidence in 2020 was analyzed as to how they affected the continuous change in HZ incidence since 2014. All age groups among the changes from 2014 to 2020, did not see any specific changes from 2019 to 2020, which should be affected by the COVID-19 pandemic in Figs. 1–4 indicating that the COVID-19 pandemic in 2020 had no significant influence on HZ incidence in the Miyazaki Prefecture.

4. Discussion

Universal varicella vaccination was introduced in Japan in 2014, and the varicella vaccination rates for the first and second inoculation were 149.2% and 46.3% in 2014, and 105.9% and 106.9% in 2015, respectively [14]. We have reported a reduction in the number of varicella patients and HZ incidence in vaccine recipients and an increase in HZ incidence in the child-rearing generation up to 2017

Table 1
Transition of herpes zoster incidence in each age group before and after 2014.

Target Groups		HZ incidence*(per 1000 person-years)				Mean variation** (per 1000 person-years)			
Age (years)		1997	2014	2020	Incidence comparison***	1997 –2014		2014 –2020	Variation comparison****
Total population	Total	3.61	5.20	6.50	< 0.001	0.91	>	0.83	
	Male	3.23	4.72	5.77	< 0.001	0.77	>	0.61	
	Female	3.94	5.63	7.14	< 0.001	1.02	=	1.02	
0–4	Total	1.67	1.98	0.37	< 0.001	0.22	>	-0.97	< 0.001
	Male	1.45	2.20	0.37	< 0.001	0.40	>	-1.20	< 0.001
	Female	1.91	1.76	0.38	< 0.001	0.04	>	-0.73	< 0.001
5–9	Total	2.76	3.80	2.87		0.68	>	0.13	
	Male	2.60	3.33	2.61		0.60	>	0.35	
	Female	2.92	4.28	3.14		0.76	>	0.10	< 0.01
10–19	Total	2.82	3.23	4.41	< 0.001	0.10	<	0.53	< 0.05
	Male	2.88	3.47	4.81	< 0.001	0.15	<	0.48	< 0.01
	Female	2.75	2.98	4.00	< 0.001	0.04	<	0.58	< 0.01
20–29	Total	2.08	2.42	3.66	< 0.001	0.24	<	0.80	< 0.01
	Male	1.95	2.17	3.35	< 0.001	0.24	<	0.79	< 0.01
	Female	2.20	2.66	3.98	< 0.001	0.24	<	0.81	< 0.001
30–39	Total	1.61	2.82	4.80	< 0.001	0.54	<	0.81	Before and after 2012 (P < 0.05)
	Male	1.68	2.75	4.18	< 0.001	0.44	<	0.51	
	Female	1.54	2.89	5.37	< 0.001	0.64	<	1.10	
40–49	Total	2.38	2.92	4.58	< 0.001	0.26	<	0.76	< 0.01
	Male	1.92	2.94	4.14	< 0.001	0.43	<	0.52	
	Female	2.84	2.91	5.00	< 0.001	0.08	<	0.99	< 0.001
50–59	Total	5.21	5.22	6.65	< 0.001	0.09	<	0.83	< 0.001
	Male	4.10	3.78	5.45	< 0.001	-0.15	<	0.85	< 0.001
	Female	6.22	6.56	7.76	< 0.01	0.37	<	0.80	< 0.05
60–69	Total	6.17	7.76	8.84	< 0.001	1.05	>	0.74	
	Male	5.87	6.74	7.45	< 0.001	0.55	<	0.59	
	Female	6.42	8.70	10.11	< 0.001	1.51	>	0.87	
70–79	Total	6.52	9.47	10.45	< 0.001	1.83	>	1.01	< 0.05
	Male	6.22	9.44	9.95	< 0.001	1.97	>	0.37	< 0.001
	Female	6.71	9.49	10.87	< 0.001	1.75	>	1.53	
80–89	Total	5.70	8.59	10.01	< 0.001	1.90	>	1.31	
	Male	6.70	9.34	9.50	< 0.001	1.35	>	0.67	
	Female	5.21	8.15	10.32	< 0.001	2.17	>	1.68	
≥ 90	Total	4.67	6.36	7.64	< 0.001	1.22	<	1.64	
	Male	3.57	5.93	8.78	< 0.05	3.02	>	2.47	
	Female	5.04	6.48	7.26	< 0.001	0.65	<	1.40	

