DATA NOTE

Worldwide Index of Serotype-Specific Pneumococcal Antibody Responses (WISSPAR): A curated database of clinical trial data [version 1; peer review: 2 approved]

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v1 **First published:** 13 Jul 2023, **7**:109
https://doi.org/10.12688/gatesopenres.14768.1
Latest published: 13 Jul 2023, **7**:109
https://doi.org/10.12688/gatesopenres.14768.1

Abstract

The Worldwide Index of Serotype Specific Pneumococcal Antibody Responses (WISSPAR; https://wisspar.com), is a centralized, online platform housing data on immunogenicity from clinical trials of pneumococcal vaccines. The data on WISSPAR are primarily curated from outcomes tables from clinical trials and are made available in a searchable format that can be readily used for downstream analyses. The WISSPAR database includes trials covering numerous vaccine products, manufacturers, dosing schedules, age groups, immunocompromised groups, and geographic regions. Customizable data visualization tools are embedded within the site, or the data can be exported for further analyses. Users can also browse summary information about the clinical trials and their results. WISSPAR provides a platform for analysts and policy makers to efficiently gather, compare, and collate clinical trial data about pneumococcal vaccines.

Keywords

clinical trials, pneumococcal disease, pneumococcal conjugate vaccines, immunogenicity, Streptococcus pneumoniae

Open Peer Review

Approval Status ✓ ✓

	1	2
version 1 13 Jul 2023	✓ view	✓ view

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Any reports and responses or comments on the article can be found at the end of the article.

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Author roles: Perniciaro S: Data Curation, Writing – Original Draft Preparation, Writing – Review & Editing; **Cooper-Wooton D**: Data Curation, Software; **Knoll M**: Resources, Supervision, Writing – Review & Editing; **Weinberger D**: Conceptualization, Data Curation, Formal Analysis, Funding Acquisition, Investigation, Methodology, Project Administration, Resources, Software, Supervision, Validation, Visualization, Writing – Review & Editing

Competing interests: DMW has received consulting fees from Pfizer, Merck, Affinivax, Matrivax, and GSK for work unrelated to this manuscript and is principal investigator on grants from Pfizer and Merck to Yale University for work unrelated to this manuscript. SP has received consulting fees from Global Diagnostic Solutions, Inventprise, and Vaxcyte and is principal investigator on a grant from Merck to Yale University. MDK has received consulting fees from Merck for work unrelated to this manuscript and receives funding from Pfizer and Merck contracts with the Johns Hopkins University for work unrelated to this manuscript. DC-W has no competing interests to disclose.

Grant information: This work was supported by the Bill and Melinda Gates Foundation [INV-007834].

How to cite this article: Perniciaro S, Cooper-Wooton D, Knoll M and Weinberger D. **Worldwide Index of Serotype-Specific Pneumococcal Antibody Responses (WISSPAR): A curated database of clinical trial data [version 1; peer review: 2 approved]** Gates Open Research 2023, **7**:109 https://doi.org/10.12688/gatesopenres.14768.1

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Introduction

Pneumococcal disease, caused by *Streptococcus pneumoniae*, includes common, noninvasive infections such as otitis media, and severe, life-threatening infections including pneumonia, sepsis and meningitis Pneumococcal disease causes hundreds of thousands of deaths per year worldwide, most of these occurring in children, older adults, and people with immunocompromising conditions. The burden of pneumococcal disease is greatest in low- and middle- income countries, but there are high burdens of disease in infants and older adults in both high- and low-income settings[1,2].

Pneumococcal conjugate vaccines (PCVs) have been shown to have high efficacy against disease and mortality[3]. Vaccines targeting different serotypes and used with various dosing schedules have been employed in a wide array of populations globally[4,5]. With several new pneumococcal vaccines recently licensed and in development, there is a need to compare PCVs and ensure maintenance of vaccine effectiveness[6–9]. New PCVs are typically licensed based on comparisons of immunogenicity with existing vaccines. Therefore, there is a need to be able to readily compare the immunogenicity of different PCVs across studies. These immunogenicity data are used by regulators and by national immunization technical advisory groups (NITAGs) to determine which vaccine products, dosing schedules, and age groups will be included in immunization policy recommendations for their respective populations.

