ResPECT Study

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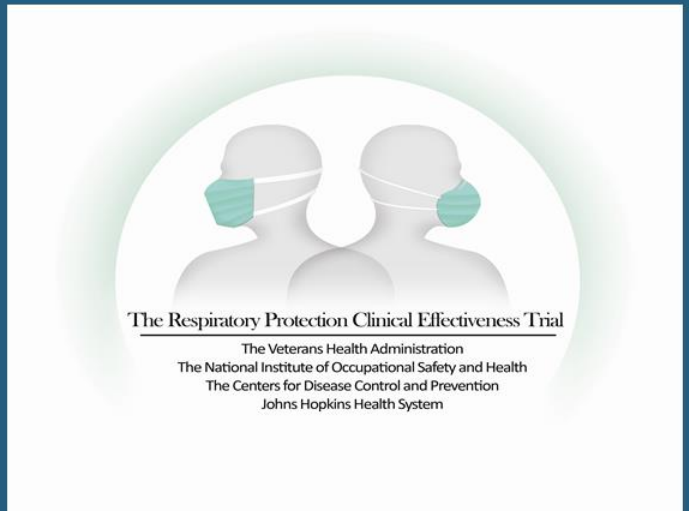
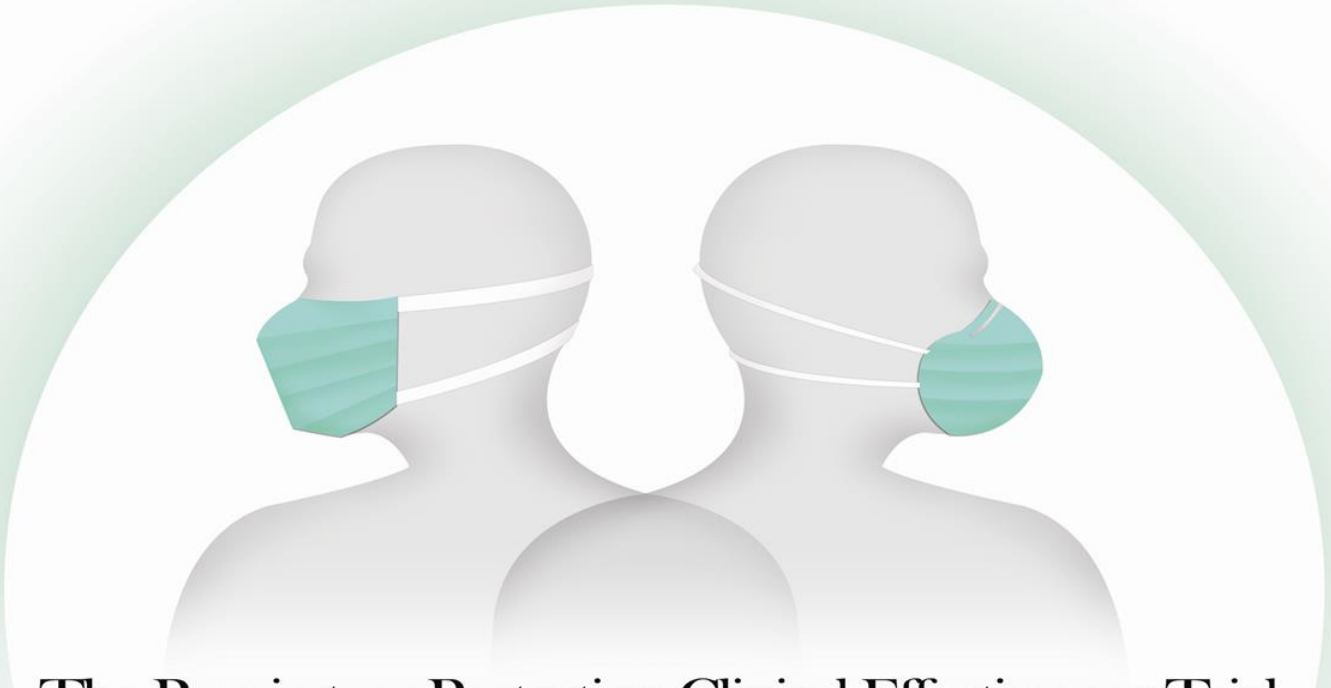




The Respiratory Protection Clinical Effectiveness Trial

The Veterans Health Administration
The National Institute of Occupational Safety and Health
The Centers for Disease Control and Prevention
Johns Hopkins Health System

Principle investigators:

Lew Radonavich and Trish Perl

Co Investigators:

Mary Bessensen, Derek Cummings, Charlotte Gaydos, Cynthia Gibert, Justin Lessler, Chris Nyquist, Connie Price, Nick Reich, Maria Rodriguez-Barrados, & Mike Simberkoff

Sponsors:

CDC (NIOSH, DHQP-Ron Shaffer, Ed Fischer, Mike Bell) & The Veterans Health Administration

Universities

Johns Hopkins University

University of Massachusetts

University of Colorado

VA: NY, Washington DC and Houston

Scientific Advisory Board

Daniel Morgan, Arnold Monto, Kristin Nichols, Richard P. Wenzel

DSMB:

Allison McGeer, Elizabeth Johnson, Tia Powell

Background

- Respiratory infections are common among HCPs
- Transmission thought to be primarily via large droplets, airborne hypothesized by some and contact increasingly recognized as important
- Appropriate level of respiratory protection has been disputed with
  - H1N1
  - SARS
  - MERS-CoV
  - H7N9
  - Other emerging respiratory viruses