* Comparison of the HZ incidence from 1997 to 2014 and from 2014 to 2020.
**Comparison of the increase of the mean annual HZ incidence between 1997 and 2014 and between 2014 and 2020.
*** Comparison of the HZ incidence between 1997 and 2014 and between 2014 and 2020.
**** Comparison of the HZ incidence variation between 1997 and 2014 and between 2014 and 2020, assuming HZ incidences of 1997 and 2014 of zero, respectively.

[1,2]. Reduction of HZ in vaccine recipients is due to the attenuated nature of the Oka varicella vaccine to reactivate HZ [21–23]. The increase in HZ cases in the child-rearing generation is due to the loss of boosting immunity to VZV by the reduction of varicella in their children.

We planned to analyze the HZ incidence in 2024 as a follow-up study to determine the natural HZ incidence without the effect of varicella epidemic, because the booster immunity to VZV by Oka varicella vaccine in the elderly continues for 8 years, and the effect of varicella epidemics on the HZ incidence would become minimal in 2024, 10 years after 2014. Protective booster immunity against HZ by the Oka varicella vaccine in elderly people begins to decline in 1 year and is maintained for 5 years, but the significant protective effect disappears in 8 years [12,13]. The preventive effect of Oka varicella vaccine on HZ diminishes in 8 years. However, as revealed in this study, the HZ incidence of those aged 30–39 years were most affected by varicella and had a reduced HZ incidence before universal varicella vaccination. Although 6 years have passed since universal varicella vaccination in 2014, the increasing trend of the HZ incidence has not diminished, but rather has increased more and more. This suggests that the increase in the HZ incidence due to the decrease in varicella epidemics has not yet reached its peak, even though 6 years have passed, since the preventive effect of current Oka varicella vaccine, Zostavax®, on HZ significantly diminished to 47% in 3 years [13]. Since the HZ incidence is increasing since 2014, this indicates that varicella contact has a longer duration of the preventive effect on HZ than the preventive effect of Zostavax®. It is not clear whether the cause of this difference is due to the booster immunization route of natural varicella infection or subcutaneous injection, or the wild or attenuated vaccine strain of VZV, or immunoreactivity of the target age groups between < 50 and > 50. The HZ-preventive effect of another HZ-preventive vaccine, gE-based Shingrix®, was sustained for at least 7 years [24]. Since the HZ incidence continues to rise, the preventive effect of varicella contact on HZ seems to be as persistent as Shingrix®.

Although it is not clear how lifestyle and behavioral changes and the associated stress affect the incidence of HZ [25–27], we examined how lifestyle and behavioral changes for preventing COVID-19 spread in 2020 affected HZ epidemiology. Since a total of 757 COVID-19 patients were recorded on December 31, 2020 and COVID-19 vaccine was not available in 2020 [18], the HZ incidence change is among the general population and not in patients with COVID-19. Lifestyle and behavioral changes as countermeasures against COVID-19 infection and the associated stress did not significantly affect HZ