Immunogenicity data for pneumococcal vaccine trials should be compared and interpreted with caution, and the web interface has prominent statements about the caveats of the data. Data on immunogenicity alone cannot be used to infer differences in effectiveness between vaccines. These data need to be combined with information on the protective concentration of antibodies required to protect against each serotype in different populations for meaningful comparisons[10]. Despite these cautions, pulling immunogenicity data together into a single location will make this necessary process of comparison easier and less labor-intensive.

Review and synthesis of the data to inform these policy decisions can be labor intensive and cumbersome. Streamlining this process and making immunogenicity data available in a format that can be readily searched and extracted has value for policy makers and for researchers interested in vaccine efficacy, effectiveness, impact, and optimization. WISSPAR is a resource that provides an interactive platform to summarize and compare the immunogenicity data from clinical trials of pneumococcal vaccines.

Methods

Data sources

Data currently displayed on WISSPAR are from the Outcome Measures subsection of the Results section on clinicaltrials.gov. Several other datasets and types are available, including adverse events reporting, subject demographics, retention patterns. There are currently data from more than 57 trials available to compare, though these are updated frequently. If users need data from a trial that is not yet included on WISSPAR, users are encouraged to contact the authors with requests.

Outcome data

The current version of WISSPAR is focused on two measures of serotype-specific immunogenicity: geometric mean concentrations of immunoglobulin G levels measured by enzyme-linked immunosorbent assay (ELISA) or Electrochemiluminescence (ECL) assay and geometric mean titers measured with opsonophagocytic assays (OPA). These two measurements are commonly taken from blood serum of clinical trial participants at specified time intervals following doses of pneumococcal vaccines (e.g. 1 month following a dose received between 11–15 months of age), and provide a largely standardized basis for comparison, though differences between assays can cause variation. These data are extracted from outcomes tables from clinical trials, and can be filtered, visualized, or exported according to the specifications of the user, including selecting trials of certain vaccine products, manufacturers, dosing schedules, geographic regions, immunocompromised populations, or age groups.

Dataset validation

Data are manually validated for completeness, clarity and formatting from the customized WISSPAR backend. Data from clinical trials are imported exactly as they are recorded in clinicaltrials.gov, so if data are incorrectly entered into clinicaltrials.gov, the accuracy of WISSPAR could be affected.

Dashboard contents

Public-facing WISSPAR content is organized into Data Dashboards, Analysis Tools, and Resources (Table 1). The Data Dashboards provide customizable visualizations of the serotype-specific immunogenicity data in the Graphical Overview (Figure 1), and summary information from the included trials in the Clinical Trials Overview. The analysis tools allow users to efficiently pinpoint trials of interest in the Look up a trial tool, and export custom .csv files for downstream analyses using the Immunogenicity Data Export tool. There are community resources available, including a blog to keep users abreast of updates and demonstrate WISSPAR capabilities example analyses. An example of how WISSPAR can be used to make comparisons of serotype-specific differences in immunogenicity between three vaccine products is published on the WISSPAR blog[11].

Data hosting and database structure

The WISSPAR platform consists of a few different services hosted on Digital Ocean (Figure 2). The backend database is PostgreSQL (V13) with connection pools set up for security

Table 1. Descriptions of page content for the Worldwide Index of Serotype-Specific Antibody Responses, WISSPAR. WISSPAR has a suite of tools to summarize, compare, and export immunogenicity data from clinical trials of pneumococcal vaccines.

