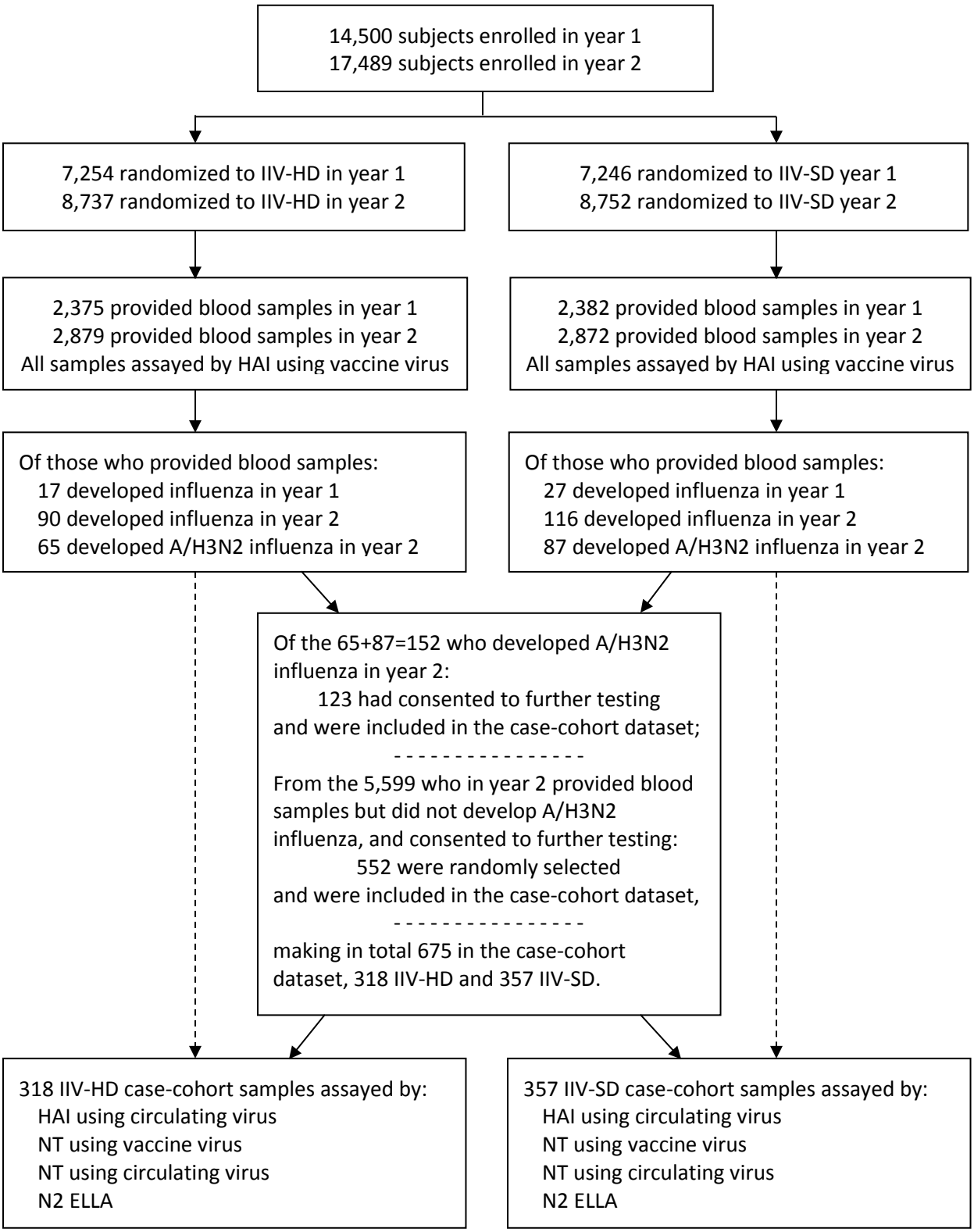
Supplemental Figure 1. Flowchart of subjects and assays



Supplemental Table 1. Associations between occurrence of A/H3N2 influenza illness and assay titers