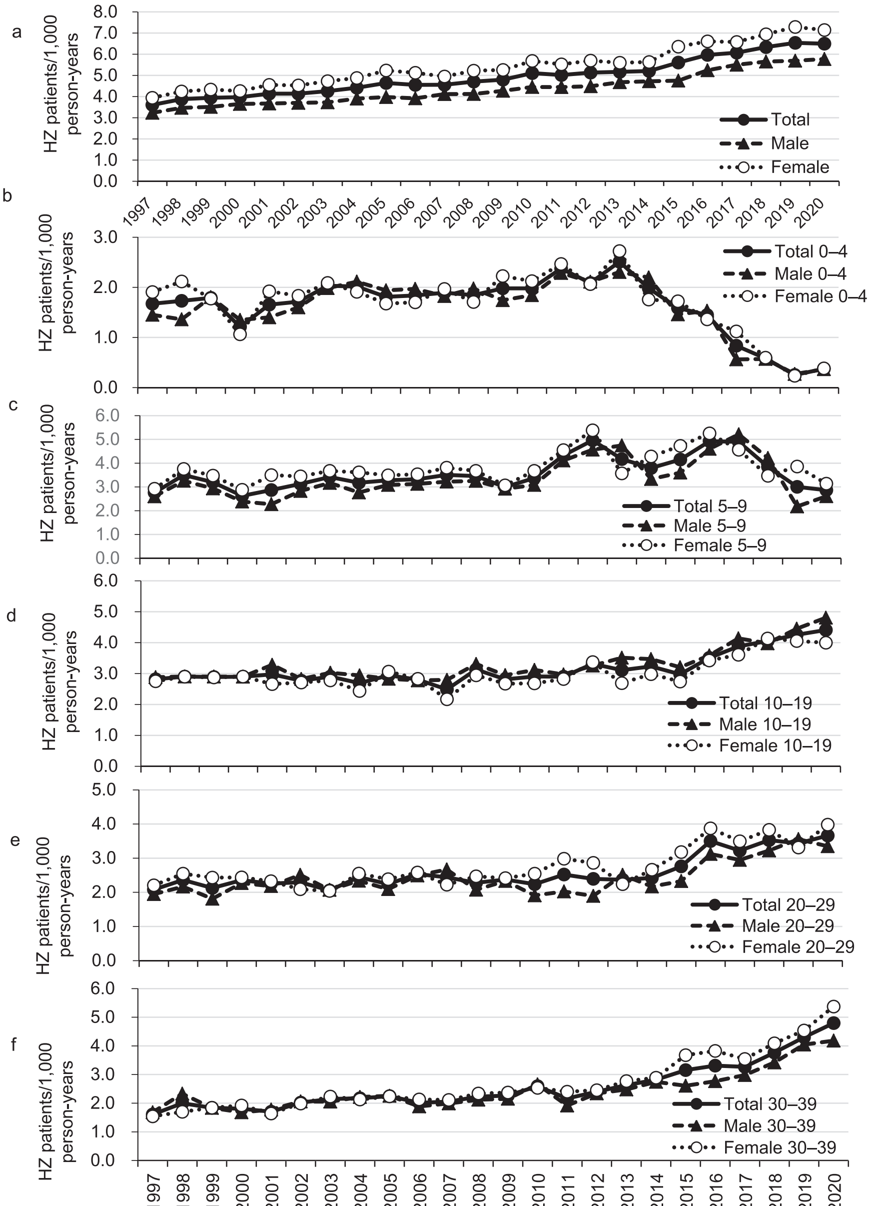

Fig. 3. Transition of the HZ incidence of each age group from 1997 to 2020. The HZ incidence of total population (closed circles), male (closed triangles), and female (open circles) of the age group. (a) Total population, (b) 0–4 years, (c) 5–9 years, (d) 10–19 years, (e) 20–29 years, (f) 30–39 years.

epidemiology. Therefore, it was clarified that the lifestyle and behavioral changes and stress associated with them and the stress associated with them that we are experiencing this time do not trigger the onset of HZ.

The HZ incidences after natural varicella and Oka varicella vaccine in children with leukemia were 0.80 and 2.46 cases per 100 person-years, respectively, and children who did not develop rash after vaccination had significantly lower HZ incidence, indicating that varicella vaccine reduced to at least 32.5% of HZ incidence after wild varicella [21]. The mean HZ incidence in patients aged 0–4 years from 1997 to 2012 was 1.85 per 1000 person-years after infection with wild varicella and 0.37 (20%) per 1000 person-years in 42,720 children in 2020. Pediatric HZ incidence was compared by the pattern of Oka varicella vaccine administration among 199,797 children [28], overall HZ incidence was 18.6/100,000 person-years in the first-dose measles-mumps-rubella (MMR) and varicella (V) vaccines separately, 17.9/100,000 person-years in the MMRV group, and 7.5/100,000 person-years in the varicella-alone group. The HZ incidence in our pediatric vaccinated people is about twice that in the United States, but there may be differences in the survey method and capture rate. In any case, the HZ incidence in Oka varicella vaccine recipients will be reduced from 37 to 7.5 per 100,000 person-years, with an increasing population of Oka varicella vaccine recipients. With this, the HZ incidence in young people is expected to decline to 20–35% of the current HZ incidence.