Key Objectives & Questions

- Determine the incidence of influenza & other respiratory viral pathogens causing symptomatic and asymptomatic infections among HCWs in outpatient settings
- Determine the magnitude of reduction of influenza & respiratory infections in HCPs wearing masks and N95 respirators

Design

- Primary outcome-respiratory RT-PCR confirmed respiratory virus infection or serologic evidence of infection
- Two arms
- Designed to detect an effect in four-five years
  - Assumed cumulative incidence of LC respiratory viruses among usual precautions group-10%
  - Effect size-25% reduction in cumulative incidence between the surgical mask and N95 group compared to usual precautions

Comparison

- *2007* CDC Respiratory Protection Guidelines for Flu (**Medical Masks**)

- *2009* CDC Respiratory Protection Guidelines for Flu (**N95 Respirators**)

Hypothesis

- The incidence of RT-PCR confirmed respiratory virus infection will be at least lower among health care personnel working in outpatient settings and wearing N95 respirators than those wearing surgical masks exposed to patients with respiratory viral infections

Methods

- Study with a prospective timeline, non-blinded, cluster randomized interventions, a two-arm, “head-to-head” comparison, multiple sites and multiple geographic locations, with longitudinal cohorts recruited for multiple years
- Will be conducted in outpatient clinics, emergency departments and/or urgent care settings in multiple geographic locations
- Subjects will be recruited and randomized to one of two study arms, medical masks or N95 Respirators
- The duration of the intervention (mask wearing) period of the study is dependent on surveillance and incidence of viral respiratory illness at each site, but it is not expected to extend longer than 16 weeks

Methods, cont.

- During the pre-study period, demographic information (baseline survey), knowledge, attitudes, and beliefs regarding FPE will be administered, a blood sample will be collected for baseline serology testing, and subjects educated about the study, including the fit testing process
- Weeks 1-16 are the 'intervention period'. A cluster-randomized design will be utilized such that a group ("cluster") of approximately 16 people will be assigned (randomized) to wear the same device (Mask or N95) for up to 16

Methods, cont.

- Participants will also be asked to provide upper respiratory specimen during the intervention period
- The research team will also observe participants' adherence to mask use and hand hygiene
- Two weeks after the final week of wearing FPE (post-study period), subjects will be asked to provide a final serological sample and to complete a post-study survey

Cluster-Randomized Trial

- Unit of randomization is the “cluster”, not the individual
  - Cluster = clinic/ward/department
- Why CRT?
  - Basic feasibility considerations
  - Mass education
  - Reduces inter-group “contamination”
    - “Clustering effect”

Setting

- Outpatient clinics
  - Emergency Departments
  - General Medicine and Pediatrics clinics
  - Family Medicine clinics
- Includes adult and pediatrics
- JHHS
- Denver Health, Denver Children's and Denver VA
- NY (manhattan) VA
- Houston VA
- Washington VA

Timeline

- 2010-1: Pilot Johns Hopkins University (Johns Hopkins Health System) sites
- 2011-2: 3 sites activated:
  - JHU (site PI: TM Perl)
  - University of Colorado—Denver Health (site PI: CS Price)
  - VA Manhattan (site PI: M Simberkoff)
- 2012-3: Added 4 additional sites:
  - VA Hospital sites
    - Washington DC (site PI: C Gibert)
    - Houston, TX (site PI: MC Rodriguez-Barradas)
    - Denver, CO (site PI: M Bessesen)
  - University of Colorado Children's Hospital (site PI: AC Nyquist)

Procedures

- Clinic site randomized (clusters within each site)
- Study Briefing
- Collect Baseline Information
  - Demographic
  - Recent health history
    - Possible exclusion
    - Recent flu symptoms
  - Exposure
  - Household/family information
  - Flu Vaccination history
- Obtain Blood Sample
- N95 Fit Testing if needed

Weeks 2-13

- Wear Assigned PPE for exposure to patients with respiratory symptoms
  - Compliance monitored
    - weekly by research staff
    - self reported diary
- Daily and Weekly Symptom Diaries
  - Electronic, web-based collection
- Daily Exposure assessment
- Daily Patient Roster/Complexity Classification

Daily and Weekly Diaries

- Daily
  - Monitor signs and symptoms of flu
    - Fever
    - Shortness of breath/upper respiratory symptoms
    - Other flu-like symptoms
  - Call in if Fever + Cough or Sore Throat
- Weekly
  - Risk Factor Assessment
    - Use of nasal sprays or ointments
    - Recent problems with allergies
    - Use of immune suppressing drugs
    - Symptoms of others in household
- Paper and/or web-based

Symptoms Procedure

- Fever + Cough or Sore Throat
  - Greater than 37.8° C or 100.1° F
- Nasopharyngeal Swab or Aspirate
  - Two samples
- Coordinate with Local Occupational Health and Follow Clinic/Hospital Furlough Policy

Completion of Study

- Blood Serology
  - Test for antibodies to……

Planned Outcomes

- Primary outcome variable: Viral Respiratory Incidence
  - Rates of participant infection with influenza between study arms – N95, surgical masks, and "usual protection"
- Secondary outcomes
  - Incidence of influenza and other respiratory virus infections infections
  - Comparison of influenza rates based on self-reported symptoms & clinical criteria with influenza rates detected by serology
  - Comparison of detection by NP swab vs. serology
  - Comparison of PPE's effects on productivity

Sample Size Calculation

- In an effort to maximize compliance and ensure generalizability, the investigators have selected a cluster randomization in which all subjects on the same clinical unit are outfitted with the same type of protective devices. Although the model of N95 may vary at each study site and within each cluster, the type of respirator will not change
- Selection of clinic sites will be based on the size of the clinic. Each cluster/clinic will have a median of 20 HCPs
- Selection of clinic sites will also be based, in part, on the interest-level and enthusiasm of the HCP-subjects and the numbers of patients who present for healthcare with a diagnosable respiratory illness

Lab Methods

- ***Respiratory Pathogen Identification***
  - Swab specimens designated for processing within 10 days will be processed and stored at JHU. Frozen samples will be sent to Johns Hopkins University at agreed upon intervals
- ***Nucleic Acid Extraction, PCR***
  - A multiplex PCR assay(s) at JHU will be used to identify human respiratory pathogens. Currently, we plan to process and store samples for further analysis until such a time that logistic and funding resources are made available.

