



Immunogenicity of 2-dose pre-exposure rabies vaccine co-administered with quadrivalent influenza vaccine in children

Napaporn Chantasrisawad^{1,2*}, Watsamon Jantarabenjakul^{1,2,3}, Suvaporn Anugulruengkitt^{1,2}, Suda Punrin⁴, Kornvika Limsuwun⁴, Panadda Sawangsinth², Chayapa Phasomsap², Jiratchaya Sophonphan², Chitsanu Pancharoen^{1,2}, Thanyawee Puthanakit^{1,2}

¹ Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
² Center of Excellence for Pediatric Infectious Diseases and Vaccines, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
³ Thai Red Cross Emerging Infectious Diseases Clinical Center (TRC-EID), King Chulalongkorn Memorial Hospital, Bangkok, Thailand
⁴ Queen Saovabha Memorial Institute, The Thai Red Cross Society, Bangkok, Thailand
*Email address: Napaporn.cha@chula.ac.th



Introduction

The World Health Organization recommends a 2-dose rabies pre-exposure prophylaxis (PrEP) regimen. Annual influenza vaccine visits provide an opportunity to add rabies PrEP as concomitant immunization without any additional cost for transportation or minimal additional health care worker manpower.

Objectives

This study aimed to compare the immunogenicity of rabies PrEP regimens co-administered with inactivated quadrivalent influenza vaccine (IIV4).

