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Review Article

Stratified Risk of Medical Symptoms after Concurrent Vaccination in Military Personnel: A PWP-CP Model Approach

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Abstract

Vaccination plays an important role in preventive healthcare, especially for populations like military personnel, who are at heightened risk of infectious diseases due to their unique environments and exposure levels. This study aimed to evaluate the impact of concurrent vaccinations on the risk of medical encounters in military personnel, considering both deployed and non-deployed groups. We analyze the dataset from 275550 service members, including 179997 deployed and 95553 non-deployed personnel.

Using Prentice-Williams-Peterson Counting Process (PWP-CP) model, we assessed the association between various concurrent vaccines (influenza, hepatitis B, anthrax, typhoid, and others) and the occurrence of symptoms such as headache, myalgia, and malaise. Our findings indicated that two or three concurrent vaccines generally reduced the risk of symptoms in the overall and deployed groups. However, receiving four or more vaccines concurrently may slightly increase the risk.

These findings suggest that concurrent vaccinations may help mitigate the risk of certain medical symptoms, particularly in deployed personnel, highlighting the need for vaccination strategies within the military context.

INTRODUCTION

Vaccination is a cornerstone of preventive healthcare, especially for military personnel who face elevated risks of infectious diseases due to their operational environments and deployment to high-exposure regions. To ensure timely protection, military service members often receive multiple vaccines simultaneously-including those targeting influenza, hepatitis B, anthrax, and typhoid-during pre-deployment immunization schedules [1-4].

While concurrent vaccination is efficient, it raises concerns about potential adverse health outcomes such as increased medical encounters. Previous studies have offered mixed findings: some report a higher incidence of local or systemic reactions with multiple vaccines, while others find no significant increase in serious outcomes like hospitalization. Most of these studies, however, use univariate analyses or assume independence between events, which may not adequately reflect real-world scenarios where individuals can experience multiple, correlated medical encounters over time [5-11].

To address this gap, we apply the Prentice-Williams-Peterson Counting Process (PWP-CP) model [12], which is specifically designed for recurrent event data. This model accounts for time-varying covariates and the dependence between successive events, offering a more robust framework for evaluating the relationship between concurrent vaccinations and subsequent medical encounters in military populations.

DATA DESCRIPTION

The study data were compiled by the Armed Forces Health Surveillance Branch (AFHSB). The cohort included individuals on active duty for at least one year between January-01-2004 and December-31-2014, and had received at least one vaccination. A total of 275,550 subjects were divided into two groups: the single vaccine group, consisting of individuals who received only one vaccine, and a concurrent vaccine group, which was randomly selected and matched to the single vaccine group based on vaccine date, gender, age, branch of service, military grade, and race/ethnicity. In this study, concurrent vaccinations

were defined as receiving two or more vaccinations within a 7-day period—an approach deemed most practical and analytically sound based on preliminary analyses cooperated with AFHSB. This definition maximized inclusion of personnel while preserving a sufficient number of matched individuals in both groups. Among the 137,775 subjects who received concurrent vaccinations, 109,717 (79.63%) subjects received two concurrent vaccinations, 20,189 (14.65%) subjects received three vaccinations, and 7,869 (5.71%) subjects received four or more concurrent vaccinations.

The medical encounter data encompassed inpatient and outpatient visits within 14 days after vaccination, with diagnoses classified using 3-digit International Classification of Diseases, 9th Revision (ICD-9), codes. Based on a summary of encounter frequencies, the top 12 most frequent symptoms included back pain, pain in limbs, pharyngitis, headache, dyspnea/wheezing, nausea/vomiting, myalgia, dermatitis, cough, diarrhea, dizziness, rash, and malaise/fatigue. To assess the impact of specific medical encounter types, we also conducted further analysis to determine whether these symptoms vary between the single and concurrent vaccine groups.

Table 1 presents the top 10 vaccines, showing consistent percentage distributions between the single and concurrent vaccine groups. There are only minor differences in the order, with Meningococcal appearing in the top 10 of the concurrent vaccine group but not in the single vaccine group, while 'Influenza, unspecified' is in the top 10 of the single vaccine group but not in the concurrent vaccine group. Since individuals in the concurrent vaccine group received multiple vaccines, the sum of counts for this group is larger than the total number of subjects.

