Science and Public Health in the Pharma World

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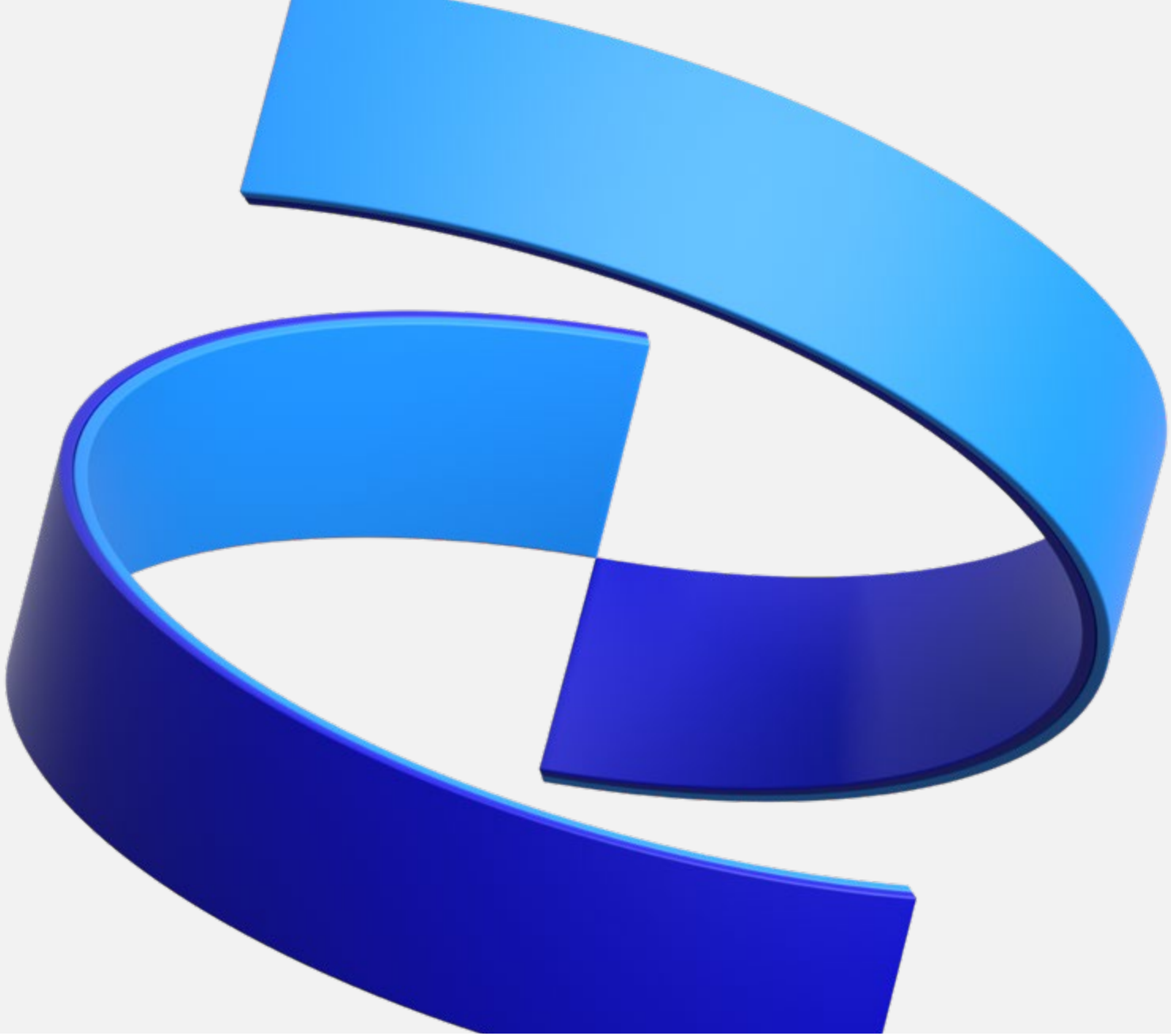
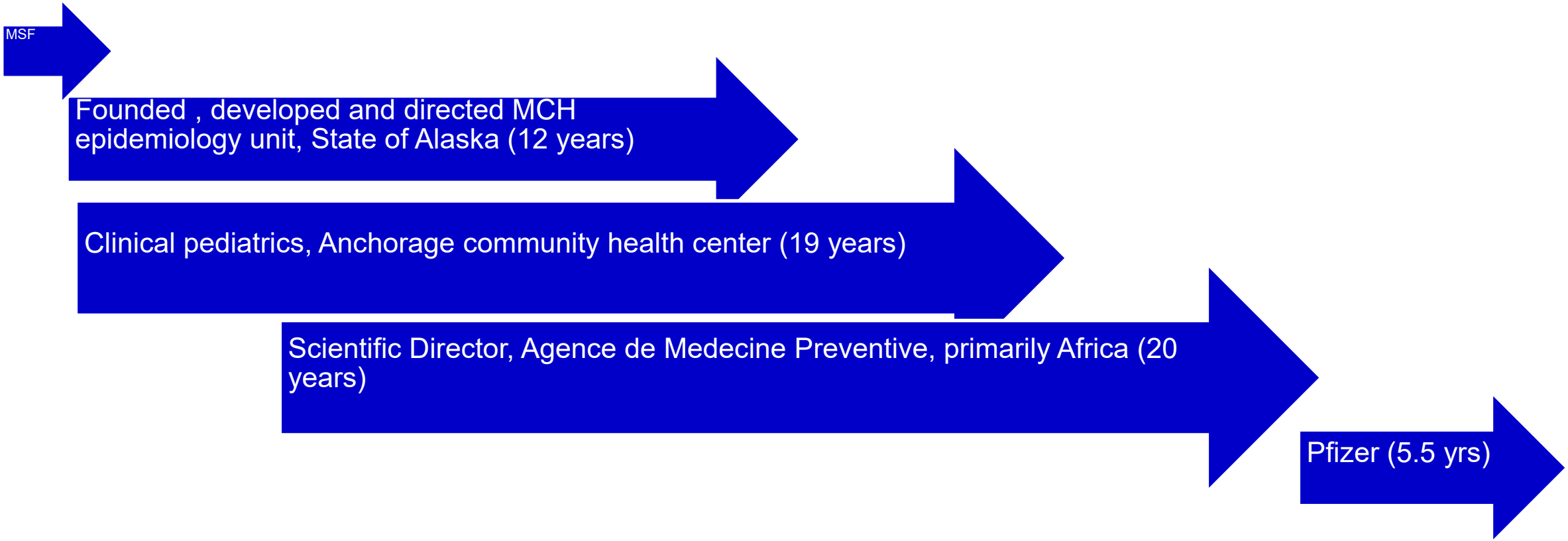