	Coefficient for slope by logistic regression (95% confidence interval)				
Case definition (n=no. of cases*)	HAI, vaccine virus N = 5752	HAI, circulating virus N = 673	NT, vaccine virus N = 675	NT, circulating virus N = 675	N2 ELLA N = 675
Laboratory-confirmed Influenza associated with RI (n=152/123)	-0.50 (-0.65;-0.34)	-0.64 (-0.87;-0.41)	-0.48 (-0.70;-0.27)	-0.62 (-0.84;-0.41)	-0.36 (-0.56;-0.16)
Laboratory-confirmed Influenza associated with PD-ILI (n=121/98)	-0.54 (-0.72;-0.37)	-0.61 (-0.85;-0.37)	-0.52 (-0.76;-0.29)	-0.69 (-0.93;-0.45)	-0.38 (-0.60;-0.16)
Laboratory-confirmed Influenza associated with CDC-ILI (n=52/48)	-0.79 (-1.06;-0.53)	-0.79 (-1.14;-0.43)	-0.77 (-1.11;-0.43)	-0.81 (-1.13;-0.49)	-0.55 (-0.86;-0.25)
Antigenically similar Influenza associated with RI (n=37/34)	-0.51 (-0.82;-0.19)	-0.70 (-1.10;-0.30)	-0.43 (-0.80;-0.06)	-0.53 (-0.88;-0.17)	-0.68 (-1.04;-0.32)
Antigenically similar Influenza associated with PD-ILI (n=30/28)	-0.57 (-0.92;-0.22)	-0.91 (-1.38;-0.44)	-0.50 (-0.91;-0.09)	-0.72 (-1.12;-0.32)	-0.78 (-1.18;-0.38)
Antigenically similar Influenza associated with CDC-ILI (n=18/17)	-0.76 (-1.21;-0.31)	-0.91 (-1.51;-0.31)	-0.53 (-1.05;-0.01)	-0.75 (-1.26;-0.25)	-0.81 (-1.31;-0.30)

*no. of cases: the first number is for the HAI, vaccine virus assay; the second is for the other assays.

Supplemental Table 2. Increase in proportion of treatment effect on A/H3N2 influenza illness occurrence explained by pairs of assays

	Proportion of treatment effect explained by two assays [by greater of each assay taken singly] (increase)				
Case definition (n=no. of cases*)	HAI, circulating virus, and NT, circulating virus N = 673	HAI, vaccine virus, and N2 ELLA N = 675	HAI, circulating virus, and N2 ELLA N = 673	NT, vaccine virus, and N2 ELLA N = 675	NT, circulating virus, and N2 ELLA N = 675
Laboratory-confirmed Influenza associated with RI (n=123)	1.24 [1.32] (-0.08)	1.29 [0.82] (0.46)	0.99 [0.97] (0.02)	1.17 [0.85] (0.32)	1.42 [1.32] (0.09)
Laboratory-confirmed Influenza associated with PD-ILI (n=98)	1.69 [1.81] (-0.12)	1.74 [0.95] (0.79)	1.21 [1.13] (0.09)	1.61 [1.12] (0.49)	1.97 [1.81] (0.15)
Laboratory-confirmed Influenza associated with CDC-ILI (n=48)	0.93 [0.99] (-0.06)	1.15 [0.86] (0.29)	0.76 [0.65] (0.10)	1.06 [0.75] (0.31)	1.15 [0.99] (0.16)
Antigenically similar Influenza associated with RI (n=34)	0.48 [0.49] (-0.01)	0.73 [0.53] (0.20)	0.65 [0.53] (0.12)	0.71 [0.53] (0.18)	0.75 [0.53] (0.23)
Antigenically similar Influenza associated with PD-ILI (n=28)	0.74 [0.75] (-0.01)	0.91 [0.65] (0.27)	0.84 [0.65] (0.19)	0.88 [0.65] (0.23)	1.06 [0.75] (0.31)
Antigenically similar Influenza associated with CDC-ILI (n=17)	0.31 [0.32] (-0.00)	0.44 [0.28] (0.16)	0.36 [0.28] (0.08)	1.17 [0.85] (0.32)	0.43 [0.32] (0.12)

*no. of cases: the first number is for the HAI, vaccine virus assay; the second is for the other assays.