Table 1: Distribution of Top 10 Vaccines in Single and Concurrent Vaccine Groups

Concurrent Vaccine Group			Single Vaccine Group		
N=137775*			N=137775		
Vaccine	Count	Percent (%)	Vaccine	Count	Percent (%)
Influenza, injectable	74483	54.06	Influenza, injectable	51587	37.44
Typhoid, injectable	60374	43.82	Influenza, intranasal	28907	20.98
Hepatitis B	28868	20.95	Typhoid, injectable	16186	11.75
Influenza, intranasal	25180	18.28	Anthrax	12218	8.87
Hepatitis A	17883	12.98	Hepatitis B	5901	4.28
Anthrax	17432	12.65	Influenza, unspecified	4055	2.94
TD	15632	11.35	TD	3743	2.72
Hep A-Hep B	15388	11.17	Hep A-Hep B	3024	2.19
DTP	10666	7.74	DTP	2606	1.89
Meningococcal	9750	7.08	Hepatitis A	2545	1.85

*Note: Individuals in the concurrent vaccine group may receive multiple vaccines, so the sum of counts for this group is larger than the total number of subjects.

Subsequent subgroup analyses were conducted by vaccine type to assess whether the outcomes varied between the single and concurrent vaccine groups.

Table 2 demonstrates a well-matched demographic distribution between single and concurrent vaccine groups. Gender, race and service are exactly matched, while marital status, grade level, and vaccine years are nearly matched. Minor age differences across categories reflect the within one-year range used in the matching

Table 2: Demographic Distribution Table - Gender, Age, Race, Marriage Status, Grade Level, Service, Deployment, and Vaccination Year of Single vaccine and Matched Concurrent Vaccine Group (Percentage in Parentheses)

Variable	Single	Concurrent	Total
	N=137775	N=137775	N=275550
SEX			
Female	22197(16.11)	22197(16.11)	44394(16.11)
Male	115578(83.88)	115578(83.88)	231156(83.88)
AGE			
0-20	70552(51.20)	66514(48.27)	137066(49.74)
21-25	47078(34.17)	50454(36.62)	97532(35.39)
26-30	14794(10.73)	15064(10.93)	29858(10.83)
>30	5329(3.867)	5732(4.160)	11061(4.014)
Unknown	22(0.015)	11(0.007)	33(0.011)
RACE_ETHNIC			
American Indian/ Alaskan Native	1724(1.251)	1724(1.251)	3448(1.251)
Asian/Pacific Islander	4752(3.449)	4752(3.449)	9504(3.449)
Black	20969(15.21)	20969(15.21)	41938(15.21)
Hispanic	12868(9.339)	12868(9.339)	25736(9.339)
Other or Unknown	5518(4.005)	5518(4.005)	11036(4.005)
White	91944(66.73)	91944(66.73)	183888(66.73)
MARRIAGE STATUS			
Other or Unknown	5475(3.973)	5127(3.721)	10602(3.847)
Married	78711(57.1)	77830(56.49)	156541(56.81)
Single	53589(38.8)	54818(39.78)	108407(39.34)
GRADE			
E1-E4	48502(35.2)	52431(38.05)	100933(36.62)
E5-E9	61323(44.50)	57231(41.53)	118554(43.02)
O1-O5	24932(18.09)	24589(17.84)	49521(17.97)
O6-O10	1955(1.418)	2147(1.558)	4102(1.488)
W1-W5	1063(0.771)	1377(0.999)	2440(0.885)
SERVICE			
Air Force	44750(32.48)	44750(32.48)	89500(32.48)
Army	15877(11.52)	15877(11.52)	31754(11.52)
Coast Guard	6572(4.770)	6572(4.770)	13144(4.770)
Marine Corps	19007(13.79)	19007(13.79)	38014(13.79)
Navy	51569(37.42)	51569(37.42)	103138(37.42)
DEPLOYED			
NO	58748(42.64)	36805(26.71)	95553(34.67)
YES	79027(57.35)	100970(73.28)	179997(65.32)
VACCINATION YEAR			
2004-2005	73870(53.61)	73828(53.58)	147698(53.60)
2006-2008	36309(26.35)	36358(26.38)	72667(26.37)
2009-2011	13194(9.576)	13188(9.572)	26382(9.574)
2012-2014	14402(10.45)	14401(10.45)	28803(10.45)