Main Protocol Differences

Pilot

- 6 clusters
- Weekly nasopharyngeal swabs
- Weekly payments
- PPE/HH audits on paper (10 weekly)
- SurveyMonkey for diaries

Year 1

- 53 clusters
- 2 randomized nasal & throat swabs with take-home kits
- 2 lump payments—incentivized
- PPE/HH audits via web-based program
- RedCap for surveys/diaries
- Extended enrollment period

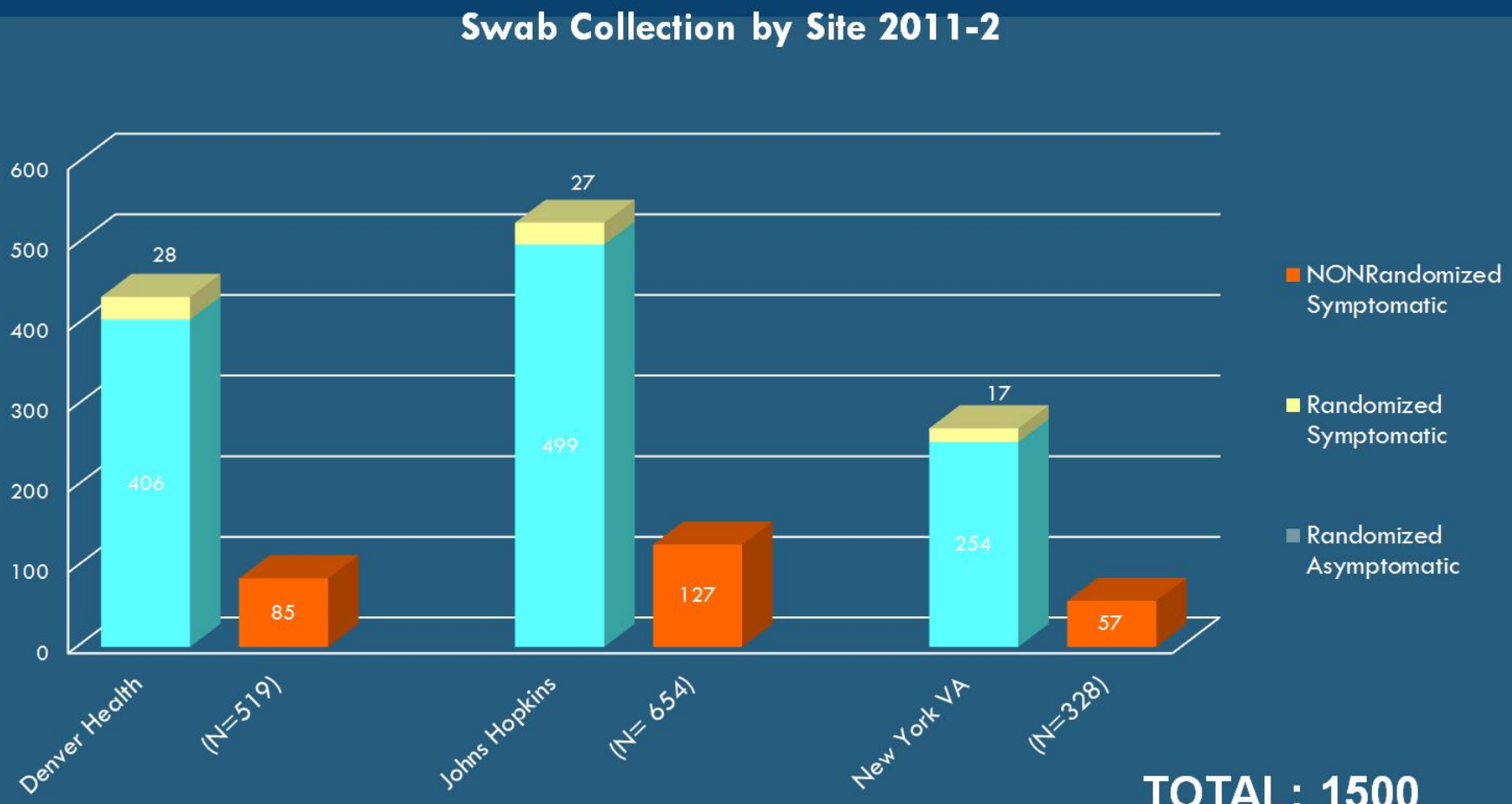
Year 2

- 117 clusters
- 2 randomized nasal & throat swabs with take-home kits
- 2 lump payments—incentivized
- PPE/HH audits via web-based program
- Redcap for surveys/diaries

