HHS Public Access

Author manuscript

J Adolesc Health. Author manuscript; available in PMC 2024 October 01.

Published in final edited form as:

J Adolesc Health. 2024 April ; 74(4): 696–702. doi:10.1016/j.jadohealth.2023.11.005.

Incidence of Adolescent Syncope and Related Injuries Following Vaccination and Routine Venipuncture

Holly C. Groom, M.P.H.[a,*], **Neon B. Brooks, Ph.D.**[a], **Eric S. Weintraub, M.P.H.**[b], **Matthew T. Slaughter, M.S.**[a], **Kathleen F. Mittendorf, Ph.D.**[c], **Allison L. Naleway, Ph.D.**[a]

[a]Kaiser Permanente Center for Health Research, Portland, Oregon

[b]National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia

[c]Vanderbilt-Ingram Cancer Center, Vanderbilt University Medical Center, Nashville, Tennessee

Abstract

Purpose: Vaccination is associated with syncope in adolescents. However, incidence of vaccine-associated syncope and resulting injury, and how it compares to syncope incidence following other medical procedures, is not known. Here, we describe the incidence of syncope and syncope-related injury in adolescents following vaccination and routine venipuncture.

Methods: We identified all Kaiser Permanente Northwest members ages 9–18 years with a vaccination or routine venipuncture and a same-day International Classification of Diseases diagnosis of syncope from 2013 through 2019. All cases were chart reviewed to establish chronology of events (vaccination, venipuncture, syncope, and injury, as applicable) and to attribute cause to vaccination or venipuncture. Incidence rates for vaccine-associated and venipuncture-associated syncope were calculated overall, by sex and age group. Syncope events resulting in injury were assessed for each event type.

Results: Of 197,642 vaccination and 12,246 venipuncture events identified, 549 vaccination and 67 venipuncture events had same-day syncope codes. Chart validation confirmed 59/549 (10.7%) events as vaccine-associated syncope, for a rate of 2.99 per 10,000 vaccination events (95% confidence interval (CI): 2.27–3.85) and 20/67 (29.9%) events as venipuncture-associated syncope, for a rate of 16.33 per 10,000 venipuncture events (95% CI: 9.98–25.21). The incidence rate ratio of vaccine-associated to venipuncture-associated syncope events was 0.18 (95% CI: 0.11–0.31). The incidence of vaccine-associated syncope increased with each additional

[*]Address correspondence to: Holly C. Groom, M.P.H., Kaiser Permanente Center for Health Research, 3800 N. Interstate Avenue, Portland, OR 97232. holly.c.groom@kpchr.org (H.C. Groom).

Holly Groom: Conceptualization, Methodology, Validation, Data curation, Writing- Original Draft, Writing- Review & editing, Visualization. Neon Brooks: Data curation, Writing,- Original Draft, Writing- Review & editing, Visualization. Eric Weintraub: Conceptualization, Methodology, Writing- Review & editing. Matthew Slaughter: Methodology, Data curation, Software, Formal analysis, Writing- Review & editing. Kate Mittendorf: Conceptualization, Methodology, Writing- Review & editing. Allison Naleway: Conceptualization, Methodology, Validation, Data curation, Writing- Review & editing.

Supplementary Data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jadohealth.2023.11.005.

Conflicts of interest: ALN has received research funding from Pfizer and Vir Biotechnology for unrelated studies.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

simultaneously administered vaccine, from 1.51 per 10,000 vaccination events (95% CI: 0.93–2.30) following a single vaccine to 9.94 per 10,000 vaccination events (95% CI: 6.43–14.67) following three or more vaccines. Syncope resulted in injury in about 15% of both vaccine and venipuncture events.

Discussion: Syncope occurs more commonly following venipuncture than vaccination. The number of simultaneously administered vaccines is a risk factor for postvaccination syncope in adolescents.

Keywords

Vaccination; Vasovagal syncope; Adolescent preventive medicine

Vasovagal syncope, or fainting, can be precipitated by vaccinations and other medical procedures [1,2]. While syncope itself poses little risk, resultant falls can lead to injury, including head trauma, that can cause concussion, hospitalization, or rarely, death [3–6]. Syncope is most common in adolescent and elderly populations [7–9]. Following an increase in reports to the Vaccine Adverse Events Reporting System (VAERS) for syncope in adolescents after the licensure of the human papillomavirus (HPV), meningococcal conjugate (MCV4), and tetanus-diphtheria-acellular pertussis (Tdap) vaccines [6], the Advisory Committee on Immunization Practices (ACIP) noted that an observation period should be “strongly considered”, particularly when vaccinating adolescents, to decrease the risk of syncope-related injury [10]. Understanding the risk of syncope and resulting injury in adolescents is important to inform preventive interventions.

Since 2008, studies have consistently associated syncopal events with the newly licensed adolescent vaccines [11–15]. However, since the vaccines were introduced in the United States at the same time and often administered concurrently, it is difficult to isolate the effects of particular vaccines or to distinguish these from the effects of receiving multiple simultaneous vaccinations. Females were disproportionately represented in reports of syncope to VAERS during the time when HPV vaccine was only recommended to females, leading to speculation that HPV vaccine may be associated with greater syncope risk than other vaccines [12]. However, the only study comparing risk of syncope following HPV vaccine to other adolescent vaccines found no increased risk specific to HPV vaccine [16]. Subsequently, a summary of 12 publications on syncope following vaccination compiled by the Institute of Medicine in 2011 concluded that a causal relationship exists between syncope and any injected vaccine [17].