WISSPAR Website Pages	Content Summary	
PUBLIC DATA DASHBOARDS		
Graphical View	An interactive Shiny app that allows users to visualize measurements of serotype-specific immunogenicity and export images. Available variables include: • Vaccine • Serotypes • Age category • Schedule • Doses received and timing • Trial phase • Sponsor Users can visualize measurements of IgG Geometric Mean Concentrations (GMCs), Opsonophagocytic Activity assays (OPAs), and GMC and OPA ratios.	
Clinical Trials Overview	Filterable listing of clinical trials included on WISSPAR, allowing users to search for particular clinical trials or criteria of interest, including: • Vaccines • Schedule • Manufacturers • Age Category • Ethnicity • Continent • Immunocompromised Groups • Gender	
ANALYSIS TOOLS		
Look up a trial	Quick-search function that allows users to access complete trial information by entering the NCT ID from clinicaltrials.gov	
Immunogenicity Data Export	Highly customizable data export tool where users can create customized datasets for downstream analyses. Variables include:	
	Filters	**Fields**
	• Income group • Trial phase • Vaccine • Age category • Immunocompromised group • Responsible party	• Clinical trial data • Study eligibility • Study location • Outcome Measures • Outcome Overview
RESOURCES		
Blog	Link to WISSPAR blog posts, which includes updates from the team, examples of how to use WISSPAR to compare trial data, and more.	
Videos	Video walk-through of WISSPAR features and functions	

and guaranteed availability; there are also automated backups for recovery. The web application is written in Golang (1.16) for the backend connecting to the database and integrating with the clinicaltrials.gov website. On the front end of the web application, the javascript framework is SvelteJS to allow for quick component loading times and better code organization

Figure 1. Data visualization app on the Worldwide Index of Serotype-Specific Antibody Responses, WISSPAR. WISSPAR's data visualization app is based in R Shiny and allows users to generate customizable, downloadable figures showing immunogenicity measurements stratified by serotype, vaccine product, vaccine manufacturer, trial sponsor, and vaccination schedule.

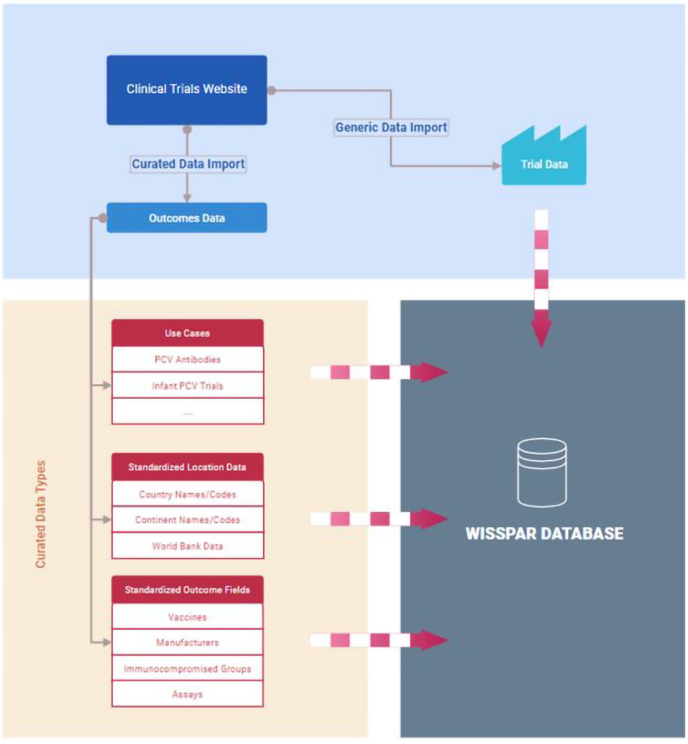

Figure 2. Organizational Schematic of the Worldwide Index of Serotype-Specific Antibody Responses, WISSPAR. The data import process from clinicaltrials.gov and the sources of data and the data types used in WISSPAR are described here.

over traditional javascript. We used GitLab for our software version control, when a change is made in the repository on GitLab it is detected by our Digital Ocean repository and automatically deployed. We also have fail safes built in so that if a code build fails to deploy it will revert to the last working version without any downtime to the web application. Interactive plots, with filters and selectors, was created in RShiny and deployed through the shiny.io server.