Increased HZ incidence due to the loss of booster immunity to VZV with the disappearance of varicella epidemics was observed even in 2018–2020 between the ages of 10 and 59, especially in the

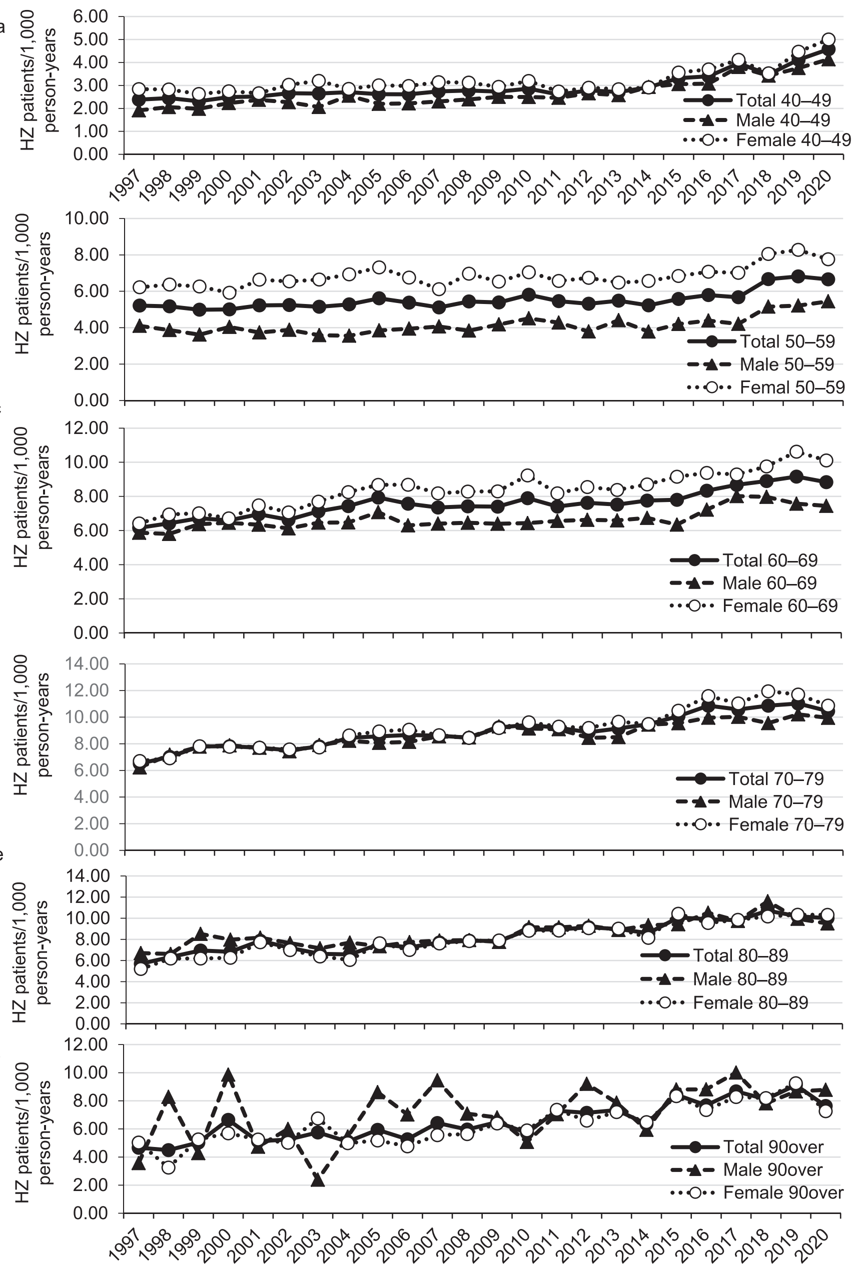

Fig. 4. Transition of the HZ incidence of each age group from 1997 to 2020. The HZ incidence of total population (closed circles), male (closed triangles), and female (open circles) of the age group. (a) 40–49 years, (b) 50–59 years, (c) 60–69 years, (d) 70–79 years, (e) 80–89 years, (f) ≥ 90 years.