Precise incidence of vaccine-associated syncope has been difficult to determine due to differences in definition and underreporting of syncope, which is perceived by providers as relatively benign [18]. The variability in methods for validating syncope events makes it challenging to compare incidence rates across studies, or to compare rates following vaccination to rates following other medical procedures. Further, little is known about the risk of injury from vaccine-associated syncope. While serious injuries and death are rare but documented in VAERS, rates of more minor syncope-related injuries following vaccination are unknown.

Here, we describe the incidence of vasovagal syncope and syncope-related injury reported in the electronic medical record (EMR) following vaccination in adolescents ages 9–18 years in a large integrated health system from 2013 to 2019. We compare these to rates of syncope following routine venipuncture for lipid screening, as both are part of routine adolescent care and both involve needle insertion. We also compare incidence of syncope following HPV vaccination with incidence following other adolescent vaccinations.

Methods

The study population included Kaiser Permanente Northwest members ages 9–18 years with a vaccination or lipid screening venipuncture (index event) between January 1, 2013, and December 31, 2019, who had at least12 months of continuous health plan enrollment before the index event. Within this population, we identified all coded diagnoses of syncope (International Classification of Diseases [ICD]-9 780.2 syncope and collapse, ICD-10 R55 syncope and collapse) that occurred during an outpatient or inpatient visit on the same day as an index event. Individuals could be represented more than once. Following ascertainment of syncope events, we identified any injury diagnoses coded on the index date or the following day (see Table S1 for a list of injury diagnosis codes).

Lipid screening venipuncture events were identified by *Current Procedural Terminology* codes 80061 (lipid panel), 82,465 (cholesterol, serum or whole blood, total), 83,719 (very low-density lipoprotein cholesterol), 83,721 (low-density lipoprotein cholesterol), and 84,478 (triglycerides). For vaccination, only injectable vaccines were included because injection is understood to precipitate vasovagal syncope [17]. Additionally, we excluded Tdap vaccination outside of preventive health (well-child or routine gynecological exam, codes ICD-9 V20.2, V70.0, V70.3, V72.31 and ICD-10 Z00.129, Z00.00, Z01.4, Z01.411, Z01.419), as Tdap vaccines administered in urgent or emergent situations are likely due to injury, which may independently lead to syncope events.

Each coded syncope diagnosis was chart reviewed to validate that a syncope event occurred on the index date. We excluded cases where syncope was not diagnosed during the index visit (miscoded diagnosis), or the medical record could not be located. Syncope events were then categorized as historical (the syncope event occurred at least 1 day before the index event) or incident (occurring on the same day as the index event) (Figure 1). Incident syncope events were reviewed to establish the chronology of events (vaccination, venipuncture, syncope, and injury, as applicable). Incident syncope events were categorized as related or unrelated to vaccination or venipuncture based on chronology and the provider's attribution of causation in the EMR (Table S2). Syncope events following both vaccine and venipuncture were attributed to only one event based on which event immediately precipitated the syncope event and attribution in chart notes. Clinician comments on the specific vaccine believed to have caused the syncope event were abstracted when available.

Chart abstraction also included review of any injuries documented as occurring on the same day as the syncope event, including injuries described in provider notes that did not receive a

diagnosis code. Abstracted information included the type of injury, the body part(s) affected, and whether subsequent medical care was sought or provided.

Incidence was calculated as the number of syncope cases per 10,000 vaccination or venipuncture events. 95% confidence intervals (CIs) for the binomial proportion were calculated according to the Clopper-Pearson exact method [19]. A vaccination event could involve one or more simultaneously administered vaccines. Incidence rates for vaccine-associated and venipuncture-associated syncope were calculated overall, by sex, and by age group (ages 9–12, 13–15, 16–18). Incidence rates for vaccine-associated syncope were also calculated by number of vaccines received (one, two, three or more), and by whether the HPV vaccine was received. Finally, an incidence rate ratio was used to compare incidence rates by number of vaccines administered, vaccine-type (HPV vs. non-HPV) and vaccine-associated versus venipuncture-associated syncope.

This study was reviewed and approved by the Kaiser Permanente Northwest institutional review board and was conducted with a waiver of informed consent.

Results

A total of 197,642 vaccination events and 12,246 lipid screening venipuncture events were identified in 9-year-olds to 18-year-olds from 2013 through 2019. In 70% of vaccination events, a single vaccine was administered, in 17%, two vaccines were administered simultaneously, and in 13%, three or more vaccines were administered. Of the 25,159 events where three or more vaccines were administered, 77% occurred among 9–12-year-olds, 8% among 13–15-year-olds, and 15% among 16–18-year-olds.

Vaccine and syncope identification

A total of 549 vaccination index events had a syncope diagnosis coded on the same day in the EMR; 24 of these (4%) also occurred on the same day as a venipuncture event (Figure 1). Five hundred forty-two (99%) were chart-confirmed as valid syncope events; seven were excluded because a provider determined it was not a syncope event (n = 3), syncope was not diagnosed at the specified visit (n = 2), or the chart was not located (n = 2) (Figure 1). Characteristics of individuals with validated syncope events are shown in Table 1.

Eighty-one percent (437/542) of confirmed syncope events were classified as historical (syncope occurring before the index visit); 105 (19%) were incident (occurring on the day of the visit). Thirty-five incident syncope events (33%) occurred before vaccination and 70 (67%) occurred after vaccination.