process. However, there is an imbalance in deployment status, with 57.35% of individuals in the single vaccine group having deployed, compared to 73.28% in the concurrent vaccine group. Based on a noticeable imbalance in the deployment status between the two vaccine groups, the relationship between vaccination and subsequent medical encounters may differ between deployed and non-deployed individuals due to differing health risks, disease exposure, or healthcare access. To evaluate the effect of the concurrent vaccine within each deployment status, we also performed subgroup analysis by deployment.

ANALYSES AND RESULTS

The PWP-CP model (conditional model A) uses a counting process formulation, which is an extension of the Cox model. The key difference between PWP-CP model and the traditional counting process model is the inclusion of a stratum variable. In this model, the time interval of a subsequent event starts at the end of the time interval for the previous event. The hazard function for the kth event of the ith subject at time t, $\lambda_{ik}(t)$ could be represented as:

$$\lambda_{ik}(t) = \lambda_{0k}(t)e^{X_{ik}\beta}$$

where λ_{0k} represents the event-specific baseline hazard for the kth event, β is the vector of regression coefficients, and X_{ik} is the covariate matrix [12].

Overall Analyses

The model is stratified by the number of concurrent vaccinations to assess whether the impact differs by the number of vaccines received (2, 3, >=4). The independent variables include sex (F, M), age (17-25, 26-30, >30, unknown), vaccine year (continuous), and deployment status (never, ever). If a subject has multiple medical encounters in a single day, these are considered as one encounter. Based on a noticeable imbalance in deployment status between the two vaccine groups, as shown in Table 2, we also fitted the PWP-CP model by deployment subgroup to account for potential confounding effects. Table 4 presents the hazard ratios (HRs) and 95% confidence intervals (CIs) for the concurrent vaccine group compared to the single vaccine group (Table 3).

Based on the results in Table 3:

- In the overall cohort, individuals who received two, three, or four or more concurrent vaccines had a significantly lower risk of medical encounters compared to those who received a single vaccine. Specifically, the hazard ratios (HR) for two, three, and four or more vaccines were 0.879 (CI: 0.867–0.891, p<0.0001), 0.856 (CI: 0.828–0.886, p<0.0001), and 0.891 (CI: 0.847–0.936, p<0.0001), respectively, indicating a consistent reduction in risk.

Table 3: Hazard Ratios (HRs), 95% Confidence Intervals (CIs), and P-values by Number of Concurrent Vaccines (Num), for the Full Data and Stratified by Deployment Status.

Num of Vaccines	All data (N=275550)		Both Deployed (N=127334)		Both not deployed (N=42890)	
	HR(CI)	P-value	HR(CI)	P-value	HR(CI)	P-value
2	0.879 (0.867,0.891)	$<10^{-3}$	0.84 (0.823,0.858)	$<10^{-3}$	0.98 (0.823,0.858)	0.23
3	0.856 (0.828,0.886)	$<10^{-3}$	0.813 (0.772,0.856)	$<10^{-3}$	1.01 (0.935,1.091)	0.80
≥4	0.891 (0.847,0.936)	$<10^{-3}$	0.737 (0.673,0.807)	$<10^{-3}$	1.125 (1.029,1.23)	0.0095

- In the deployed subgroup, the HRs for receiving two, three, and four or more concurrent vaccines were 0.840 (CI: 0.823–0.858, p<0.0001), 0.813 (CI: 0.772–0.856, p<0.0001), and 0.737 (CI: 0.673–0.807, p<0.0001), demonstrating a reduced risk of medical encounters in individuals who received concurrent vaccinations.