Overview by Site

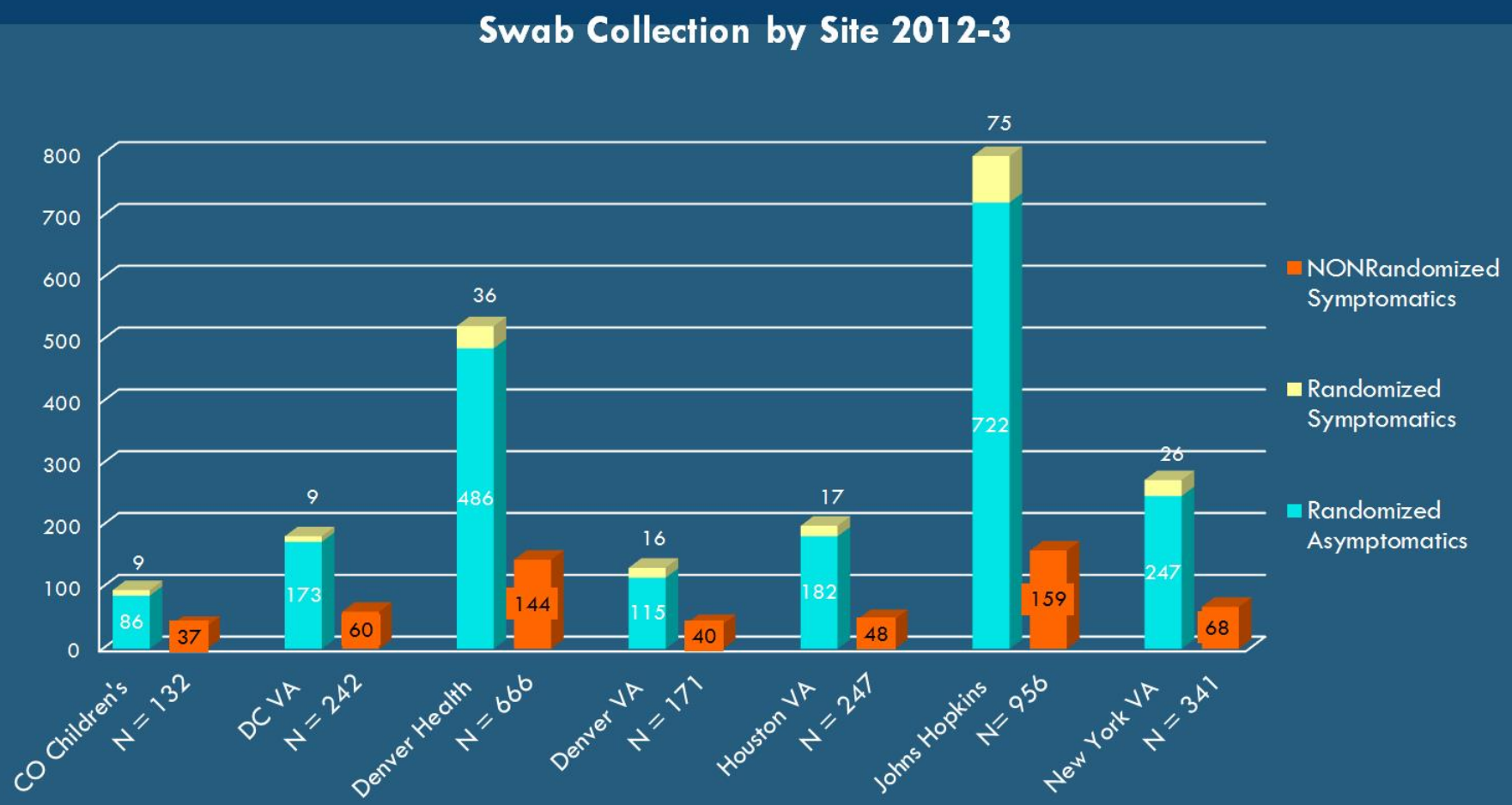
	Total Clusters	Total Enrolled	Total Withdrawn (to date)	Total Participants (after withdrawals)	Total Enrollees that received flu vaccine	Total Symptomatic Swabs Performed	Total Asymptomatic Swabs Performed
JHU – Pilot	*6*	*148*	*38 (26%)*	*110*	*59 (40%)*	*36*	*1083*
JHU – Year 1	*16*	*276*	*22 (8%)*	*254*	*225 (82%)*	*127*	*526*
JHU – Year 2	21	438	47 (11%)	391	367 (84%)	95	690
Denver Health – Yr 1	*14*	*228*	*20 (9%)*	*208*	*225 (82%)*	*127*	*526*
Denver Health – Yr 2	20	275	22 (8%)	253	254 (93%)	149	533
Colorado Children's	2	48	2 (4%)	46	48 (100%)	41	93
Denver VA	10	70	6 (9%)	64	50 (72%)	55	106
NY VA –Yr 1	*23*	*153*	*6 (4%)*	*147*	*83 (54%)*	*51*	*238*
NY VA-Yr 2	20	151	16 (11%)	135	75 (53%)	94	290
DC VA	18	97	7 (7%)	90	55 (57%)	61	165
Houston VA	8	106	8 (8%)	98	66 (62%)	64	123
TOTALS [for YEAR 2]	**99**	**1185**	**108 (9%)**	**1,077**	**1199**	**722**	**3609**