When incident syncope events occurred before vaccination, they most often occurred at school or at home (25/35, 71%), with individuals receiving due or past-due vaccines while seeking follow-up care. In five cases (14%), individuals had syncope during their clinical encounter, and the clinician proceeded with scheduled vaccine(s) after the patient had recovered. In five cases (14%), the individual had syncope and an injury (in either order) and came to the clinic specifically for the Td/Tdap vaccine.

Rates of postvaccination syncope

Of the 70 confirmed postvaccination syncope events, 59 (84%) were indicated by a provider to have occurred immediately following vaccination and to be a result of vaccination; the remaining 11 were attributed to a venipuncture event that occurred after vaccination. Thus, the final chart validation rate to identify vaccine-associated syncope was 10.7% (59/549), and the overall rate of postvaccination syncope was 2.99 per 10,000 vaccination events (95% CI: 2.27–3.85).

Rates of postvaccination syncope were similar by sex (3.72 and 2.28 per 10,000 for females and males, respectively; data not shown). Overall rates of postvaccination syncope were higher among 9–12-year-olds (4.58 per 10,000; 95% CI: 3.24–6.29) than 13–15-year-olds (1.52; 95% CI: 0.65–2.99), with 16–18-year-olds not differing from either group (2.10; 95% CI: 1.12–3.59; Figure 2).

The syncope rate per 10,000 vaccination events following administration of a single vaccine was 1.51 (95% CI: 0.93–2.30), compared to 3.92 (95% CI: 2.09–6.70) following administration of two vaccines, and 9.94 (95% CI: 6.43–14.67) following administration of three or more vaccines (Figure 2). When stratified by number of vaccines received, differences in syncope rates by age were no longer significant. Among those aged 9–12 years and 16–18 years, rates of syncope following three or more vaccines were significantly higher than rates following receipt of one vaccine (Figure 3, Table S3). When stratified by the number of vaccines received, rates of syncope were similar following vaccination events with and without the HPV vaccine (Figure 4, Table S3).

Venipuncture and syncope identification

Sixty-seven venipuncture index events had a same-day syncope diagnosis in the EMR, including the 24 events that occurred on the same day as vaccination (see above). Of these 67, 64 (96%) were chart-confirmed as valid syncope events; three were excluded because there was not a syncope diagnosis at the specified visit (n = 2), or a chart was not located (n = 1) (Figure 1).

Chart abstraction determined that 37 of the 64 (58%) syncope events were historical and 27 (42%) were incident. Of the incident events, 7 (26%) occurred before venipuncture and 20 occurred after venipuncture. None of the seven events occurring before venipuncture were attributed to venipuncture-related anxiety.

Rates of post-venipuncture syncope

All 20 confirmed postvenipuncture syncope events (100%) were indicated by provider notes to be due to venipuncture (including 11 in which a vaccination occurred before venipuncture), resulting in a final chart validation rate of 20/67 or 29.9%, and an overall postvenipuncture syncope rate of 16.33 per 10,000 venipuncture events (95% CI: 9.98–25.21). Syncope was significantly less common following vaccination than following venipuncture (incidence rate ratio 0.18; 95% CI: 0.11–0.31; Figure 4). Although the crude rate of postvenipuncture syncope was highest among the 13–15-year-old age group (24.93 per 10,000 events, 95% CI: 11.96–45.80), CIs for all three age groups were wide and

overlapping (9–12-year-olds: 4.3 per 10,000, 95% CI: 0.11–23.93; 16–18-year-olds: 15.23 per 10,000, 95% CI: 6.97–28.89). The rate of postvenipuncture syncope was higher among females (20.28, 95% CI: 10.49–35.41) than males (12.64, 95% CI: 5.46–24.89; data not shown).

Postsyncope injury

Injury identification.—We identified 18 coded injuries that occurred within 24 hours of a vaccination or venipuncture event and a syncope event through automated data extraction. However, chart abstraction identified only one of these injuries as related to postevent syncope. Sixteen injuries occurred in patients with syncope that was not attributed to vaccination or venipuncture, and one injury occurred before a visit at which a qualifying syncope event occurred.

Through abstraction, we identified an additional 11 injuries following postevent syncope, for a total of 12 injuries: nine resulting from vaccine-associated syncope, and three resulting from venipuncture-associated syncope. The proportion of syncope events resulting in injury was 15% following both vaccination and venipuncture.

Eleven of the 12 injuries occurred on the face or head, one of which required follow-up care: this patient suffered a concussion following vaccination that took over a month to resolve and limited participation in athletics. The remaining injuries were minor contusions or abrasions which did not require further medical attention beyond basic first aid at the visit, although one patient visited the emergency department for evaluation of facial abrasions.

Discussion

Incidence of vaccine-associated syncope among adolescents was 2.99 per 10,000 vaccination events. This was significantly lower than rates of syncope following a lipid blood draw (16.33 per 10,000 events). Syncope rates increased significantly with the number of simultaneous vaccines given at a visit; when controlling for number of vaccines, we observed no significant differences in vaccine-associated syncope by age or whether the patient received the HPV vaccine. Injuries occurred following 15% of postvaccination or postvenipuncture syncope events, but most required no medical care beyond basic first aid.

To our knowledge, only one other US study has reported on syncope following administration of all vaccine types. This assessment relied on reports from a passive reporting system to capture syncope events and used a doses-distributed denominator, reporting a syncope rate of 0.0054 per 10,000 doses distributed in the United States for all individuals aged 5 years and older from 2005 to 2007 [6].