- In the non-deployed group, there were no significant differences in risk for individuals receiving two or three concurrent vaccines, with HRs of 0.980 (CI: 0.948–1.013) and 1.010 (CI: 0.935–1.091). While for individuals receiving four or more concurrent vaccines, a modes increased risk was observed, with an HR of 1.125 (CI: 1.029–1.23, p=0.0095). Overall, concurrent vaccinations generally correlate with a lower risk of medical encounters, particularly in deployed individuals, but further investigation is warranted for non-deployed individuals receiving higher numbers of concurrent vaccines.

Exploratory Analysis for Top 12 Medical Encounters

To assess the impact of specific types of medical encounter, we conducted an analysis to evaluate the relative risk of experiencing the top 12 symptoms in the concurrent vaccine group compared to the single vaccine group. As in the previous model, the analysis was stratified by the number of vaccines received (2, 3, >=4) and further sub grouped by deployment status.

Table 4 below presents the hazard ratios (HRs), and corresponding 95% confidence intervals (CIs) for medical encounters related to various symptoms. In the overall dataset, receiving two or three concurrent vaccines generally reduced the risk of symptoms such as ‘pain in limb’, ‘headache’, ‘dyspnea/wheezing’, ‘nausea/vomiting’, ‘myalgia’, ‘dermatitis’, ‘diarrhea’, ‘dizziness’ and ‘malaise/fatigue’. The association was less pronounced for symptoms like ‘pharyngitis’, with significant results

Table 4: Hazard Ratios (HRs), 95% Confidence Intervals (CIs), and P-values of Concurrent Vaccine Effects by Symptom Type and Number of Concurrent Vaccines (Num), for the Full Data and Stratified by Deployment Status.