Use of data

All data on WISSPAR are publicly available or previously published.

Data availability

Zenodo: weinbergerlab/WISSPAR: v1_1_1, https://doi.org/10.5281/zenodo.7055186[12].

Acknowledgments

We thank representatives from the CDC, Merck, Pfizer, and the Gates Foundation for critical feedback about the development of the dashboard.

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PubMed Abstract | Publisher Full Text | Free Full Text

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PubMed Abstract | Publisher Full Text

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Open Peer Review

Current Peer Review Status: ✔ ✔

Version 1

Reviewer Report 08 August 2023

https://doi.org/10.21956/gatesopenres.16094.r34280

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The Worldwide Index of Serotype Specific Pneumococcal Antibody Responses (WISSPAR) is a helpful and comprehensive online tool including immunogenicity data from clinical trials of pneumococcal vaccines (PCVs) according to numerous vaccine products, manufacturers, dosing schedules, age groups, immunocompromised groups, and geographic regions.

The platform is user-friendly and without a doubt will be a very useful tool for researchers, regulators and technical advisory groups that need to compare the immunogenicity of different PCVs across studies. At present data of WISSPAR come from more than 57 trials but WISSPAR curators update the database frequently. In addition, if users need data from a trial that is not yet included on WISSPAR, they are encouraged to contact the authors with requests. Measures of serotype-specific immunogenicity include IgG Geometric Mean Concentrations (GMCs), Opsonophagocytic Activity assays (OPAs), and GMC and OPA ratio.

My only minor concern is about data validation: data from clinical trials are imported exactly as they are recorded in clinicaltrials.gov, so if data are incorrectly entered into clinicaltrials.gov, the accuracy of WISSPAR could be affected. My suggestion would be including an alert if they or the scientific community detect any data that might reasonably considered to be erroneous. On the other hand, it could be interesting to provide a brief audit on the methodological quality of data reported in the clinical trials included in the tool, using widely accepted review checklists such as those of CONSORT reporting guidelines.

Is the rationale for creating the dataset(s) clearly described?

Yes

Are the protocols appropriate and is the work technically sound?

Yes

Are sufficient details of methods and materials provided to allow replication by others?
Yes

Are the datasets clearly presented in a useable and accessible format?
Yes

Competing Interests: I have received fees as speaker from GSK, Pfizer and Sanofi-Pasteur.

Reviewer Expertise: Pediatric Infectious Diseases; molecular epidemiology; invasive pneumococcal disease

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 02 August 2023

https://doi.org/10.21956/gatesopenres.16094.r34277

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The WISSPAR database presented by Perniciaro *et al.,* provides an extremely valuable tool to keep track of clinical trials data on pneumococcal vaccines. The tool allows any user to easily access the clinical trial data and compare different datasets. Having a tool that allows to compare PCVs and assess vaccine effectiveness would greatly help vaccine research. The new resource is especially useful for vaccines in early development stages or discovery phase, providing access and facilitating the comparison to previously published data. The rationale for creating the dataset is clearly described by the authors and both the methodology and data sources are reported in details.

Overall the database presented is certainly suitable for indexing, my only comment would be about future updates. It would be interesting to know if the authors have already planned how future updates of the system will be released. If new datasets will become available, will they be immediately included? What's the planned frequency of the updates? Will the frequency of the system updates be time-dependent or data-dependent? Is there any plan to add any extra function?

Is the rationale for creating the dataset(s) clearly described?
Yes

Are the protocols appropriate and is the work technically sound?
Yes

Are sufficient details of methods and materials provided to allow replication by others?
Yes

Are the datasets clearly presented in a useable and accessible format?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Vaccine development / infectious diseases

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.