Vaccine-specific safety studies based on passive reporting have identified syncope as associated with Tdap (0.13 per 10,000 doses distributed) [15], MCV4 (observed rates in VAERS data exceeding 7 times the expected rate following vaccine) [14] and HPV vaccines (0.47^{13} to 0.82^{12} per 10,000 doses distributed in the United States and 0.78 per 10,000 doses distributed in Australia) [20]. One study estimate from Australia found a rate of 2.69 syncope events per 10,000 HPV doses administered among youth ages 12–13 in 2013–

2014 during a school-based campaign which included enhanced training of school nurses to improve documentation of adverse events following vaccination, including syncope [21]. This estimate may be most comparable to our study estimate, which also relied on real-time documentation of events from vaccination providers.

Prior studies of syncope rates did not account for the number of vaccines received. In our data, syncope was strongly associated with the number of vaccines administered, with rates reaching 9.9 per 10,000 events in those receiving three or more vaccines. This is consistent with findings from a study of adults in the Armed Services, where syncope rates increased by 286% when three vaccines were simultaneously administered, compared to one vaccine [22]. Another study found that both receipt of multiple vaccines and younger age (11–14 vs.15–21 years) were associated with higher rates of presyncope [23]. In our data, 9–12-year-olds had the highest rate of postvaccination syncope following three or more simultaneous vaccines, however, differences between age groups were not statistically significant. Importantly, the ACIP vaccine schedule includes a recommendation for three, coadministered vaccines (HPV, Tdap, MCV) sometime between ages 9–12 years, which explains why we observed a much higher rate of three or more vaccines in this age group. Given the small number of visits where three or more vaccines were administered among those ages 13 and older, we had limited ability to compare rates of syncope where three or more vaccines were administered between age groups. A larger study population would be needed to fully disentangle effects of age and number of simultaneous vaccines on rates of syncope.

In our data, HPV vaccination was not independently associated with higher rates of syncope than non-HPV vaccination when accounting for number of vaccines received. While several prior studies have reported an association between HPV vaccination and syncope [11–13], they did not account for simultaneous vaccination. Notably, the HPV vaccine was administered to 90% of adolescents who received three or more vaccines in a visit; failing to account for number of vaccines could lead to the impression that the HPV vaccine is specifically associated with syncope events. Indeed, when not accounting for number of vaccines administered, visits with HPV vaccination had significantly higher rates of syncope in our data (4.40, 95% CI: 3.11–6.03) than those without (1.89, 95% CI: 1.17–2.89). In our chart review of vaccine-associated syncope events, 26 (44%) of 59 events included notes attributing the syncope to a specific vaccine, 15 (58%) of which specified the HPV vaccine. Of these, eight involved HPV administered along with other vaccines, with HPV administered last. Thus, it cannot be determined if the HPV vaccine or the effect of multiple vaccines caused these syncope events.

While almost all (99%) syncope events identified through data extraction were valid, chart review was critical, as 81% of identified syncope events occurred ≥1 days before the vaccination and/or venipuncture event. Our confirmation rates were 10.8% for identifying vaccine-associated syncope, and 29.9% for venipuncture-associated syncope. Using extraction of coded diagnosis data alone is likely to result in highly inflated estimates of vaccine-associated or venipuncture-associated syncope.

About 15% of vaccine-associated and venipuncture-associated syncope events led to documented injuries. Medical record review is critical for accurately describing syncope-related injuries: almost all syncope-related injuries were missed when relying only on extracted diagnosis codes. All but one injury involved the patient hitting their head, although this could reflect higher likelihood of providers documenting head injury than other forms of injury. The rate of 15% is somewhat higher than prior estimates from the literature: a study in adults from the US Armed Forces found that 6.9% of postimmunization syncopal events resulted in diagnosis of injury [22], and an Australian study of adolescents reported that 2% of syncope events had resultant injuries [21]. Adherence to the ACIP recommendation of a seated observation period following adolescent vaccinations would likely reduce injury risk, and may be particularly warranted for patients receiving multiple vaccines. However, of the nine injuries observed following vaccination, four occurred among individuals who fell while seated on the exam table or a chair; these injuries may have been prevented had the person been lying down.

Vaccination-associated syncope was significantly less common than venipuncture-associated syncope in our data. Given the similar proportions of syncope-associated injury following venipuncture compared to vaccination, the risk of injury following venipuncture may also warrant additional precautionary measures. However, with few injuries overall, it is hard to make any definitive conclusions about the frequency of these events.

While there is a clinical recommendation for routine lipid screening among adolescents, one study limitation was that blood draws were not routinely performed in the population. Nonetheless, we had adequate numbers to detect differences in syncope rates following vaccination compared to blood draws. As a comparison group, we also acknowledge that adolescents who receive lipid blood draws may represent a population identified as at increased risk for cardiovascular disease, sometimes identified by elevated body mass index (BMI) [24]. For this reason, we examined BMI in our study population and found a higher average BMI among those with only venipuncture events compared to those with only vaccine events (26.6 vs. 22.2, data not shown). Prior studies have found that risk of syncope is higher among those with lower BMI [25], thus we do not feel the higher BMI in our venipuncture group has any impact on our study conclusions; if anything, it may have led to an underestimate of venipuncture-associated syncope in the general population. Another limitation was the infrequency of vaccination with three or more vaccines in adolescents older than 12, limiting our power to compare syncope rates following multiple vaccines across ages. Due to the nature of our data, only provider-documented syncope was included, likely leading to underestimates. However, reporting bias should be similar among exposure groups.

