Table 1. Characteristics of 816 Participants in a Healthcare Personnel Cohort with Vaccination Records through Four Prior Years

	Sample [a]	
Categorical descriptors, N (%)		
Study site (Oregon)	361	(44)
Sex (Female)	700	(86)
Race (White)	650	(80)
Ethnicity (Hispanic)	85	(10)
Child (age <13) at home	248	(30)
Physician	52	(6)
Work in Hospital	440	(54)
Work in Emergency Dept.	155	(19)
Chronic medical condition [b]	151	(19)
Continuous descriptors, Median (SD)		
Age (years)	48	(12)
Household size (0-7)	2	(2)
Education (5-levels)	16	(2)
Self-rated health status (5-levels)	4	(1)
Body mass index (kg/m^2)	28	(28)
Direct patient care per week (hours)	34	(1)
Prior vaccinations, N (%)		
2006-07 IIV3	433	(53)
2007-08 IIV3	391	(48)
2008-09 IIV3	464	(57)
2009-10 IIV3	589	(72)
2009 MIV A(H1N1)pdm09	401	(49)
2010-11 IIV3	607	(74)
Sum of Prior IIV3, Mean (SD)	3	(1)

* $p < .05$; ** $p < .01$; *** $p < .001$

[a] Sample (N = 816) includes health care personnel with medical and vaccination records since July, 2006 and excludes those who received live attenuated influenza vaccine (LAIV) in 2010-11 and/or in any season since 2006-07.

[b] Presence of a chronic medical condition was identified by a medical visit during the prior year in the electronic medical record for a medical condition associated with increased risk of influenza complications (codes available from the authors).

Table 2. Serum Hemagglutination Inhibition Antibody (HI) Titers for A/Perth/16/2009 (H3N2) at Preseason, Post-Vaccination, and Post-Season by Number of Inactivated Influenza Vaccinations (IIV3s) during the Prior Four Seasons, including Estimated Geometric Mean Titer (GMT), Elevated Titers of ≥40 and >100, and Geometric Mean Fold Change Ratios (GMRs), among Healthcare Personnel Vaccinated and Unvaccinated with 2010-11 IIV3

Subgroup	Sum of IIV3 2006-07 to 2009-10	N	Preseason (Time 1) GMT (95% CI)	Preseason (Time 1) GMT ≥40 % (95% CI)	Preseason (Time 1) GMT >100 % (95% CI)	Post-Vaccination (Time 2) GMT (95% CI)	Post-Vaccination (Time 2) GMR (95% CI)	Post-Vaccination (Time 2) GMT ≥40 % (95% CI)	Post-Vaccination (Time 2) GMT >100 % (95% CI)	Post-Season (Time 3) GMT (95% CI)	Post-Season (Time 3) GMR (95% CI)	Post-Season (Time 3) GMT ≥40 % (95% CI)	Post-Season (Time 3) GMT >100 % (95% CI)
2010-11 Vaccinated													
	4 IIV3s	227	10 (9 - 11)	14 (9 - 18)	3 (1 - 10)	23 (20 - 27)	2.3 (2.1 - 2.6)	46 (40 - 51)	11 (6 - 15)	14 (12 - 16)	0.6 (0.6 - 0.7)	23 (17 - 29)	5 (2 - 8)
	3 IIV3s	153	12 (11 - 14)	19 (13 - 25)	2 (0 - 13)	32 (28 - 38)	2.6 (2.3 - 3.0)	55 (48 - 61)	8 (3 - 13)	17 (15 - 20)	0.5 (0.5 - 0.6)	32 (25 - 39)	2 (0 - 6)
	2 IIV3s	85	10 (8 - 12)	17 (9 - 25)	3 (0 - 7)	33 (25 - 44)	3.4 (2.8 - 4.3)	56 (47 - 65)	20 (13 - 26)	16 (13 - 21)	0.5 (0.4 - 0.6)	34 (24 - 43)	11 (5 - 16)
	1 IIV3s	86	13 (10 - 17)	26 (18 - 33)	9 (1 - 4)	57 (42 - 76)	4.3 (3.3 - 5.5)	63 (54 - 72)	32 (26 - 39)	26 (20 - 32)	0.5 (0.4 - 0.6)	40 (31 - 50)	19 (14 - 24)
	0 IIV3s	27	8 (6 - 11)	12 (0 - 25)	4 (0 - 6)	50 (29 - 88)	6.2 (3.4 - 11.3)	69 (54 - 85)	37 (26 - 48)	15 (11 - 23)	0.4 (0.2 - 0.5)	25 (9 - 41)	4 (0 - 14)
2010-11 Unvaccinated													
	4 IIV3s	7	15 (8 - 28)	26 (3 - 50)	1 (0 - 15)					16 (8 - 32)	0.9 (0.9 - 0.9)	15 (11 - 42)	1 (0 - 15)
	3 IIV3s	15	12 (8 - 19)	13 (0 - 29)	7 (0 - 16)					15 (10 - 25)	0.8 (0.9 - 1.9)	18 (1 - 36)	1 (0 - 8)
	2 IIV3s	33	12 (9 - 16)	18 (7 - 29)	6 (0 - 12)					13 (10 - 19)	0.9 (0.9 - 1.3)	25 (13 - 37)	3 (0 - 9)
	1 IIV3s	44	11 (8 - 14)	18 (8 - 27)	7 (0 - 12)					10 (8 - 14)	1.1 (0.9 - 1.4)	14 (3 - 25)	7 (1 - 12)
	0 IIV3s	110	7 (6 - 7)	7 (1 - 13)	1 (0 - 6)					8 (7 - 9)	1.2 (1.6 - 1.3)	11 (5 - 18)	3 (0 - 7)