ResPECT Swab Collection Year 1



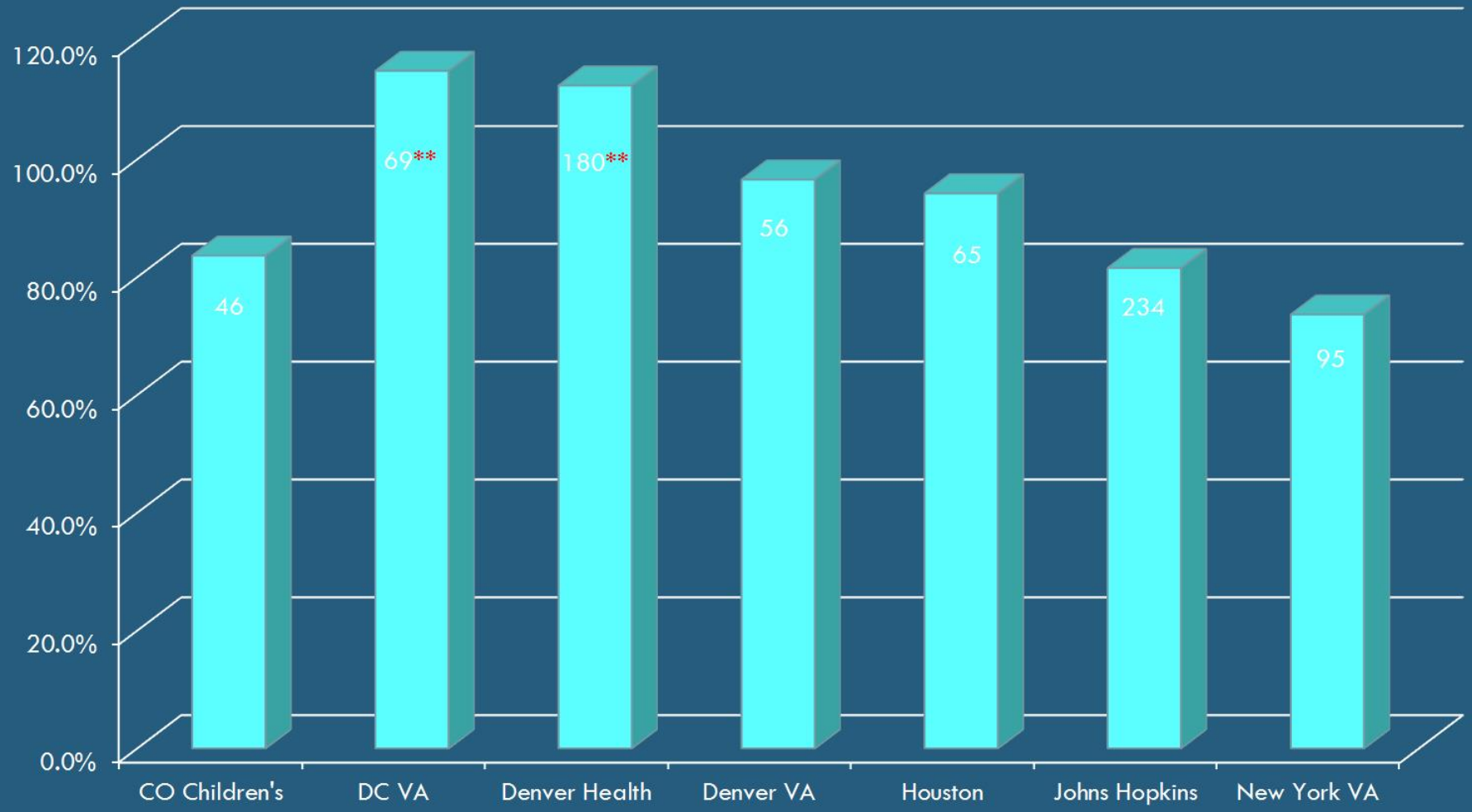
TOTAL: 1500

Swab Collection Year 2



TOTAL: 2755

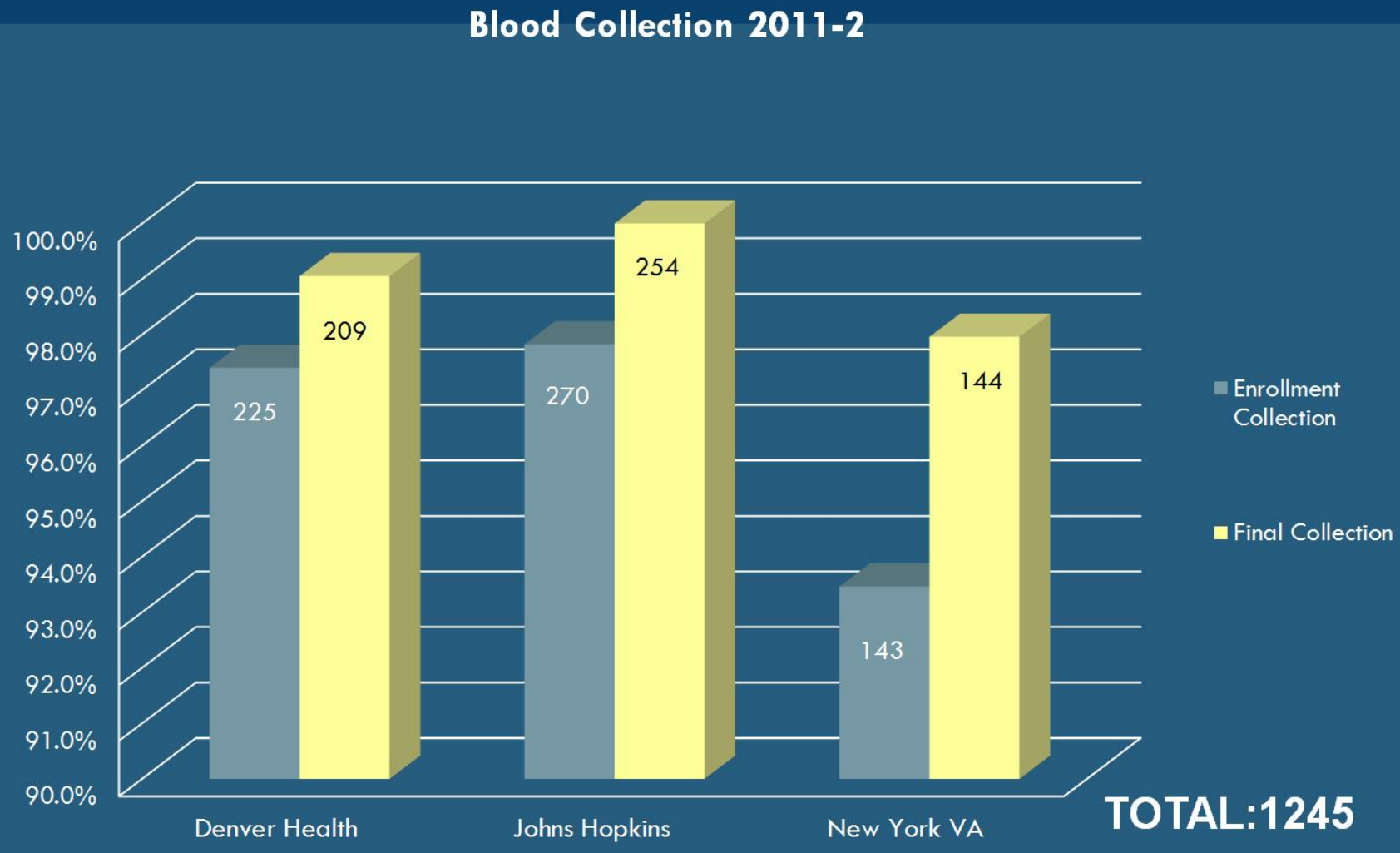