These data suggest that vaccine-associated syncope rates increase with simultaneous vaccination, with the highest rates occurring in those receiving three or more vaccines in one visit. About 15% of syncope events result in injuries, a proportion that could be reduced with seated, possibly even supine, observation and monitoring of patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We would like to extend acknowledgements to Mara Kalter and Judy Donald for their assistance with chart review.

References

[1]. Ganzeboom KS, Colman N, Reitsma JB, et al. Prevalence and triggers of syncope in medical students. Am J Cardiol 2003;91:1006–8. A8. [PubMed: 12686351]

[2]. Myers TR, McNeil MM, Ng CS, et al. Adverse events following quadrivalent meningococcal CRM-conjugate vaccine (Menveo(R)) reported to the Vaccine Adverse Event Reporting system (VAERS), 2010–2015. Vaccine 2017; 35:1758–63. [PubMed: 28262331]

[3]. Woo EJ, Ball R, Braun MM. Fatal syncope-related fall after immunization. Arch Pediatr Adolesc Med 2005;159:1083.

[4]. Miller ER, Moro PL, Cano M, Shimabukuro TT. Deaths following vaccination: What does the evidence show? Vaccine 2015;33:3288–92. [PubMed: 26004568]

[5]. Mahajan D, Cook J, Dey A, et al. Supplementary report: Surveillance of adverse events following immunisation among children aged less than seven years in Australia, 1 January to 30 June 2012. Commun Dis Intell Q Rep 2013;37:E130–4. [PubMed: 24168086]

[6]. CDC. Syncope after vaccination — United States, January 2005–July 2007. MMWR Morb Mortal Wkly Rep 2008;57:457–60. [PubMed: 18451756]

[7]. Kenny RA, McNicholas T. The management of vasovagal syncope. QJM 2016;109:767–73. [PubMed: 27340222]

[8]. da Silva RM. Syncope: Epidemiology, etiology, and prognosis. Front Physiol 2014;5:471. [PubMed: 25538626]

[9]. Task Force for the D, Management of S, European Society of C, et al. Guidelines for the diagnosis and management of syncope (version 2009). Eur Heart J 2009;30:2631–71. [PubMed: 19713422]

[10]. Kroger AT, Atkinson WL, Marcuse EK, Pickering LK, Advisory Committee on Immunization Practices Centers for Disease C, Prevention. General recommendations on immunization: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2006; 55(RR-15):1–48.

[11]. Klein NP, Hansen J, Chao C, et al. Safety of quadrivalent human papillomavirus vaccine administered routinely to females. Arch Pediatr Adolesc Med 2012;166:1140–8. [PubMed: 23027469]

[12]. Slade BA, Leidel L, Vellozzi C, et al. Postlicensure safety surveillance for quadrivalent human papillomavirus recombinant vaccine. JAMA 2009;302: 750–7. [PubMed: 19690307]

[13]. Arana JE, Harrington T, Cano M, et al. Post-licensure safety monitoring of quadrivalent human papillomavirus vaccine in the Vaccine Adverse Event Reporting System (VAERS), 2009–2015. Vaccine 2018;36:1781–8. [PubMed: 29477308]

[14]. Myers TR, McNeil MM, Ng CS, et al. Adverse events following quadrivalent meningococcal diphtheria toxoid conjugate vaccine (Menactra(R)) reported to the Vaccine Adverse Event Reporting System (VAERS), 2005–2016. Vaccine 2020;38:6291–8. [PubMed: 32747215]

[15]. Chang S, O'Connor PM, Slade BA, Woo EJ. U.S. Postlicensure safety surveillance for adolescent and adult tetanus, diphtheria and acellular pertussis vaccines: 2005–2007. Vaccine 2013;31:1447–52. [PubMed: 23142308]

[16]. Gee J, Naleway A, Shui I, et al. Monitoring the safety of quadrivalent human papillomavirus vaccine: Findings from the vaccine safety datalink. Vaccine 2011;29:8279–84. [PubMed: 21907257]

[17]. Institute of Medicine. Adverse effects of vaccines: Evidence of causality. Washington, DC: National Academies Press; 2011.

[18]. Driscoll DJ, Jacobsen SJ, Porter CJ, Wollan PC. Syncope in children and adolescents. J Am Coll Cardiol 1997;29:1039–45. [PubMed: 9120157]

[19]. Clopper CJ, Pearson ES. The use of confidence or fiducial limits illustrated in the case of the binomial. Biometrika 1934;26:404–13.

[20]. Crawford NW, Clothier HJ, Elia S, et al. Syncope and seizures following human papillomavirus vaccination: A retrospective case series. Med J Aust 2011;194:16–8. [PubMed: 21449862]

[21]. Phillips A, Hickie M, Totterdell J, et al. Adverse events following HPV vaccination: 11 years of surveillance in Australia. Vaccine 2020;38: 6038–46. [PubMed: 32709432]

[22]. Armed Forces Health Surveillance C. Syncope, active and reserve components, U.S. Armed Forces, 1998–2012. MSMR 2013;20:5–9.