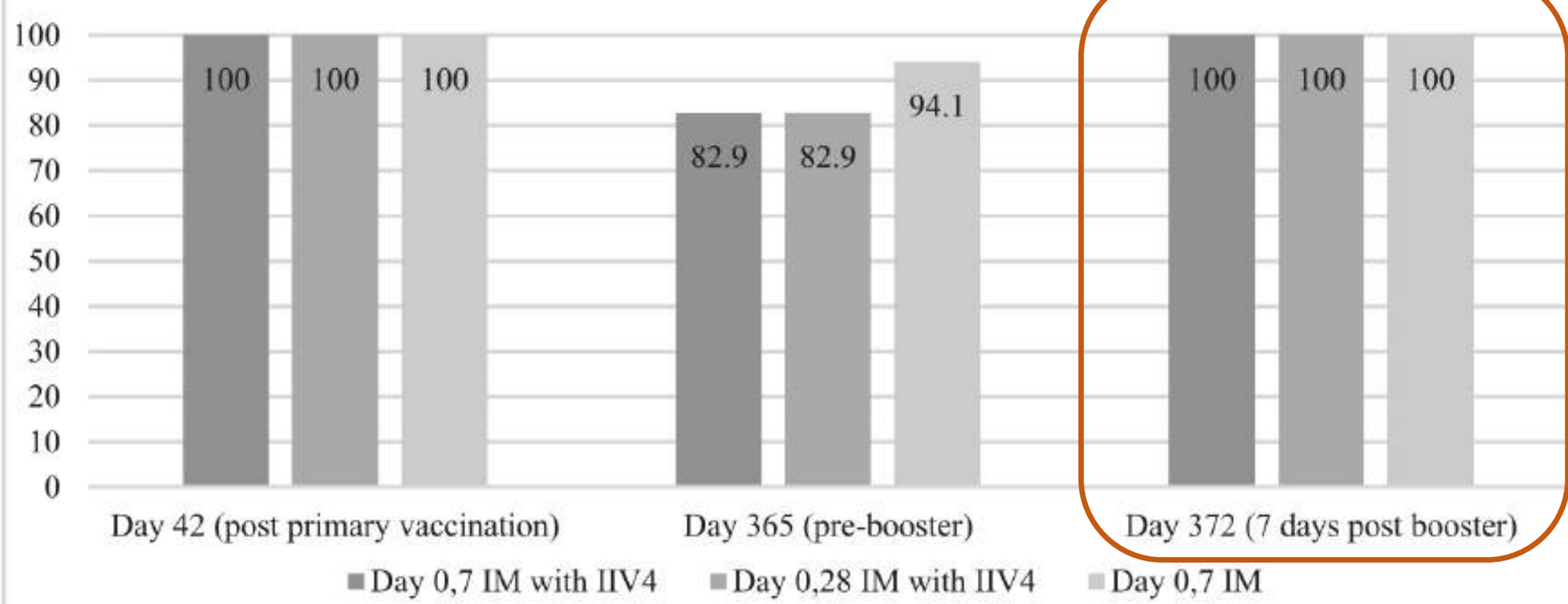
Methods

Children aged 3 to 9 years were randomly assigned (2:2:1) to receive 0.25 mL of chromatographically purified Vero cell rabies vaccine (CPRV) intramuscularly. Group A at day 0, 7 with IIV4; Group B at day 0, 28 with IIV4; Group C at day 0, 7. A booster-dose of CPRV was given on day 365. Primary outcome was the proportion of children with protective rabies virus neutralizing antibody (RVNA) ≥ 0.5 IU/mL, on day 42- and 7-days post-booster.

Results

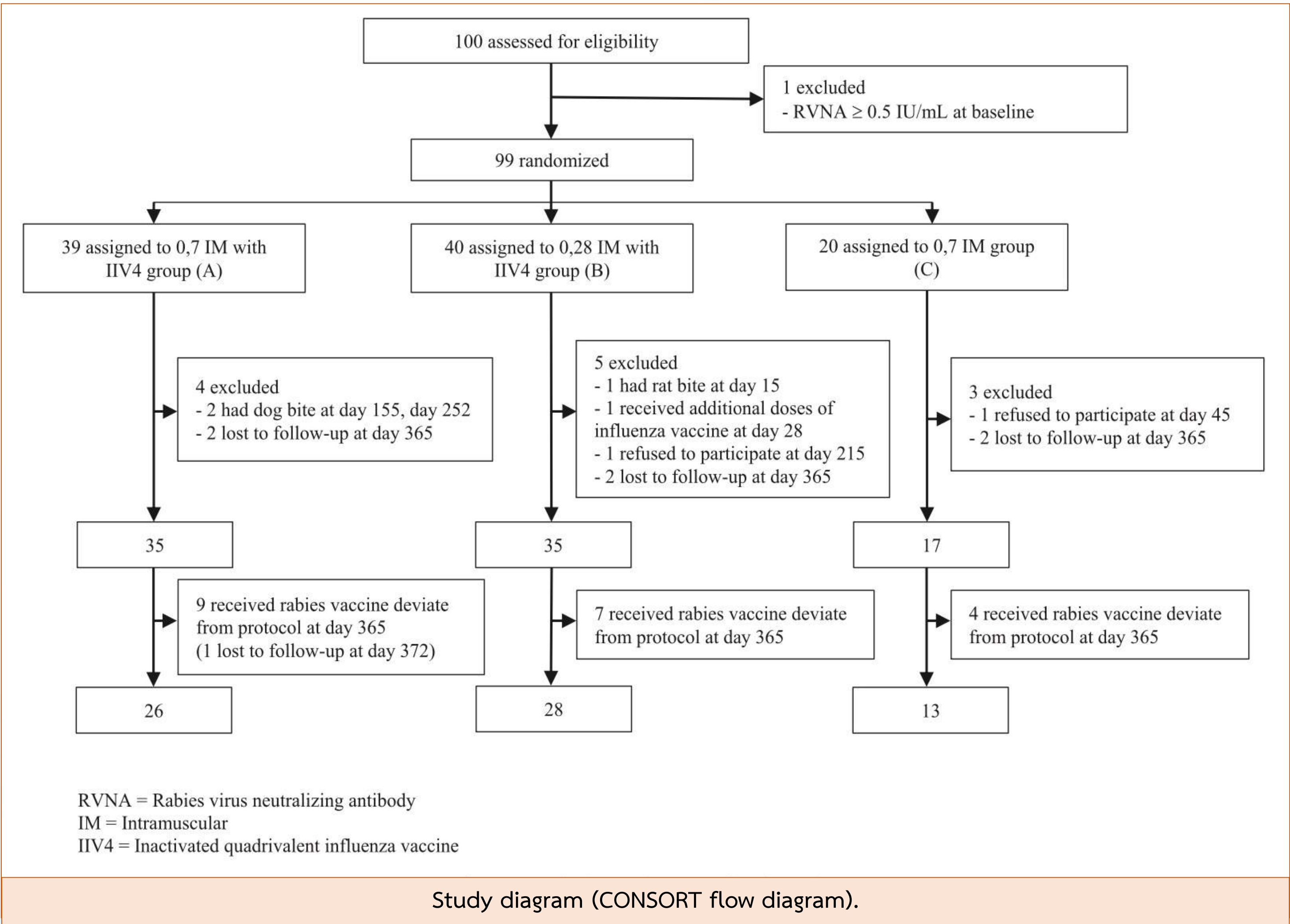
From November 2019 to January 2020; 100 children with a median age (IQR) of 5.4 years (4.8-7.3) were enrolled. All participants achieved protective RVNA titers on day 42 and 7-day post booster.