% Symptomatic Samples Collected* 2012-3



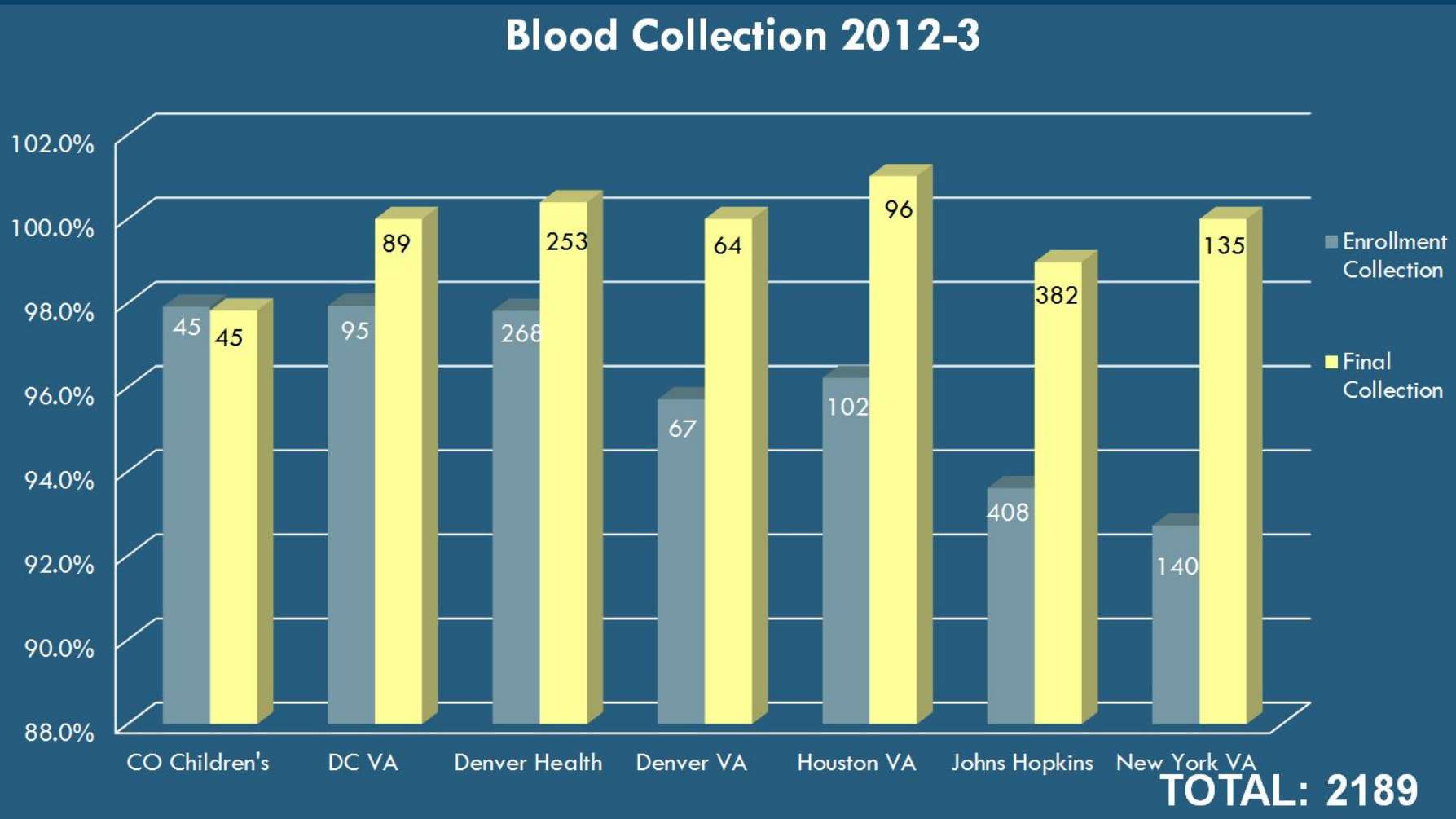
*Based on # Symptomatic Event Report Forms Submitted