[23]. Kemper AR, Barnett ED, Walter EB, et al. Drinking water to prevent postvaccination presyncope in adolescents: A randomized trial. Pediatrics 2017;140:e20170508. [PubMed: 29061871]

[24]. Expert Panel on Integrated Guidelines for Cardiovascular H, Risk Reduction in C, Adolescents, National Heart L, Blood I. Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: Summary report. Pediatrics 2011;128 Suppl 5(Suppl 5):S213–56. [PubMed: 22084329]

[25]. Yamada T, Yanagimoto S. Dose-response relationship between the risk of vasovagal syncope and body mass index or systolic blood pressure in young adults undergoing blood tests. Neuroepidemiology 2017;49: 31–3. [PubMed: 28810256]

IMPLICATIONS AND CONTRIBUTION

Chart review of adolescent syncope events in a large healthcare system demonstrated low overall incidence of vaccine-related syncope; a rate which is significantly lower than the rate of venipuncture-associated syncope. Simultaneous vaccination was associated with higher incidence of vaccine-associated syncope. Fifteen percent of vaccine-associated and venipuncture-associated syncope events resulted in injury. Diagnosis-code data for syncope is insufficient and chart review is required to identify these cases.

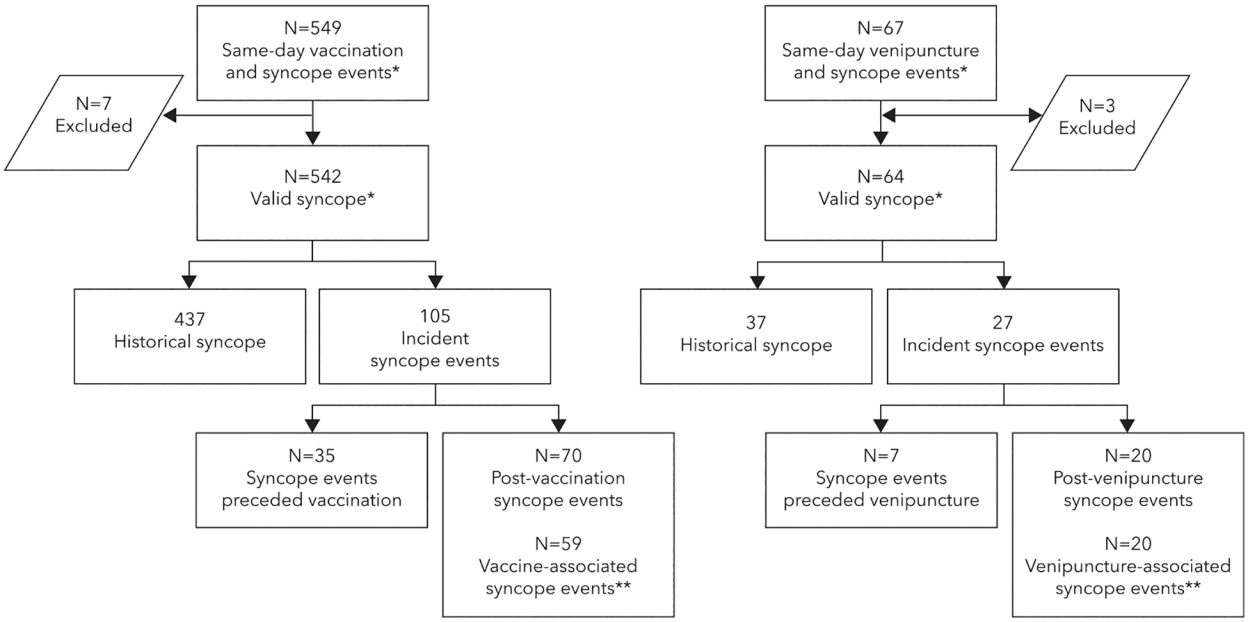

Figure 1.

Consort diagram of chart-reviewed syncope events. “Excluded” indicates syncope not diagnosed at the specified visit (n=4), final diagnosis is not syncope (n=3), and chart not located (n=3); “Historical” indicates syncope diagnosed at the visit but the event occurred ≥1 day prior to the vaccine and/or venipuncture event; “Incident” indicates syncope occurred the same day (day 0) as the vaccine and/or venipuncture event. *Includes 24 syncope events on the same day as vaccine and venipuncture events. **Includes 11 syncope events on the same day as vaccine but attributed to venipuncture.