Geometric mean titer (GMT) at day 42 were Group A, 8.98 (95%CI 7.06-11.42); Group B, 23.89 (95%CI 19.33-29.51); Group C, 9.94 (95%CI 7.03-14.06). Likewise, RVNA GMT at 7 days post-booster were Group A, 42.53 (95%CI 18.41-66.64); Group B, 23.19 (95%CI 17.28-29.10); Group C, 57.75 (95%CI 35.86-79.67).



RVNA = Rabies virus neutralizing antibody
IM = Intramuscular
IIV4 = Inactivated quadrivalent influenza vaccine

The proportion of participants with RVNA titers ≥ 0.5 IU/mL at day 42, day 365, and day 372.



GMT of Rabies virus neutralizing antibody (RVNA) compared between groups					
	IU/mL	0,7 IM with IIV4 (Group A)	0,28 IM with IIV4 (Group B)	0,7 IM (Group C)	P-value
Day 42 (N=97)	N	39	38	20	
	GMT(95%CI)	8.98 (7.06-11.42)	23.89 (19.33-29.51)	9.94 (7.03-14.06)	<0.001
	Min-Max	1-136.59	7.38-128	2.38-54.17	
Day 365 (N=87)	N	35	35	17	
	GMT(95%CI)	1.90 (0.88-2.93)	1.12 (0.85-1.39)	2.69 (0.89-4.49)	0.04
	Min-Max	0.27-17.45	0.11-3.67	0.44-14.67	
Day 372 (total) (N=82) ^a	N	32 ^b	35	15	
	GMT(95%CI)	25.83 (21.44-30.23)	23.19 (17.28-29.10)	45.75 (30.53-61)	0.002
	Min-Max	4.05-56.57	6.82-91.7	10-100	
Day 372 (per-protocol) (N=63) ^a	N	24	28	11	
	GMT(95%CI)	24.26 (19.05-29.47)	24.15 (16.93-31.37)	48.21 (27.38-69.03)	0.02
	Min-Max	4.05-45.85	6.82-91.7	10-100	
Day 372 (full dose booster of CPRV) (N=19)	N	8	7	4	
	GMT(95%CI)	30.55 (21.23-39.87)	19.35 (10.24-28.47)	39 (14.3-63.71)	0.02
	Min-Max	21.81-56.57	9.17-36.68	25.9-56.57	

P-value from ANOVA; IM = Intramuscular; IIV4 = Inactivated quadrivalent influenza vaccine; GMT = Geometric mean titer; CPRV = Chromatographically purified Vero cell rabies vaccine
^a Potential outlier removal results
^b One participant lost to follow-up at day 372

Conclusion

This study revealed a 100% adequate RVNA response to 0.25 mL of intramuscular chromatographically purified Vero cell rabies vaccine without interference with influenza vaccine in healthy children 3 to 9 years old. This finding suggests that 2 doses of IM CPRV with either 0,7 or 0,28 regimens could be administered concomitantly with IIV4 in rabies-endemic countries.

Funding

This study was supported by the Ratchadapiseksomphot Fund, Chulalongkorn University (Bangkok, Thailand) (grant number CU_GR_63_143_30_50) and the Ratchadaphiseksomphot Fund, Faculty of Medicine, Chulalongkorn University (grant number RA-MF- 36/63). The chromatographically purified Vero cell rabies vaccine (CPRV), SPEEDATM was supported by Biovalys.

Reference

Chantasrisawad N, Jantarabenjakul W, Anugulruengkitt S, Punrin S, Limsuwun K, Sawangsinth P, Phasomsap C, Sophonphan J, Pancharoen C, Puthanakit T. Immunogenicity of 2-dose pre-exposure rabies vaccine co-administered with quadrivalent influenza vaccine in children. Int J Infect Dis. 2021 Nov;112:89-95. doi: 10.1016/j.ijid.2021.09.025.