Career trajectory



Gavi Board of Directors, WHO IVIR-AC and IPAC commiittees, SAGE working groups

Pfizer Vaccines Organizational Structure

*MDSCA = Medical and Scientific Affairs

- Scientific affairs: evidence generation
- Medical affairs: evidence dissemination

Communication is bidirectional except commercial, which does not inform medical decisions

**Three common contractual structures for research with external groups

- Investigator sponsored research (ISR)
- Investigator sponsored collaborative research
- Pfizer sponsored research

Why is Real-World, End-to-End Evidence Generation Important?

Objectives	Outcomes / Impacts
Clinical Development Planning	• High quality disease incidence inputs for clinical trial sample size estimates • Feasibility for clinical trial operational success • Case detection to inform clinical trial design decisions
Estimations of Public Health Value Based on Burden of Disease (BOD) and Cost Effectiveness (CE) Models	• Demonstrate the value of our vaccines by evaluating clinical characteristics of disease, transmission dynamics, risk group populations, etc. • Inform Vaccine Technical Committee (VTC) recommendations for use and pricing
Demonstrating Vaccine Effectiveness (VE) in Real-world Settings Post-approval	• Fulfill regulatory commitments • Accelerated approval of indications and label enhancement • Ongoing monitoring of real-world vaccine use to confirm & re-evaluate public health impact • Inform adaptation of vaccine formulations, evaluate duration of protection / boosting
Translating Innovative Scientific Research into Public Health Interventions	• Discovery of biomarkers to customize vaccination strategies • Discovery of immune mechanisms of protection, helping to establish new correlates of protection for simplified licensure pathways • Generate evidence to differentiate Pfizer vaccines from competitors and estimate public health value
Strengthening Pfizer's Credibility as a Scientific Leader and Public Health Partner	• Approximately 150 high-quality publications in <24 months from MDSCA evidence generation activities allow Pfizer to lead the conversation and advance our vaccine science • Collaborative partnerships with institutions, public health authorities and experts • Aligns with Pfizer Vaccines '3P' strategy: Prevention, People, Partnerships