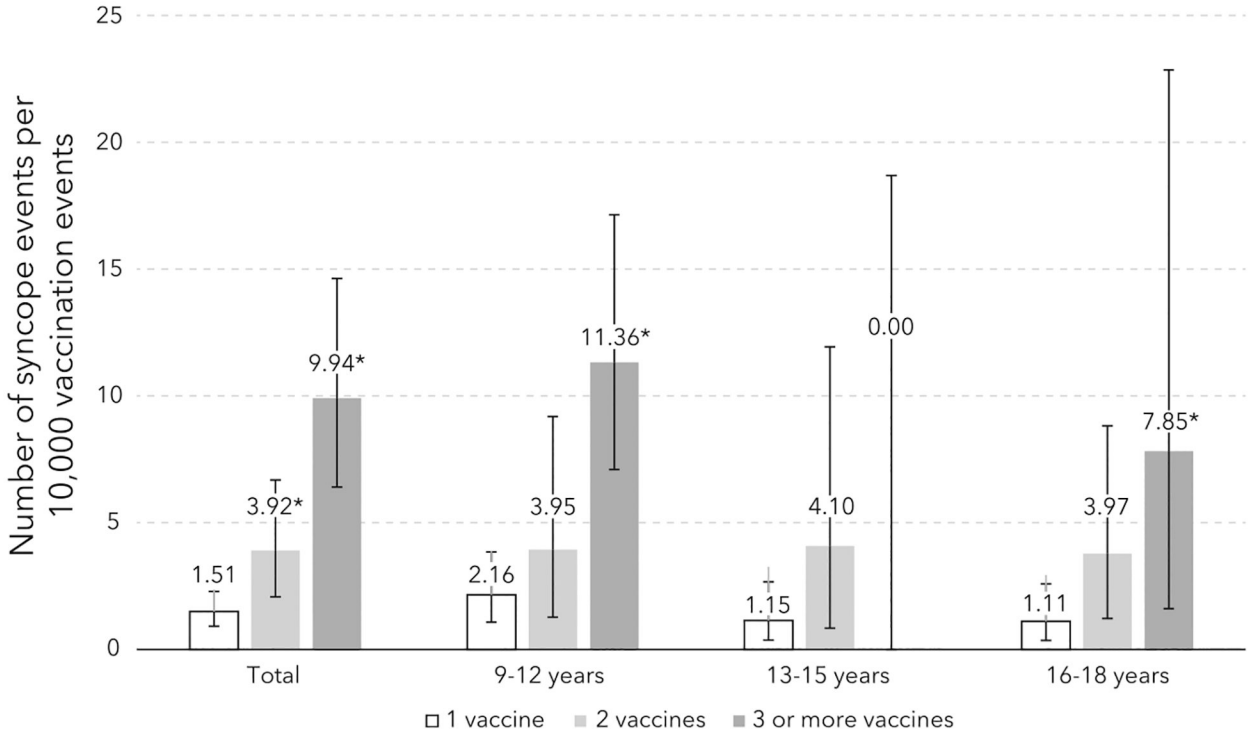

Figure 2.

Incidence of syncope per 10,000 events by age and preceding event type (vaccine or venipuncture), 2013–2019, Vaccine Safety Datalink. Error bars represent 95% CIs. *Significant difference between incidence rate of vaccine-associated syncope and venipuncture-associated syncope, $p < .05$.

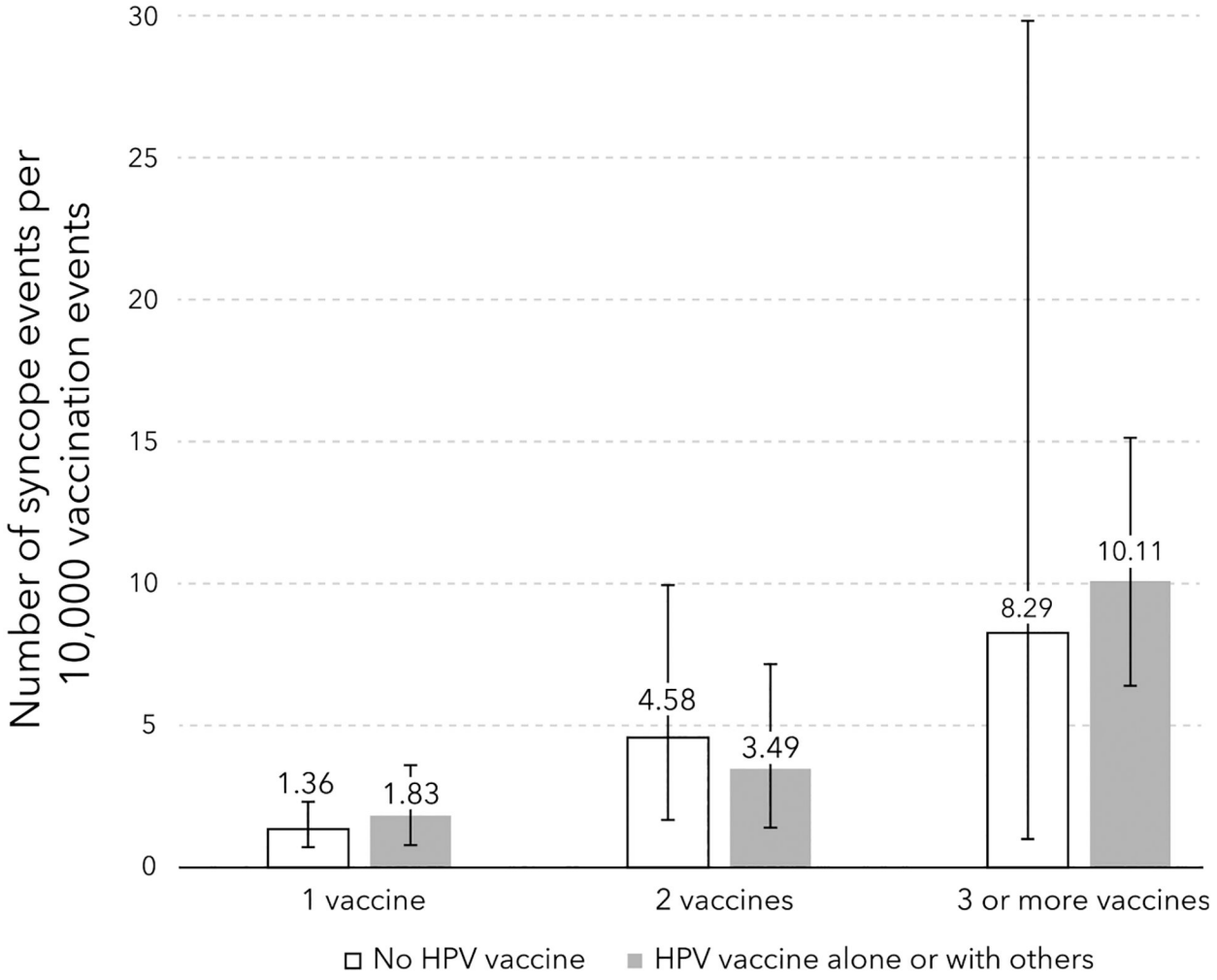

Figure 3.