Note: All estimates adjusted for sex, race (White), age (years) and age-squared, study site, work in a hospital setting or not, household size, and education (years). Among vaccinees, GMR at time 2 describes change in GMT post-vaccination (or since Time 1); at Time 3, GMR describes change in GMT from post-vaccination to the end of season. Among unvaccinated HCP, GMR at Time 3 describes change in GMT since preseason (Time 1). GMRs were calculated using the log-transformed HI titers. GMTs were converted back to original GMT values. The GMR estimate was calculated by 2 to the power of mean difference estimate. The percentage with elevated tiers was estimated using generalized linear models with the same adjusted covariates. In addition, among vaccinees, estimates of post-vaccination elevated titers adjusted for preseason or baseline titers.

Supplemental Table A. Vaccine components for seasonal inactivated trivalent influenza vaccines (IIV3)

Seasonal Vaccines	Influenza vaccine components
2010-11 IIV3	A/California/7/2009 (H1N1)-like virus A/Perth/16/2009 (H3N2)-like virus B/Brisbane/60/2008-like virus (B/Victoria)
2009-10 IIV3	A/Brisbane/59/2007 (H1N1)-like virus A/Brisbane/10/2007 (H3N2)-like virus B/Brisbane/60/2008-like virus (B/Victoria)
2008-09 IIV3	A/Brisbane/59/2007 (H1N1)-like virus A/Brisbane/10/2007 (H3N2)-like virus B/Florida/4/2006-like virus (B/Yamagata)
2007-08 IIV3	A/Solomon Islands/3/2006 (H1N1)-like virus A/Wisconsin/67/2005 (H3N2)-like virus B/Malaysia/2506/2004-like virus (B/Victoria)
2006-07 IIV3	A/New Caledonia/20/99 (H1N1)-like virus A/Wisconsin/67/2005 (H3N2)-like virus B/Malaysia/2506/2004-like virus (B/Victoria)

Supplemental Table B. Characteristics of 816 Participants and the Spearman Correlations Between These Factors and the Total Number of Inactivated Trivalent Influenza Vaccinations (IIV3s) during the Prior 4 Seasons, Receipt of the 2010-11 IIV3, Preseason Geometric Mean Titer (GMT) for A/Perth/16/2009 (H3N2), and Post-Vaccination Fold-Change in Titers

	Sample [a]	Number of Prior Vaccinations	Received 2010-11 IIV3	Preseason A(H3N2) GMT	Post-Vaccination Fold Change [b]
Categorical descriptors, N (%)					
Study site (Oregan)	361 (44)	.14 ***	- .05	.05	- .17 ***
Sex (Female)	700 (86)	.06	.00	.00	.05
Race (White)	650 (80)	.08 **	.05	.08 *	- .07
Ethnicity (Hispanic)	85 (10)	- .05	- .01	.01	.02
Child (age <13) at home	248 (30)	- .08 **	- .10 *	.03	- .02
Physician	52 (6)	.01	.07 *	- .05	- .07
Work in Hospital	440 (54)	- .11 ***	.03	.00	.10 *
Work in Emergency Dept.	155 (19)	- .09 **	- .08 *	.00	.01
Chronic medical condition [c]	151 (19)	.04	.05	- .02	.03
Continuous descriptors, Median (SD)					
Age (years)	48 (12)	.20 ***	.12 **	- .05	- .02
Household size (0-7)	2 (2)	- .11 *	- .09 **	- .03	.08 *
Education (5-levels)	16 (2)	.10 ***	.06	- .09 *	- .09 *
Self-rated health status (5-levels)	4 (1)	.02	.01	- .05	- .02
Body mass index (kg/m^2)	28 (28)	.08 *	.07 *	.01	.07
Direct patient care per week (hours)	34 (1)	- .09 **	- .03	.03	.02
Prior vaccinations, N (%)					
2006-07 IIV3	433 (53)	.78 ***	.40 ***	.05	- .18 ***
2007-08 IIV3	391 (48)	.80 ***	.38 ***	.08 *	- .21 ***
2008-09 IIV3	464 (57)	.78 ***	.41 ***	.08 *	- .11 **
2009-10 IIV3	589 (72)	.66 ***	.54 ***	.20 ***	- .03