MDSCA Evidence Generation – Case Study Overview (1 of 2)

Support of Clinical Development Planning

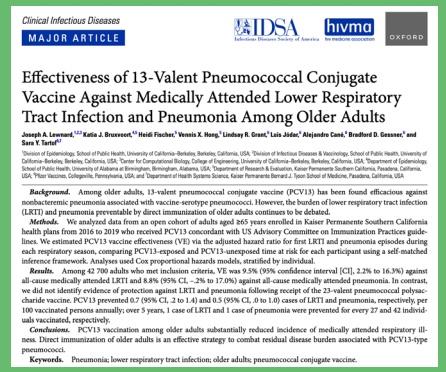
BOLD Study (Lyme)

Lyme incidence data for phase 3 site selection and power calculations

Reductions in all-cause pneumonia from direct PCV vaccination of adults

Kaiser N. California, S. California; Saxony, Germany; CAPiTA public health analysis

VE data used by VTCs globally to inform policy decisions



Clinical Infectious Diseases

MAJOR ARTICLE

IDSA hivma OXFORD

Effectiveness of 13-Valent Pneumococcal Conjugate Vaccine Against Medically Attended Lower Respiratory Tract Infection and Pneumonia Among Older Adults

Joseph A. Lewnard, Katie J. Bruxvoort, Heidi Fischer, Vennis X. Hong, Lindsay R. Grant, Luis Jódar, Alejandro Cané, Bradford D. Gessner, and Sara Y. Tartof

Background. Among older adults, 13-valent pneumococcal conjugate vaccine (PCV13) has been found efficacious against nonbacteremic pneumonia associated with vaccine-serotype pneumococci. However, the burden of lower respiratory tract infection (LRTI) and pneumonia preventable by direct immunization of older adults continues to be debated.

Methods. We analyzed data from an open cohort of adults aged ≥65 years enrolled in Kaiser Permanente Southern California health plans from 2016 to 2019 who received PCV13 concordant with US Advisory Committee on Immunization Practices guidelines. We estimated PCV13 vaccine effectiveness (VE) via the adjusted hazard ratio for first LRTI and pneumonia episodes during each respiratory season, comparing PCV13-exposed and PCV13-unexposed time at risk for each participant using a self-matched inference framework. Analyses used Cox proportional hazards models, stratified by individual.

Results. Among 42 700 adults who met inclusion criteria, VE was 9.5% (95% confidence interval [CI], 2.2% to 16.3%) against all-cause medically attended LRTI and 8.8% (95% CI, −2% to 17.0%) against all-cause medically attended pneumonia. In contrast, we did not identify evidence of protection against LRTI and pneumonia following receipt of the 23-valent pneumococcal polysaccharide vaccine. PCV13 prevented 0.7 (95% CI, 2 to 1.4) and 0.5 (95% CI, .0 to 1.0) cases of LRTI and pneumonia, respectively, per 100 vaccinated persons annually; over 5 years, 1 case of LRTI and 1 case of pneumonia were prevented for every 27 and 42 individuals vaccinated, respectively.

Conclusions. PCV13 vaccination among older adults substantially reduced incidence of medically attended respiratory illness. Direct immunization of older adults is an effective strategy to combat residual disease burden associated with PCV13-type pneumococci.

Keywords. Pneumonia; lower respiratory tract infection; older adults; pneumococcal conjugate vaccine.

Interactions between viruses and pneumococci in upper airway; PCV use and reduction in viral LRI

Kaiser S. California; Liverpool School of Tropical Medicine

PCVs may prevent more disease than estimated from UAD confirmed CAP

JCI The Journal of Clinical Investigation

Streptococcus pneumoniae colonization associates with impaired adaptive immune responses against SARS-CoV-2

Elena Mitsi, … , Bradford D. Gessner, Daniela M. Ferreira

J Clin Invest. 2022;132(7):e157124. https://doi.org/10.1172/JCI157124.