** Does not account for those that did not fill out SEF (e.g. called staff with symptoms).

Blood Draw Completion Year 1



Blood Draw Completion Year 2



TOTAL: 2189

Sample Testing Overview

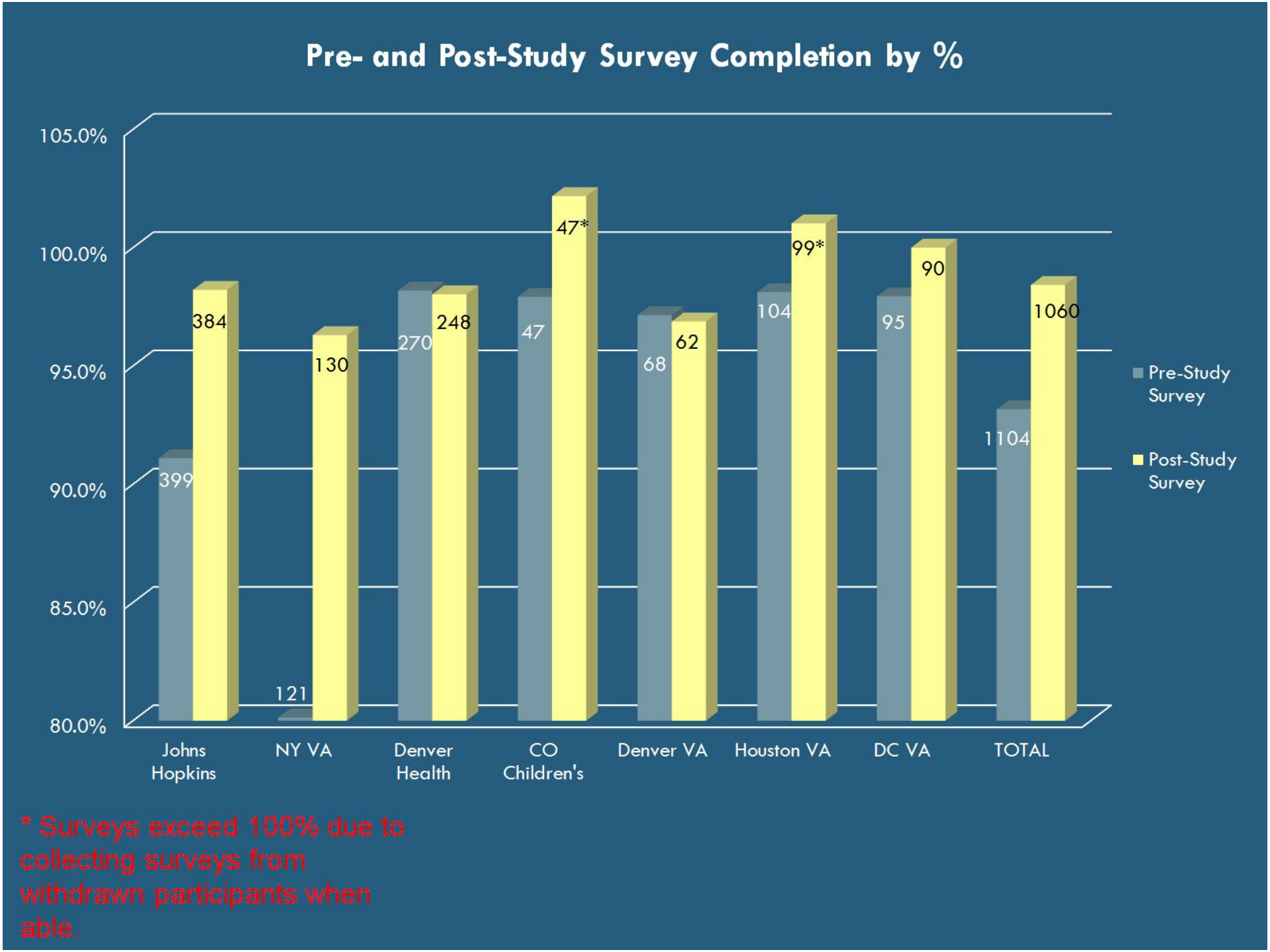
N/P Swab samples tested to date:

	Asymptomatic	Symptomatic	Total
Swabs YR1	1035	335	1370
Swabs YR2	*Not yet tested*	209	209
Total	**1035**	**544**	**1579**