2009 MIV A(H1N1)pdm09	401	(49)	.43 ***	.40 ***	.08 *	- .14 ***
2010-11 IIV3	607	(74)	.55 ***	--	.12 ***	--
Sum of Prior IIV3, Mean (SD)	3	(1)	--	.55 ***	.12 ***	- .20 ***

* p < .05; ** p < .01; *** p < .001

[a] Sample (N = 816) includes health care personnel with medical and vaccination records since July, 2006 and excludes those who received live attenuated influenza vaccine (LAIV) in 2010-11 and/or in any season since 2006-07.

[b] The post-vaccination sample consists of 578 of 607 vaccinees with sera collected at both preseason and post-vaccination.

[c] Presence of a chronic medical condition was identified by a medical visit during the prior year in the electronic medical record for a medical condition associated with increased risk of influenza omplications (codes available from the authors).

Supplemental Table C. Serum Hemagglutination Inhibition Antibody (HI) Titers for A/Perth/16/2009 (H3N2) at Preseason, including Estimated Geometric Mean Titer (GMT) and Elevated Titer ≥40 and >100, by Prior Vaccination History, among Healthcare Personnel in Fall, 2010

		Preseason (Time 1)		
	N	GMT (95% CI)	GMT ≥40 % (95% CI)	GMT >100 % (95% CI)
Sum of seasonal IIV3 2006-07 to 2009-10				
4 IIV3s	243	10 (9 - 11)	14 (9 - 17)	4 (1 - 5)
3 IIV3s	176	12 (10 - 14)	19 (13 - 24)	2 (0 - 5)
2 IIV3s	124	11 (9 - 13)	18 (11 - 24)	4 (1 - 7)
1 IIV3s	135	12 (11 - 15)	23 (17 - 29)	8 (5 - 11)
0 IIV3s	141	7 (6 - 8)	8 (2 - 14)	2 (0 - 5)

Note: All estimates adjusted for sex, race (White), age (years) and age squared (quadratic term), study site, work in a hospital setting or not, household size, and education (years)

Supplemental Table D. Serum Hemagglutination Inhibition Antibody (HI) Titers at Preseason, Post-Vaccination, and End-of-Season for A/Perth/16/2009 (H3N2) by Influenza Vaccination History, including Estimated Geometric Mean Titer (GMT), Elevated Titer ≥40, and Geometric Mean Fold Change Ratios (GMRs), among Healthcare Personnel Vaccinated and Unvaccinated with 2010-11 Inactivated Influenza Trivalent Vaccine (IIV3) Stratified by Age Group

Subgroup	Vaccination History	N	Preseason (Time 1) GMT (95% CI)	Preseason (Time 1) GMT ≥40 % (95% CI)	Post-Vaccination (Time 2) GMT (95% CI)	Post-Vaccination (Time 2) GMR (95% CI)	Post-Vaccination (Time 2) GMT ≥40 % (95% CI)
2010-11 Vaccinated							
Aged 18-34 [a]	Mixed		12 (10 - 15)	22 (16 - 27)	42 (33 - 55)	3.4 (2.8 - 4.2)	62 (53 - 71)
Aged 35-49 [a]	Mixed		10 (9 - 11)	14 (9 - 18)	25 (22 - 30)	2.5 (2.2 - 2.9)	44 (37 - 51)
Aged 50-64 [a]	Mixed		11 (10 - 12)	15 (11 - 19)	33 (28 - 38)	3.0 (2.7 - 3.4)	55 (50 - 61)
2010-11 Vaccinated	Sum of seasonal IIV3 2006-07 to 2009-10						
Aged 18-34 [b]							
	4 IIV3s	22	10 (7 - 16)	15 (0 - 30)	27 (17 - 43)	2.7 (1.9 - 3.7)	58 (38 - 77)
	3 IIV3s	32	11 (8 - 14)	15 (2 - 28)	26 (17 - 40)	2.4 (1.8 - 3.3)	52 (36 - 68)
	2 IIV3s	19	14 (8 - 23)	24 (7 - 41)	56 (33 - 94)	4.0 (2.3 - 6.9)	69 (48 - 90)
	1 IIV3s	23	18 (10 - 32)	34 (19 - 49)	82 (42 - 162)	4.5 (2.7 - 7.5)	73 (54 - 93)
	0 IIV3s	11	10 (5 - 20)	25 (1 - 48)	66 (21 - 206)	6.6 (2.5 - 17.9)	81 (53 - 100)
Aged 35-49 [b]							
	4 IIV3s	73	10 (8 - 13)	14 (6 - 22)	22 (17 - 29)	2.2 (1.8 - 2.7)	40 (28 - 51)
	3 IIV3s	49	13 (10 - 17)	21 (11 - 31)	25 (19 - 34)	2.0 (1.6 - 2.4)	48 (34 - 61)
	2 IIV3s	31	8 (6 - 11)	11 (0 - 23)	27 (17 - 43)	3.4 (2.4 - 4.9)	43 (26 - 60)
	1 IIV3s	30	10 (7 - 13)	16 (3 - 29)	34 (24 - 49)	3.5 (2.3 - 5.2)	55 (38 - 73)
	0 IIV3s	8	5 (4 - 7)	0 (0 - 22)	20 (5 - 84)	3.7 (0.8 - 16.0)	31 (0 - 63)
Aged 50-64 [b]							