		All data (N=275550)			Both Deployed (N=127334)			Both not deployed (N=42890)		
Symptoms	**Num**	**HR**	**CI**	**P-value**	**HR**	**CI**	**P-Value**	**HR**	**CI**	**P-value**
Pain in limb	2	0.798	(0.752,0.848)	<.0001	0.758	(0.691,0.832)	<.0001	0.889	(0.77,1.026)	0.1079
	3	0.806	(0.704,0.923)	0.0018	0.673	(0.536,0.845)	0.0006	1.300	(0.968,1.744)	0.0811
	>=4	1.124	(0.926,1.364)	0.2381	1.059	(0.678,1.654)	0.7998	1.158	(0.862,1.555)	0.3294
Pharyngitis	2	0.982	(0.918,1.05)	0.5945	0.887	(0.794,0.991)	0.0334	1.091	(0.943,1.261)	0.2408
	3	0.949	(0.811,1.109)	0.5081	0.743	(0.572,0.965)	0.0261	0.995	(0.749,1.322)	0.9721
	>=4	1.580	(1.283,1.947)	<.0001	1.386	(0.86,2.236)	0.1804	1.499	(1.103,2.036)	0.0096
Headache	2	0.807	(0.748,0.871)	<.0001	0.728	(0.645,0.822)	<.0001	0.892	(0.751,1.059)	0.1919
	3	0.854	(0.708,1.031)	0.1001	0.898	(0.648,1.244)	0.5186	0.998	(0.703,1.418)	0.9923
	>=4	0.993	(0.756,1.305)	0.9623	0.51	(0.272,0.958)	0.0363	1.124	(0.771,1.64)	0.5438
Dyspnea/ wheezing	2	0.722	(0.667,0.781)	<.0001	0.61	(0.541,0.687)	<.0001	1.022	(0.84,1.245)	0.8258
	3	0.71	(0.579,0.871)	0.0010	0.629	(0.464,0.853)	0.0028	1.071	(0.607,1.889)	0.8121
	>=4	0.847	(0.63,1.137)	0.2682	0.57	(0.346,0.939)	0.0273	1.55	(0.91,2.64)	0.1068
Nausea/ Vomiting	2	0.909	(0.826,0.999)	0.0486	0.848	(0.721,0.997)	0.0454	1.03	(0.849,1.25)	0.7621
	3	0.844	(0.676,1.054)	0.1342	0.655	(0.44,0.974)	0.0367	0.905	(0.587,1.395)	0.6516
	>=4	1.706	(1.222,2.382)	0.0017	1.086	(0.583,2.024)	0.7944	1.752	(1.043,2.941)	0.034
Myalgia	2	0.708	(0.643,0.778)	<.0001	0.691	(0.602,0.794)	<.0001	0.909	(0.696,1.188)	0.4850
	3	0.682	(0.538,0.865)	0.0016	0.564	(0.402,0.791)	0.0009	0.771	(0.403,1.474)	0.4311
	>=4	0.516	(0.336,0.793)	0.0025	0.39	(0.164,0.928)	0.0331	0.679	(0.244,1.889)	0.4581
Dermatitis	2	0.898	(0.817,0.989)	0.0281	0.878	(0.762,1.013)	0.0737	1	(0.792,1.263)	0.9992
	3	0.825	(0.657,1.036)	0.0984	0.74	(0.513,1.066)	0.1058	1.035	(0.618,1.732)	0.8973
	>=4	0.913	(0.676,1.234)	0.5551	0.791	(0.475,1.317)	0.3666	1.685	(0.931,3.051)	0.0848
Cough	2	0.937	(0.837,1.048)	0.2537	0.844	(0.707,1.007)	0.0592	1.079	(0.83,1.404)	0.5682
	3	0.935	(0.715,1.222)	0.6221	0.998	(0.641,1.553)	0.9913	1.021	(0.576,1.81)	0.9422
	>=4	0.927	(0.636,1.352)	0.6945	1.31	(0.655,2.621)	0.4455	0.859	(0.498,1.483)	0.5862
Diarrhea	2	0.873	(0.784,0.974)	0.0145	0.848	(0.713,1.007)	0.0602	1.148	(0.904,1.459)	0.2575
	3	1	(0.766,1.304)	0.9992	1.283	(0.836,1.968)	0.2534	0.864	(0.488,1.528)	0.6148
	>=4	1.018	(0.64,1.62)	0.9405	1.13	(0.503,2.541)	0.7667	1.019	(0.404,2.569)	0.9682
Dizziness	2	0.772	(0.681,0.874)	<.0001	0.714	(0.588,0.866)	0.0006	1.078	(0.809,1.437)	0.6095
	3	0.851	(0.629,1.153)	0.2985	0.705	(0.416,1.195)	0.1938	0.825	(0.428,1.592)	0.5665
	>=4	1.096	(0.664,1.811)	0.7192	0.448	(0.169,1.19)	0.1073	3.090	(1.134,8.423)	0.0275
Rash	2	0.975	(0.837,1.136)	0.7452	0.887	(0.702,1.121)	0.3159	0.975	(0.678,1.401)	0.8907
	3	1.210	(0.855,1.713)	0.2825	1.458	(0.82,2.592)	0.1987	1.408	(0.605,3.276)	0.4267
	>=4	1.276	(0.711,2.291)	0.4137	0.638	(0.207,1.963)	0.4332	2.219	(0.779,6.322)	0.1356
Malaise/Fatigue	2	0.729	(0.636,0.834)	<.0001	0.699	(0.564,0.865)	0.0010	1.024	(0.758,1.384)	0.8752
	3	0.828	(0.602,1.139)	0.2467	0.688	(0.405,1.168)	0.1659	0.843	(0.414,1.718)	0.6379
	>=4	0.944	(0.569,1.566)	0.8221	0.711	(0.311,1.629)	0.4202	1.407	(0.446,4.432)	0.5602

observed mainly for individuals receiving four or more concurrent vaccines. Additionally, "nausea/vomiting" and "myalgia" also showed a reduced risk when individuals received four or more concurrent vaccines.

In the deployed group, significant reductions in the risk of 'pain in limb', 'pharyngitis', 'headache', 'dyspnea/ wheezing', 'nausea/vomiting', 'myalgia', 'dizziness', and 'malaise/fatigue' were observed with two or three concurrent vaccines. Furthermore, a reduction in risk for 'headache', 'dyspnea/wheezing', and 'malaise/fatigue' was noted when individuals received four or more concurrent vaccines in the deployed group.

