



RESPONSE TO COMMENT ON SHIH ET AL.

# Increased Incidence of Pediatric Type 1 Diabetes With Novel Association With Coxsackievirus A Species in Young Children but Declined Incidence in Adolescents in Taiwan. *Diabetes Care* 2021;44:1579–1585

Wei-Liang Shih,<sup>1,2</sup>  
Yi-Ching Tung,<sup>3</sup> and  
Luan-Yin Chang<sup>1,3</sup>

*Diabetes Care* 2022;45:e11 | <https://doi.org/10.2337/dci21-0046>

We appreciate the comments from Dr. Yen and Dr. Wei (1). Here is our response to their concerns. First, we agree that the yearly positive isolation numbers of enterovirus (EV) serotypes from 2001 to 2015 from the nationwide laboratory surveillance system of the Taiwan Centers for Disease Control show no decreasing trend (2). This laboratory surveillance system selected some patients with respiratory tract infections or hand, foot, and mouth disease to perform viral isolation and reported the most common circulating viruses in Taiwan, but the isolation numbers of EV did not reflect the EV incidence of the general population. For the general population, seroepidemiology or nationwide database studies are more appropriate to measure serostatus or the incidence rate of certain infections. From the EV-A71 seroepidemiology studies, we demonstrated that the EV71 seropositive rates in children decreased markedly in 2017 compared with those in 1999 and 2007. For example, the EV-A71 seropositive rate of adolescents aged 12–19 years decreased from 65% in 1997 to 46% in 2017 (3).

Second, the ICD-9-CM codes used to identify the comorbid EV infection 1

year before the development of type 1 diabetes (T1D) in the report of the *Taiwan Diabetes Atlas* (4) revealed that the number of EV infections from 2000 to 2007 and 2008 to 2016 was 27 (0.7%) and 55 (1.4%), respectively ( $P = 0.0012$ ). These data demonstrated the association of EV infection with T1D was stronger in 2008 to 2016 than that in 2000 to 2007. This result is not against our speculation that the decreasing trend of adolescent T1D incidence in Taiwan is partly due to the decreasing numbers of EV infection from 2001 to 2015 in Taiwan.

Third, we think that other environmental factors and host genetic factors played more important roles in T1D than EV infection in Taiwanese adolescents after they had much lower incidence of EV infection during recent years. This may be one of the reasons why the association of EV infection with the risk of T1D was not significant in adolescents in our study (5). We thus consider that the adolescent incidence of T1D had a decreasing trend when one of the important factors, number of EV infections, declined. Further investigations are needed to verify this speculation.

**Duality of Interest.** No potential conflicts of interest relevant to this article were reported.

## References

1. Yen FS, Wei JCC. Comment on Shin et al. Increased incidence of pediatric type 1 diabetes with novel association with coxsackievirus A species in young children but declined incidence in adolescents in Taiwan. *Diabetes Care* 2021;44:1579–1585 (Letter). *Diabetes Care* 2021;44:1579–1585. DOI: <https://doi.org/10.2337/dc20-1092>
2. Taiwan Centers for Disease Control. Statistics, Viral Infectious Disease Contract Laboratory. Accessed 25 June 2021. Available from <https://www.cdc.gov.tw/File/Get/sLisbaJqybKb9KORE-43mg>
3. Lee JT, Yen TY, Shih WL, et al. Enterovirus 71 seroepidemiology in Taiwan in 2017 and comparison of those rates in 1997, 1999 and 2007. *PLoS One* 2019;14:e0224110
4. Taiwan Diabetes Atlas. Type 1 diabetes mellitus. Taiwan, Taipei: Taiwanese Association of Diabetes Educators (TADE), 2020. Accessed 25 June 2021. Available from page 42 of <https://www.tade.org.tw/upload/FileDownload/42.pdf>
5. Shih WL, Tung YC, Chang LY, Fang CT, Tsai WY. Increased incidence of pediatric type 1 diabetes with novel association with coxsackievirus A species in young children but declined incidence in adolescents in Taiwan. *Diabetes Care* 2021;44:1579–1585

<sup>1</sup>Institute of Epidemiology and Preventive Medicine, College of Public Health, National Taiwan University, Taipei, Taiwan

<sup>2</sup>Infectious Diseases Research and Education Center, Ministry of Health and Welfare and National Taiwan University, Taipei, Taiwan

<sup>3</sup>Department of Pediatrics, National Taiwan University Hospital, College of Medicine, National Taiwan University, Taipei, Taiwan

Corresponding author: Luan-Yin Chang, [lychang@ntu.edu.tw](mailto:lychang@ntu.edu.tw)

© 2021 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. More information is available at <https://www.diabetesjournals.org/journals/pages/license>.