4 IIV3s	132	10	(	8 - 11)	12	(	6 - 19)	23	(	19 - 28)	2.2	(	1.8 - 2.7)	42	(	34 - 50)
3 IIV3s	72	13	(	10 - 16)	20	(	12 - 29)	41	(	32 - 54)	2.0	(	1.6 - 2.4)	67	(	56 - 79)
2 IIV3s	35	10	(	7 - 13)	20	(	7 - 32)	30	(	19 - 49)	3.2	(	2.2 - 4.7)	54	(	38 - 70)
1 IIV3s	33	14	(	9 - 22)	27	(	14 - 39)	69	(	40 - 118)	4.9	(	3.1 - 7.9)	76	(	60 - 92)
0 IIV3s	8	9	(	3 - 31)	9	(	0 - 31)	87	(	27 - 287)	9.5	(	1.9 - 46.9)	67	(	36 - 98)

Note: Given the small number of participants in the stratified models, only age (years) and study site were included in the multivariable models; models including all covariates offered similar result. The models were calculated using the log-transformed HI titers. GMTs were converted back to original GMT values. The GMR estimate was calculated by 2 to the power of mean difference estimate. GMT >100 was not calculated given the small number of participants with highly elevated titers stratified by age.

[a] A statistically significant interaction between age and GMR was noted ($F[2, 569] = 3.41$, $p = .03$, partial $\eta 2 = .01$). Statistically significant parameters for age and age-squared were also noted in the models (p's < .0005). Taken together, this prompted secondary analyses to examine results stratified by age group. Each row includes HCP within that age group and includes a mixture of prior vaccination exposures in that strata. Due to the reduced number of participants in each strata, we did not estimate the percentage with titers >100.

[b] Statistically significant interactions between number of prior vaccinations and GMR were noted for HCP aged 18-34 years ($F[4,100] = 2.88$, $p = .026$, partial $\eta 2 = .10$), HCP aged 35-49 years ($F[4,184] = 2.47$, $p = .03$, partial $\eta 2 = .06$), and HCP aged 50-64 years ($F[4,273] = 6.13$, $p < .0005$, partial $\eta 2 = .08$).

Supplemental Table E. Serum Hemagglutination Inhibition Antibody (HI) Titers for A/Perth/16/2009 (H3N2) Post-Vaccination by Number of Inactivated Influenza Vaccinations (IIV3s) during the Prior Four Seasons, among 404 Participants with Preseason GMT of <40, including Geometric Mean Fold Change Ratios (GMRs) and the Percentage who Achieved Elevated Titers of ≥40 and >100

		Post-Vaccination (Time)		
Sum of IIV3 2006-07 to 2009-10	N	GMR (95% CI)	GMT ≥40 % (95% CI)	GMT >100 % (95% CI)
4 IIV3s	200	2.5 (2.2 - 2.8)	37 (30 - 43)	5 (1 - 9)
3 IIV3s	125	2.9 (2.5 - 3.4)	43 (35 - 51)	4 (0 - 9)
2 IIV3s	73	3.8 (2.9 - 4.8)	47 (37 - 57)	12 (5 - 18)
1 IIV3s	6	4.9 (3.6 - 6.7)	57 (47 - 68)	22 (15 - 29)

Note: These results exclude participants with preseason GMT of ≥40. Due to the reduced sample in this stratified analysis, participants with zero prior vaccinations were excluded. All estimates adjusted for sex, race (White), age (years) and age-squared, study site, work in a hospital setting or not, household size, and education (years). Post-vaccination GMR describes change in GMT from preseason to post-vaccination. GMRs were calculated using the log-transformed HI titers. GMTs were converted back to original GMT values. The GMR estimate was calculated by 2 to the power of mean difference estimate. The percentages of HCP with elevated tiers were estimated using generalized linear models with the same adjusted covariates. In addition, post-vaccinated elevated titers adjust for preseason or baseline titers.