In contrast, the non-deployed group showed less consistent findings. No significant risk reduction was found in the non-deployed group for concurrent vaccines. Additionally, the impact of ≥4 vaccines in the non-deployed

group often suggested an increased risk for certain symptoms, such as 'pharyngitis', 'nausea/vomiting', and 'dizziness'.

Overall, the results demonstrate variability in the impact of concurrent vaccines across different symptoms and deployment status. While concurrent vaccinations generally reduced the risk of certain symptoms in the deployed group, the non-deployed group showed more mixed results, emphasizing the importance of deployment status in influencing the outcomes of concurrent vaccinations. Further investigation is needed to clarify these associations and their potential underlying mechanisms.

Exploratory Analysis by Vaccine Type

We then assessed medical encounters associated with the top 11 vaccinations listed in Table 1. As in the previous model, the analysis was stratified by the number of vaccines received (2, 3, >=4) and then sub grouped by deployment status. Table 5 presents the concurrent vaccine effects on overall medical encounters by vaccine type. Concurrent vaccines generally showed reduced risk for various symptoms, though the effects varied depending on the vaccine type and group (overall, deployed, and non-deployed). For influenza (injectable), all levels of concurrent vaccines significantly reduced the risk in both the overall and deployed groups. In contrast, the non-deployed group showed a reduction only with two concurrent vaccines. However, receiving three or more vaccines did not significantly reduce risk for the non-deployed group. For influenza (intranasal), two concurrent vaccines reduced risk in both the overall and deployed groups, but no significant effects were seen for three or more vaccines in any group.

For anthrax, two concurrent vaccines showed a significant reduction in risk in the overall and deployed groups, but not in the non-deployed group. A similar pattern was observed for unspecified influenza vaccines. For Hepatitis B vaccines, two concurrent vaccines reduced risk in the overall group, while no significant reduction was seen with three or more vaccines in the deployed group. However, for the non-deployed group, two or three vaccines showed a substantial risk reduction. Typhoid and DTP vaccines showed mixed results, with concurrent

Table 5: Hazard Ratios (HRs), 95% Confidence Intervals (CIs), and P-values of Concurrent Vaccine Effects on Overall Medical Encounters by Vaccine Type and Number of Concurrent Vaccines (Num), for the Full Data and Stratified by Deployment Status.