Supplemental Table 3. Estimated titers for 80% protection against A/H3N2 influenza illness

	Titer for 80% protection (95% confidence interval)				
Case definition (n=no. of cases*)	HAI, vaccine virus N = 5752	HAI, circulating virus N = 673	NT, vaccine virus N = 675	NT, circulating virus N = 675	N2 ELLA N = 675
Laboratory-confirmed Influenza associated with RI (n=152/123)	†	79.9 (41.7; 129)	†	#	288 (73.5; 541)
Laboratory-confirmed Influenza associated with PD-ILI (n=121/98)	†	83.3 (25.9; 126)	†	#	†
Laboratory-confirmed Influenza associated with CDC-ILI (n=52/48)	422 (248; 575)	51.0 (15.6; 81.1)	#	221 (146; 685)	39.6 (12.9; 332)
Antigenically similar Influenza associated with RI (n=37/34)	1260 (206; 1883)	75.4 (26.6; 105)	#	167 (29.2; 3092)	39.4 (23.7; 54.7)
Antigenically similar Influenza associated with PD-ILI (n=30/28)	1096 (150; 1758)	36.7 (16.7; 65.1)	#	151 (38.7; 1345)	39.5 (20.8; 181)
Antigenically similar Influenza associated with CDC-ILI (n=18/17)	271 (129; 425)	27.5 (18.3; 98.1)	#	199 (62.3; 268)	20.7 (11.5; 38.7)

* no. of cases: the first number is for the HAI, vaccine virus assay; the second is for the other assays;
† 80% protection not achieved;
# goodness-of-fit < 0.5.

Supplemental Table 4. Proportions of subjects with titers falling within the 95% confidence interval for 50% protection against A/H3N2 influenza illness

	Proportion of subjects with titers within the 95% CI for 50% protection				
Case definition (n=no. of cases*)	HAI, vaccine virus N = 5752	HAI, circulating virus N = 673	NT, vaccine virus N = 675	NT, circulating virus N = 675	N2 ELLA N = 675
Laboratory-confirmed Influenza associated with RI (n=152/123)	47.3%	48.5%	73.9%	†	82.5%
Laboratory-confirmed Influenza associated with PD-ILI (n=121/98)	53.4%	55.9%	43.7%	†	76.6%
Laboratory-confirmed Influenza associated with CDC-ILI (n=52/48)	33.6%	58.0%	†	38.2%	77.7%
Antigenically similar Influenza associated with RI (n=37/34)	74.3%	68.6%	†	79.7%	18.8%
Antigenically similar Influenza associated with PD-ILI (n=30/28)	66.0%	58.5%	†	70.3%	45.3%
Antigenically similar Influenza associated with CDC-ILI (n=18/17)	25.1%	49.0%	†	31.8%	17.1%

*no. of cases: the first number is for the HAI, vaccine virus assay; the second is for the other assays;

† goodness-of-fit < 0.5.

Supplemental Table 5. Relative vaccine efficacy predicted by the models compared to observed efficacy among subjects in the model: A/H3N2 influenza illness

		Relative efficacy predicted, %				
Case definition (n=no. of cases*)	Relative efficacy observ-ed, %	HAI, vaccine virus N= 5752	HAI, circulat-ing virus N = 673	NT, vaccine virus N = 675	NT, circulat-ing virus N = 675	N2 ELLA N = 675
Laboratory-confirmed Influenza associated with RI (n=152/123)	25.4%	20.8%	33.8%	37.0%	†	29.6%
Laboratory-confirmed Influenza associated with PD-ILI (n=121/98)	24.7%	22.9%	34.3%	34.3%	†	27.0%
Laboratory-confirmed Influenza associated with CDC-ILI (n=52/48)	37.6%	32.6%	34.5%	†	44.5%	31.9%
Antigenically similar Influenza associated with RI (n=37/34)	39.2%	22.6%	36.2%	†	30.1%	37.7%
Antigenically similar Influenza associated with PD-ILI (n=30/28)	42.2%	24.0%	40.6%	†	42.7%	38.6%
Antigenically similar Influenza associated with CDC-ILI (n=18/17)	71.5%	33.8%	48.7%	†	53.6%	49.4%

*no. of cases: the first number is for the HAI, vaccine virus assay; the second is for the other assays;
† goodness-of-fit < 0.5.