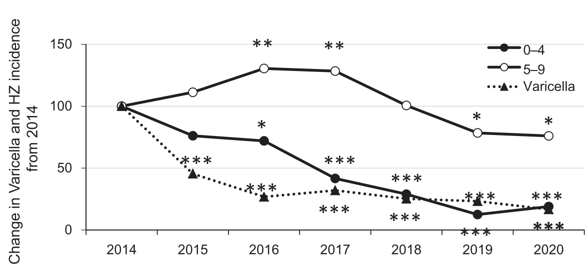

Fig. 5. Changes in the incidence of varicella (closed triangles) and the incidence of HZ among those aged 0–4 (closed circles) and 5–9 (open circles) years, with the 2014 incidence as 100%. Varicella incidence decreased followed by the HZ incidence among those aged 0–4 years. *, **, and *** indicate P < 0.05, P < 0.01, and P < 0.001, respectively, compared to 2014 by the chi-square test.

30 s. This increasing trend in HZ incidence is expected to continue in 2020 and longer, and it will take some time before the effects of varicella epidemic disappear and the natural HZ incidence at each age is settled. The effects of universal varicella vaccination are still in progress, and the epidemiology of HZ is changing. When the effects of varicella disappear, the frequency of age- and sex-specific HZ incidence becomes apparent. It is necessary to clarify how age- and sex-specific HZ incidence curves connect people aged 10–70 years in the future to assess the target age of the shingles vaccine.

Declaration of Competing Interest

There are no conflicts of interest to declare.

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Appendix

The 39 members of the Miyazaki Dermatologist Society in Miyazaki Prefecture who participated in this study. Y. Aoki, MD (Miyazaki City); I. Y. Ishii, MD (Nobeoka City); Y. Ishi, MD (Miyakonojo City); T. Inoue, MD (Miyazaki City); K. Era, MD (Nichinan City); K. Ohtuka, MD (Saito City); K. Okamura, MD (Nobeoka City); A. Kashima (Miyazaki City); R. Kaneda, MD (Miyazaki City); N. Kawana, MD (Nobeoka City); H. Kikuchi, MD (Miyazaki City); T. Kitamura, MD (Miyakonojo City); M. Kurokawa, MD (Miyazaki City); Y. Kurogi, MD (Takanabe Town, Koyu County); K. Nagatomo, MD (Takanabe Town, Koyu County); M. Kohashi, MD (Kunitomi Town, Higashi-Morokata County). K. Sakai, MD (Miyakonojo City); N. Takasaki, MD (Kobayashi City); T. Tazaki, MD (Miyazaki City); A. Tajiri, MD (Miyazaki City); S. Tada, MD (Miyazaki City); N. Toyama, MD (Nichinan City); S. Nakano, MD (Miyazaki City); H. Nagamine, MD (Hyuga City); K. Nakayama, MD (Miyazaki City); S. Narahara, MD (Miyakonojo City); H.Narita, MD (Miyazaki City); T. Nishida, MD (Miyazaki City); H. Hatisuka, MD (Miyazaki City); K. Higashi, MD (Miyazaki City); K. Horinouchi, MD (Hyuga City); E. Muroi, MD (Miyazaki City); M.Yoshiyama, MD (Saito City); E.Sakaguchi, MD (Kyoritu Hospital, Nobeoka City); Y. Oda, MD (Chiyoda Hospital, Hyuga City); M. Amono, MD (Dermatology Department in University of Miyazaki Hospital: Miyazaki City); E. Horikawa, MD (Miyazaki Prefectural Miyazaki Hospital, Miyazaki City); S. Tumori, MD (Koga General Hospital, Miyazaki City); F. Nakayama, MD (National Hospital Organization, Miyakonojo Medical Center, Miyakonojo City).

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