Num	HR	CI	P-value	HR	CI	P-Value	HR	CI	P-value
Influenza, Injectable									
	All data (N=67310)			Both Deployed (N=27450)			Both not deployed (N=12464)		
2	0.882	(0.859,0.905)	<.0001	0.872	(0.837,0.91)	<.0001	0.936	(0.882,0.994)	0.0297
3	0.803	(0.742,0.868)	<.0001	0.708	(0.623,0.803)	<.0001	1.077	(0.898,1.291)	0.4235
>=4	0.79	(0.691,0.903)	0.0005	0.605	(0.478,0.766)	<.0001	1.025	(0.774,1.358)	0.8624
Influenza, Intranasal									
	All data (N=26926)			Both Deployed (N=11362)			Both No deployed (N=4938)		
2	0.907	(0.873,0.943)	<.0001	0.83	(0.784,0.879)	<.0001	1.097	(0.995,1.21)	0.0631
3	0.952	(0.851,1.066)	0.395	0.883	(0.745,1.046)	0.1489	1.032	(0.778,1.368)	0.8294
>=4	1.031	(0.837,1.271)	0.7749	1.024	(0.74,1.415)	0.8877	1.204	(0.797,1.817)	0.3779
Anthrax									
	All data (N=9390)			Both Deployed (N=7430)			Both No deployed (N=148)		
2	0.903	(0.829,0.984)	0.0206	0.866	(0.785,0.956)	0.0044	1.022	(0.562,1.859)	0.9436
3	0.878	(0.735,1.05)	0.1542	0.84	(0.678,1.039)	0.1085	1.262	(0.448,3.552)	0.6598
>=4	0.689	(0.476,0.998)	0.0489	0.643	(0.398,1.038)	0.0704	0.278	(0.05,1.561)	0.1459
Typhoid									
	All data (N=19832)			Both Deployed (N=12062)			Both No deployed (N=1172)		
2	0.9	(0.841,0.963)	0.0023	0.957	(0.874,1.048)	0.3428	0.801	(0.621,1.032)	0.0862
3	0.843	(0.734,0.968)	0.0153	0.827	(0.684,1)	0.0503	1.439	(0.874,2.369)	0.1525
>=4	0.776	(0.627,0.96)	0.0197	0.803	(0.599,1.076)	0.1417	1.379	(0.502,3.787)	0.5327
Hepatitis B									
	All data (N=3942)			Both Deployed (N=1492)			Both No deployed (N=888)		
2	0.804	(0.698,0.926)	0.0025	0.783	(0.609,1.007)	0.0572	0.642	(0.479,0.862)	0.0031
3	0.834	(0.651,1.07)	0.1534	0.864	(0.564,1.326)	0.5048	0.27	(0.135,0.544)	0.0002
>=4	0.483	(0.327,0.712)	0.0002	0.265	(0.114,0.613)	0.0019	0.888	(0.449,1.758)	0.7337
Hepatitis A									
	All data (N=1664)			Both Deployed (N=396)			Both No deployed (N=470)		
2	1.101	(0.881,1.376)	0.3973	1.1	(0.534,2.263)	0.7962	1.025	(0.734,1.432)	0.883
3	0.848	(0.571,1.259)	0.4131	0.895	(0.41,1.956)	0.7811	0.372	(0.141,0.981)	0.0457
>=4	0.588	(0.32,1.077)	0.0856	0.715	(0.193,2.648)	0.6156	0.621	(0.269,1.436)	0.2655

Hep A-Hep B									
	All data (N=1830)			Both Deployed (N=420)			Both not deployed (N=728)		
2	0.761	(0.61,0.95)	0.0155	0.671	(0.262,1.72)	0.4061	0.718	(0.531,0.971)	0.0314
3	0.862	(0.532,1.397)	0.5474	1.135	(0.288,4.475)	0.856	0.834	(0.416,1.67)	0.6075
>=4	1.195	(0.895,1.595)	0.2265	1.516	(0.445,5.162)	0.5057	1.203	(0.861,1.682)	0.2795
TD									
	All data (N=2088)			Both Deployed (N=912)			Both not deployed (N=362)		
2	0.733	(0.608,0.883)	0.0011	0.823	(0.625,1.084)	0.1652			
3	0.711	(0.512,0.987)	0.0415	0.75	(0.446,1.263)	0.2796			
>=4	1.176	(0.661,2.093)	0.5804	1.05	(0.429,2.566)	0.9156			
DTP									
	All data (N=1606)			Both Deployed (N=764)			Both not deployed (N=242)		
2	0.848	(0.731,0.984)	0.0299	0.838	(0.671,1.046)	0.1183	0.801	(0.525,1.223)	0.3045
3	0.705	(0.5,0.994)	0.0462	0.706	(0.42,1.185)	0.1877	0.652	(0.286,1.49)	0.3106
>=4	0.7	(0.442,1.109)	0.1284	0.527	(0.252,1.104)	0.0895	0.837	(0.389,1.8)	0.6491
Meningococcal									
	All data (N=732)			Both Deployed (N=182)			Both not deployed (N=434)		
2	1.037	(0.688,1.563)	0.8625				1.544	(0.75,3.176)	0.238
3	2.484	(1.689,3.652)	<.0001				2.87	(1.813,4.544)	<.0001
>=4	2.345	(1.802,3.053)	<.0001				2.508	(1.9,3.311)	<.0001
Influenza Unspecified									
	All data (N=1472)			Both Deployed (N=780)			Both not deployed (N=106)		
2	0.773	(0.614,0.973)	0.0281	0.609	(0.432,0.858)	0.0046			
3	0.925	(0.502,1.706)	0.8038	0.142	(0.017,1.153)	0.0677			
>=4	3.479	(1.078,11.222)	0.0369	1.618	(0.081,32.476)	0.7532			

vaccines showing a reduction in risk in the overall group, but limited effects in the deployed and non-deployed groups. Meningococcal vaccines showed an increased risk with three or more vaccines in the overall and non-deployed groups. In conclusion, the impact of concurrent vaccines on risk reduction varies by vaccine type and deployment status. Two concurrent vaccines generally show the most consistent and significant risk reductions across the groups. In comparison, three or more vaccines often show weaker or non-significant effects, particularly for the non-deployed group.