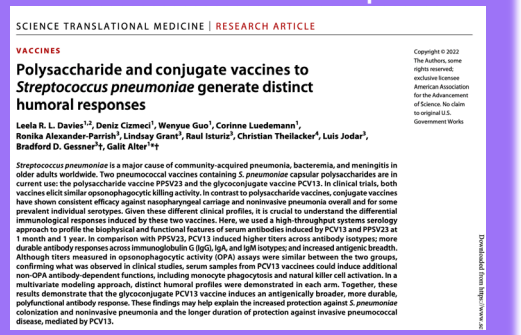
Clinical Medicine | Immunology | Virology

Graphical abstract

Innovative scientific research

Ragon Institute, Harvard, systems serology

Inform reasons why conjugates and polysaccharide pneumococcal vaccines have different clinical impact



SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

VACCINES

Polysaccharide and conjugate vaccines to *Streptococcus pneumoniae* generate distinct humoral responses

Leela R. L. Davies, Deniz Cizmeci, Wenyue Guo, Corinne Luedemann, Ronika Alexander-Parrish, Lindsay Grant, Raul Isturiz, Christian Theilacker, Luis Jodar, Bradford D. Gessner†, Galit Alter*†

Streptococcus pneumoniae is a major cause of community-acquired pneumonia, bacteremia, and meningitis in older adults worldwide. Two pneumococcal vaccines containing *S. pneumoniae* capsular polysaccharides are in current use: the polysaccharide vaccine PPSV23 and the glycoconjugate vaccine PCV13. In clinical trials, both vaccines elicit similar opsonophagocytic killing activity. In contrast to polysaccharide vaccines, conjugate vaccines have shown consistent efficacy against nasopharyngeal carriage and noninvasive pneumonia overall and for some prevalent individual serotypes. Given these different clinical profiles, it is crucial to understand the differential immunological responses induced by these two vaccines. Here, we used a high-throughput systems serology approach to profile the biophysical and functional features of serum antibodies induced by PCV13 and PPSV23 at 1 month and 1 year. In comparison with PPSV23, PCV13 induced higher titers across antibody isotypes; more durable antibody responses across immunoglobulin G (IgG), IgA, and IgM isotypes; and increased antigenic breadth. Although titers measured in opsonophagocytic activity (OPA) assays were similar between the two groups, confirming what was observed in clinical studies, serum samples from PCV13 vaccinees could induce additional non-OPA antibody-dependent functions, including monocyte phagocytosis and natural killer cell activation. In a multivariate modeling approach, distinct humoral profiles were demonstrated in each arm. Together, these results demonstrate that the glycoconjugate PCV13 vaccine induces an antigenically broader, more durable, polyfunctional antibody response. These findings may help explain the increased protection against *S. pneumoniae* colonization and noninvasive pneumonia and the longer duration of protection against invasive pneumococcal disease, mediated by PCV13.

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MDSCA Evidence Generation – Case Study Overview (2 of 2)

Epidemiologic data generation for VTCs

National surveillance globally; multiple study sites

Cross-program epidemiologic data generation for VTCs and real-world VE

Bristol (PCV20, RSV OA, BNT162b2)

Science to inform regulatory commitments

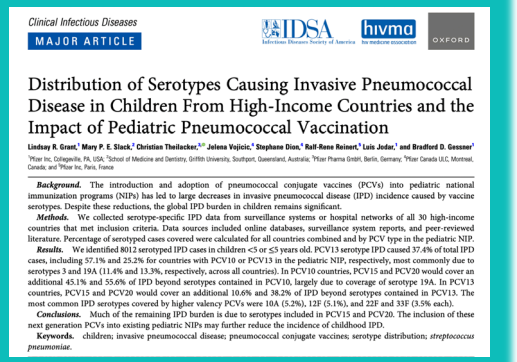
Harmonized cross-program epidemiologic data collection for VTCs

Multiple Sites (RSV older adults)

Core epidemiology

Multiple sites with harmonized protocols

Inform national recommendations



Clinical Infectious Diseases

MAJOR ARTICLE

Distribution of Serotypes Causing Invasive Pneumococcal Disease in Children From High-Income Countries and the Impact of Pediatric Pneumococcal Vaccination

Lindsay R. Grant, Mary P. E. Slack, Christian Theilacker, Jelena Vojicic, Stephane Dion, Ralf-Rene Reinert, Luis Jodar, and Bradford D. Gessner

Background. The introduction and adoption of pneumococcal conjugate vaccines (PCVs) into pediatric national immunization programs (NIPs) has led to large decreases in invasive pneumococcal disease (IPD) incidence caused by vaccine serotypes. Despite these reductions, the global IPD burden in children remains significant.