Incidence of vaccine-associated syncope per 10,000 vaccination events by age and number of simultaneous vaccines received, 2013–2019, Vaccine Safety Datalink. Error bars represent 95% CIs. *Significantly higher than incidence of syncope following administration of one vaccine, $p < .05$.

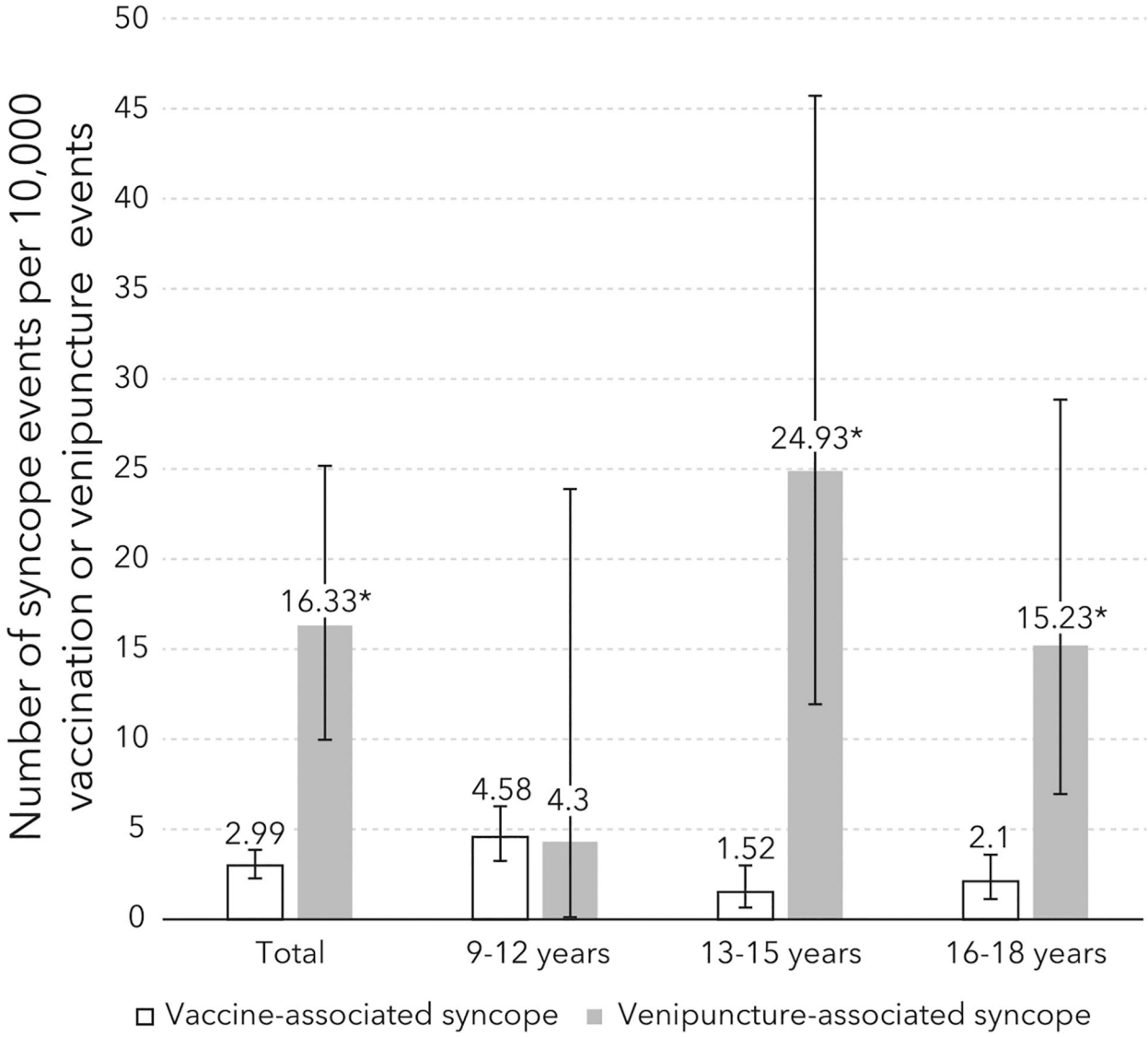

Figure 4.

Incidence of vaccine-associated syncope per 10,000 vaccination events by number and type (HPV vs. not HPV) of vaccines received, 2013–2019, Vaccine Safety Datalink. Error bars represent 95% CI.

Table 1

Characteristics of validated syncope events 2013–2019, Vaccine Safety Datalink

	Unrelated valid syncope events N = 503	**Vaccine-associated syncope events N = 59**	**Venipuncture-associated syncope events N = 20**
Sex			
Female	312 (62%)	36 (61%)	12 (60%)
Male	191 (38%)	23 (39%)	8 (40%)
Age			
9–12	133 (26%)	38 (64%)	1 (5%)
13–15	165 (33%)	8 (14%)	10 (50%)
16–18	205 (41%)	13 (22%)	9 (45%)