CONCLUSION

We utilized PWP-CP model to estimate a hazard ratio (HR) to assess the relationship between concurrent vaccinations and the risk of various medical encounters across different groups, including deployed and non-deployed populations. The HRs and corresponding 95% confidence intervals (CIs) were estimated for different vaccine types and numbers of concurrent vaccines (2, 3, and 4 or more doses). Due to the large sample sizes in several groups, p-values are reported to four decimal places to provide more precise information. Our results indicate that receiving two or three concurrent vaccines was generally associated with a reduced risk of several symptoms, including 'pain in limb', 'headache', 'dyspnea/wheezing', 'nausea/vomiting', 'myalgia', 'dermatitis', 'diarrhea', 'dizziness' and 'malaise/fatigue'. In contrast, higher doses (four or more vaccines) were associated with varying effects depending on the vaccine type and group. Notably, the deployed group showed a more consistent reduction in risk with higher doses of certain vaccines.

These findings highlight the importance of considering deployment status and vaccine type when evaluating the effects of concurrent vaccinations on health outcomes. Further research is warranted to investigate the long-term implications of these associations.

DISCUSSION

This study supports the safety of concurrent vaccinations compared to single vaccinations, aligning with findings from prior literature, including surveys of vaccination attitudes among returning troops and research on commonly used vaccines. A key methodological difference in this analysis is using a conditional model to account for multiple medical encounters, in contrast to the single-encounter logistic model employed in our previous study [11]. The results remain consistent and suggest that concurrent vaccination may offer potential benefits.

By leveraging a large sample size, this study uniquely contributes to the field by analyzing a matched cohort of military adults, with adjustments for key demographic factors such as sex, race, and age. Stratified analyses by deployment status reveal both baseline health differences and the possible influence of environmental exposures on symptom risk. These findings indicate that individuals with lower baseline health may require greater caution when receiving multiple vaccines concurrently.

In conclusion, this study provides valuable insights into the safety profile of concurrent vaccinations. It underscores the importance of tailoring vaccination strategies based on outcome types, vaccine combinations, and deployment status, particularly for deployed personnel who may face distinct environmental and physiological stressors.

This study has several limitations that should be acknowledged. First, as an observational study, it is subject to inherent biases and confounding factors that limit causal inference. Determining the optimal time window to evaluate the effects of concurrent vaccinations is inherently challenging. Our choice of a 14-day window, though guided by data, may not capture all relevant adverse outcomes or fully exclude unrelated ones. A similar challenge applies to the selection of the 7-day window used to define concurrent vaccinations.

Second, there is no universally accepted definition of which symptoms constitute vaccine-related adverse effects. Symptoms such as headache, myalgia, and malaise are nonspecific and may be influenced by multiple factors unrelated to vaccination, introducing subjectivity into outcome classification.

Third, all data analyzed in this study were collected prior to 2014. Since the COVID-19 pandemic, vaccination practices and concurrent vaccine administration have changed significantly, and more recent data may reflect different risk patterns.

Finally, our analysis focused exclusively on active-duty military personnel, a population that is predominantly young, healthy, and male (approximately 80%). As such, the findings may not be generalizable to the broader civilian population, particularly older adults, children, or individuals with underlying health conditions. Future studies using more diverse and up-to-date datasets are needed to assess the impact of concurrent vaccinations in the general population.

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DECLARATION

The views expressed in this manuscript are those of the authors and do not necessarily reflect the opinions or policies of their original affiliated institutions.

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