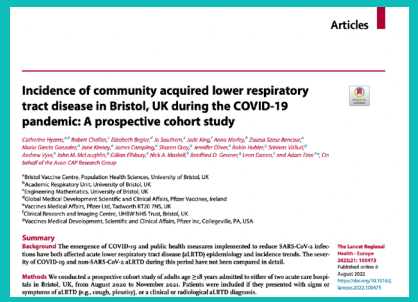
Methods. We collected serotype-specific IPD data from surveillance systems or hospital networks of all 30 high-income countries that met inclusion criteria. Data sources included online databases, surveillance system reports, and peer-reviewed literature. Percentage of serotyped cases covered were calculated for all countries combined and by PCV type in the pediatric NIP.

Results. We identified 8012 serotyped IPD cases in children <5 or ≤5 years old. PCV13 serotype IPD caused 37.4% of total IPD cases, including 57.1% and 25.2% for countries with PCV10 or PCV13 in the pediatric NIP, respectively, most commonly due to serotypes 3 and 19A (11.4% and 13.3%, respectively, across all countries). In PCV10 countries, PCV15 and PCV20 would cover an additional 45.1% and 55.6% of IPD beyond serotypes contained in PCV10, largely due to coverage of serotype 19A. In PCV13 countries, PCV15 and PCV20 would cover an additional 10.6% and 38.2% of IPD beyond serotypes contained in PCV13. The most common IPD serotypes covered by higher valency PCVs were 10A (5.2%), 12F (5.1%), and 22F and 33F (3.5% each).

Conclusions. Much of the remaining IPD burden is due to serotypes included in PCV15 and PCV20. The inclusion of these next generation PCVs into existing pediatric NIPs may further reduce the incidence of childhood IPD.

Keywords. children; invasive pneumococcal disease; pneumococcal conjugate vaccines; serotype distribution; *streptococcus pneumoniae*.

Robust incidence rates for CAP, LRTD pubs, RSV (in progress) BNT162b2 VE pubs



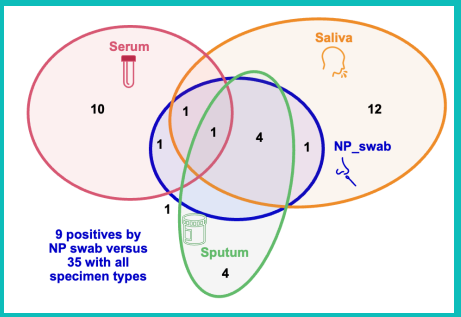
Articles

Incidence of community acquired lower respiratory tract disease in Bristol, UK during the COVID-19 pandemic: A prospective cohort study

Summary

PCV20 accelerated approval based partly on real-world VE in US (to be applied ex-US)

Assess degree of RSV underascertainment in older adults to inform incidence

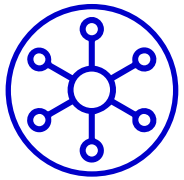


Additional MDSCA activities

- Contribute medical input to regulatory filings and strategies
- Contribute to vaccine designs
- Contribute to registrational trial designs
- Promote public health
  - Public health outcomes in clinical trials
  - Full preventable burden of disease
- Promote global equity
  - MDV PCV20

In Summary…

MDSCA Activities



- Encompass a wide range of research methodologies including retrospective ‘big data’, real-world data, prospective epidemiologic studies, and molecular / translational research
- Generate data to inform internal decisions from early clinical trial development to post-licensure
- Generate data to inform national policy recommendations, including providing accurate inputs for cost effectiveness modelling
- Fulfill post-approval commitment requirements that have supported accelerated vaccine approval
- Rely on MDSCA group’s epidemiologic, clinical, statistical, data analytics, and research operations expertise
- Rely on strong, long-term partnerships with external collaborators and sites globally that are fit-for-purpose both efficiently and effectively
- Main products are high-quality publications, scientific congress abstracts, regulatory filings, internal evidence dissemination/communication