A Quantitative Analysis on the Locations of Phase 3 Retina Trials in the United States over the past 5 Years

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Introduction

- Clinical trials are essential for advancing treatments in ophthalmology, yet comprehensive data on institutional participation in Phase 3 retina trials is not readily available.
- The U.S. National Library of Medicine Clinical Trials database (NLM database) lists individual research sites for each study; however, aggregating and visualizing this data remains challenging.
- The lack of centralized and easily interpretable data on research site participation hinders understanding of institutional contributions to retinal clinical research.
- Identifying geographic and institutional trends can improve resource allocation and research collaboration.
- We aim to
    - Quantify the number of unique institutions participating in Phase 3 clinical retina trials.
    - Assess the distribution of trials across research sites.
    - Analyze state-level variations in participation.
- Hypothesis
    - Institutional participation in Phase 3 retina trials is unevenly distributed, with a concentration in certain geographic regions and academic centers.
- Understanding trial site distribution can inform funding decisions, improve patient access to clinical trials, and guide future research efforts.
- Findings may help stakeholders optimize trial site selection and enhance equity in ophthalmic research participation.

Aims and Objectives

1. Assess U.S. involvement in Phase 3 Clinical Retina Trials (CRTs)
    1. Quantify the number of institutions participating in Phase 3 CRTs across the U.S.
2. Compare the density of research trial locations across the U.S.
    1. Identify trends in geographic distribution of trial sites.
    2. Evaluate regional disparities in trial site concentrations.
    3. Investigate factors influencing the presence or absence of research centers in specific states.

Methods

Study Design

- This study analyzed Phase 3 clinical retina trials (CRTs) conducted in the United States over a five-year period.
- Data was collected and processed to examine geographic distribution, research site participation, and trial density.

Methods

Data Collection

- Trials conducted between December 6, 2016, and December 6, 2021.
- Source: U.S. National Library of Medicine Clinical Trials database (*ClinicalTrials.gov*).
- Inclusion Criteria:
    - Phase 3 CRTs with at least one research site in the U.S.
    - Trials with publicly available research site information.
        - Information including: Study name, site name, trial location
- Exclusion Criteria:
    - Phase 1 and Phase 2 trials.
    - Trials without specific name, site, or trial listings.
- Data Retrieval Method:
    - A custom web scraper extracted categorical data, including:
        - Trial title
        - Research site names
        - Research site locations (city, state)

Data Processing & Analysis

- Software & Tools:
    - Microsoft Excel for data organization, trend analysis, and summary statistics.
    - Geospatial mapping software BatchGeo for geographic visualization.
- Key Variables Analyzed:
    - Total number of Phase 3 CRTs conducted in the U.S.
    - Number and location of research centers participating in these trials.
    - Average number of trials per research site.
    - Average number of sites per study.

Rationale for Methods

- Web scraping was chosen to efficiently compile large datasets from *ClinicalTrials.gov*, ensuring comprehensive data collection.
- Excel-based analysis allowed for streamlined trend identification and statistical summaries.
- Geospatial visualization enabled clear representation of research site density and distribution trends.

Table & Figures

- **Table 1** shows the research centers which participate in the most trials across the country
- **Table 2** shows the studies which conduct trials at the most locations across the US
- **Figure 1** is a density map of where research trials are conducted across the US
- **Figure 2** highlights the correlation between a state's population and the number of trials conducted in that state

Results

- 44 states participated in Phase 3 Clinical Retina Trials, while Alaska, Delaware, Montana, New Hampshire, North Dakota, and Wyoming did not
- 76 total studies were conducted in the US over five years
    - These were separated into 2,966 trials, for an average of 39.29 trials per study
- 709 unique research sites hosted an average of 3.06 trials
- States with the highest number of trials:
    - California & Texas (65 trials each)
    - Florida (59 trials)
    - Maryland (49 trials)
    - Massachusetts & Georgia (47 trials each)