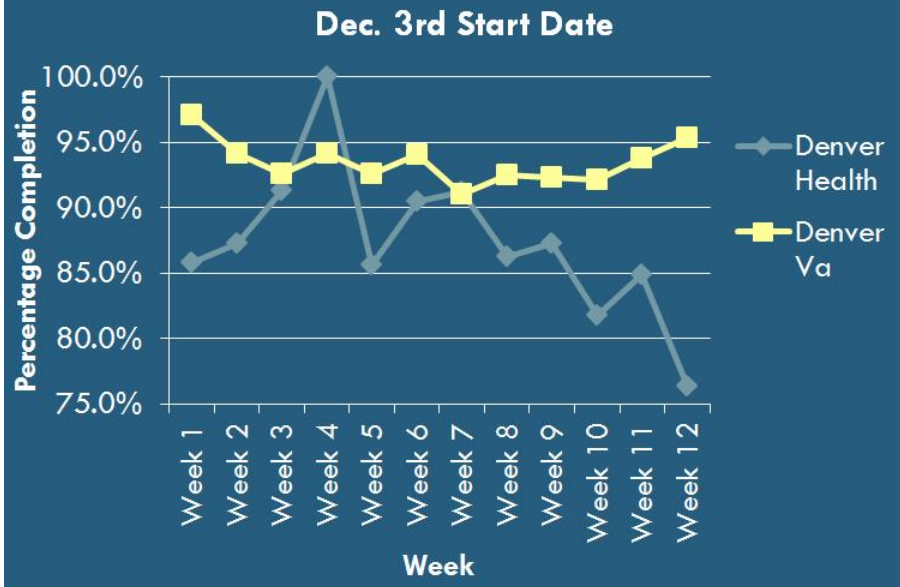
Blood samples tested to date: **1292**

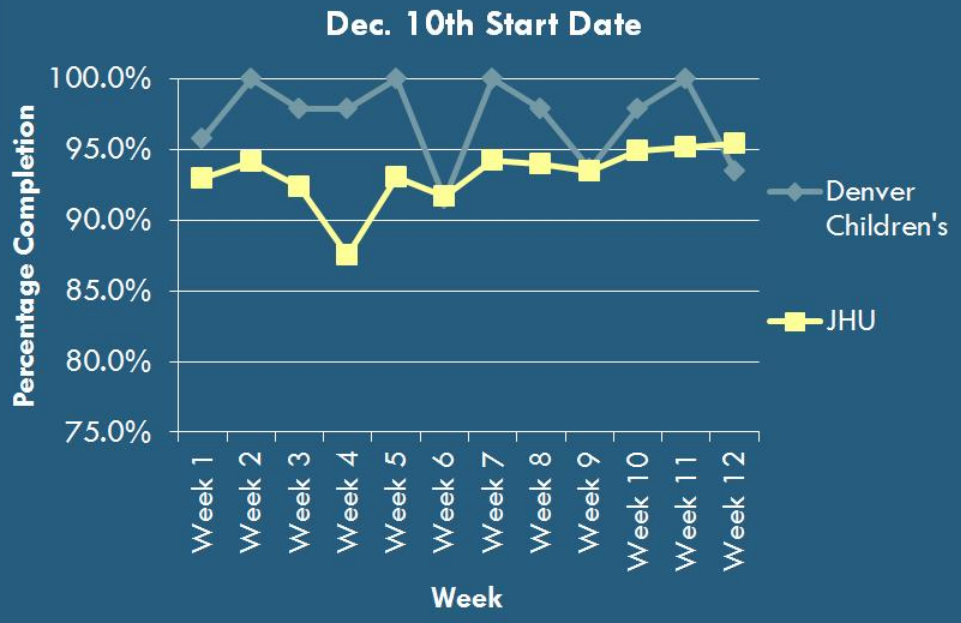
Sample Testing Overview

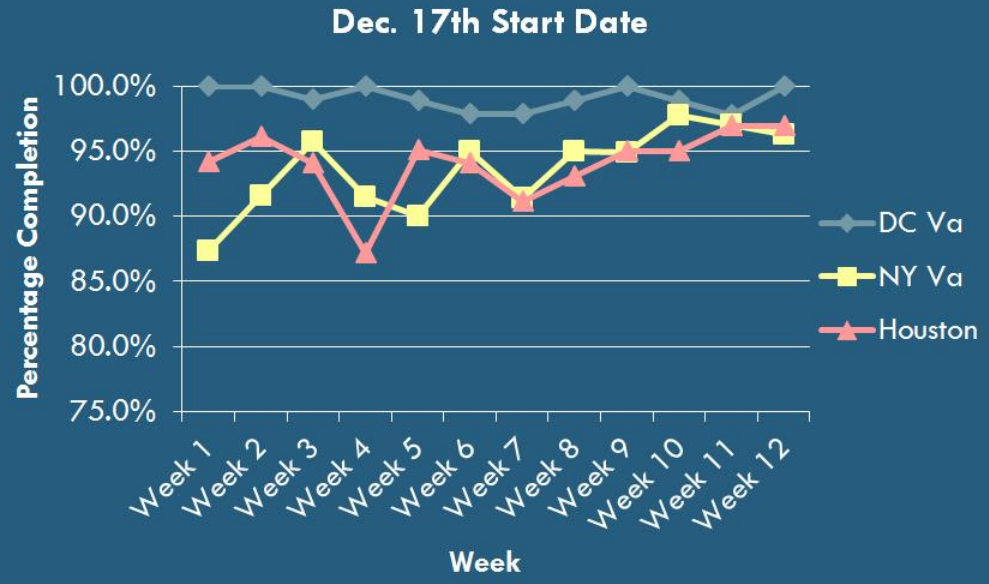
- Virus's isolated include
  - Influenza (A, B)
  - RSV
  - Rhinovirus
  - Coronavirus
  - Adenovirus
  - Parainfluenza
  - HMP


Pre- and Post-Study Survey Completion by %
105.0%
100.0%
95.0%
90.0%
85.0%
80.0%
399
384
121
130
270
248
47
47*
68
62
104
99*
95
90
1104
1060
Johns Hopkins
NY VA
Denver Health
CO Children's
Denver VA
Houston VA
DC VA
TOTAL
Pre-Study Survey
Post-Study Survey
* Surveys exceed 100% due to collecting surveys from withdrawn participants when able.

Weekly Diary Performance







Summary

- Successful cluster randomized clinical trial evaluating the efficacy of masks/respirators entering third year.
- Collaboration between CDC and VA
- Respiratory pathogens are primary outcomes
- Significant infrastructure built to support active surveillance in healthcare workers

Thank you: The ResPECT team