Table 1 – Research sites with most individual trials

Research Site	Location	Trials Conducted
Southeast Retina Center	Augusta, GA	25
Retina Research Institute of Texas	Abilene, TX	21
Ophthalmic Consultants of Boston	Boston, MA	19
Sierra Eye Associates	Reno, NV	19
Retina Associates of Florida	Tampa, FL	18

Table 2 – Research studies with most geographic sites

Study	Sponsor	Locations
Farivimab for Diabetic Macular Edema	Hoffman La Roche	118
Intravitreal Zimura (C5 inhibitor) Safety	IVERIC bio, Inc.	104
Safety and Efficacy of KSI-301 vs Aflibercept for Macular Edema via RVO	Kodiak Sciences	98
Safety and Efficacy of Port-Ranibizumab vs Intravitreal Ranibizumab for Diabetic Macular Edema	Hoffman La Roche	91
Safety and Tolerability of Faricimab in Neovascular Age-Related Macular Degeneration	Hoffman La Roche	89

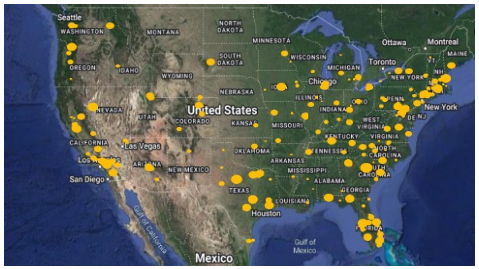

Figure 1 – Geospatial density map of research trials

Conclusions

- Suburban areas surrounding major metropolitan areas such as Dallas, New York, Chicago, and the Bay Area hosted the highest number of trials, often linked to large academic medical centers
- Rural states and those with lower population densities, fewer ophthalmic research centers, and less specialized infrastructure saw little to no trial activity.
    - This urban-rural disparity may limit access to clinical trials for rural patients, contributing to lower representation of diverse populations in research trials

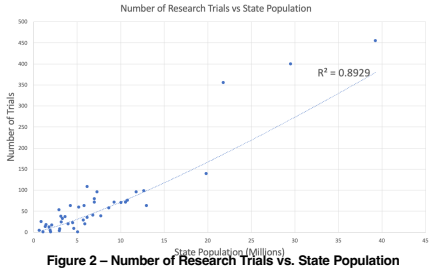

Figure 2 – Number of Research Trials vs. State Population

- One metric that can indicate the success of a phase 3 trial is the number of centers involved, where a higher number of centers is associated with fewer participants dropping out, increased funding, and a higher likelihood of statistically significant results.[1, 2]
- Research undertaken at multiple centers can also increase the reproducibility of results, generalizability to populations, and makes for easier translation into clinical practice.[3]
- Racial and ethnic minorities disproportionately have more chronic disease histories, thus overall population health can be improved with inclusion to research studies.[4]

Future Recommendations

- Identifying potential trial sites in states with lower population but high patient need can improve clinical trial efficiency and generalizability, and this can be promoted with policies to subsidize infrastructure development
- Regulators and sponsors should incentivize recruitment from diverse racial, ethnic, and socioeconomic backgrounds by establishing more inclusive trial site selection criteria.

References

1. Fogel DB. Factors associated with clinical trials that fail and opportunities for improving the likelihood of success: a review. Contemp Clin Trials Commun. 2018;11:156-164. doi:10.1016/j.conctc.2018.08.001.
2. Carlisle B, Kimmelman J, Ramsay T, MacKinnon N. Unsuccessful trial accrual and human subjects protections: an empirical analysis of recently closed trials. Clin Trials. 2014;12(1):77-83. doi:10.1177/1740774514558307.
3. Hunniford VT, Grudniewicz A, Fergusson DA, Grigor E, Lansdell C, Lalu MM. Multicenter preclinical studies as an innovative method to enhance translation: a systematic review of published studies. Preprint. Published 2019. doi:10.1101/591289.
4. Kelsey MD, Patrick-Lake B, Abdulai R, et al. Inclusion and diversity in clinical trials: Actionable steps to drive lasting change. Contemp Clin Trials. 2022;116:106740. doi:10.1016/j.cct.2022.106740

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