

The Ophthatome™ Knowledgebase : A curated knowledgebase of over 500,000 ocular disease phenotypic records coupled with analyses tools to enable novel discoveries for drug development and pharmacogenomics

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Abstract

- Medical big data analytics has applications in clinical decision, predictive/ prognostic modelling of disease progression, disease surveillance, public health and research.
- The electronic medical record (EMR), system is the digital storehouse of rich medical data that includes demographics, clinical (diagnosis, clinical diagnostic tests, treatment, prescription drugs, surgery, laboratory test reports) and administrative (bills, insurance claims) details of patients' visits to hospital(s).
- Although EMR is a repository of vast clinical data on a large patient cohort collected over many years, the data lack sufficient structure to be of any clinical value for applying deep learning methods and advanced analytics to improve disease management at an individual patient level or for the field in general.
- Aggregated data from hospital EMRs need to be captured in a structured knowledge base to support clinical and translational research (CTR)^{1,2}.

Overview of the Ophthatome

Ophthatome™ is a knowledgebase built on electronic medical records data for ophthalmic disease research, developed by MedGenome, India, in collaboration with Narayana Nethralaya, Bengaluru, India.

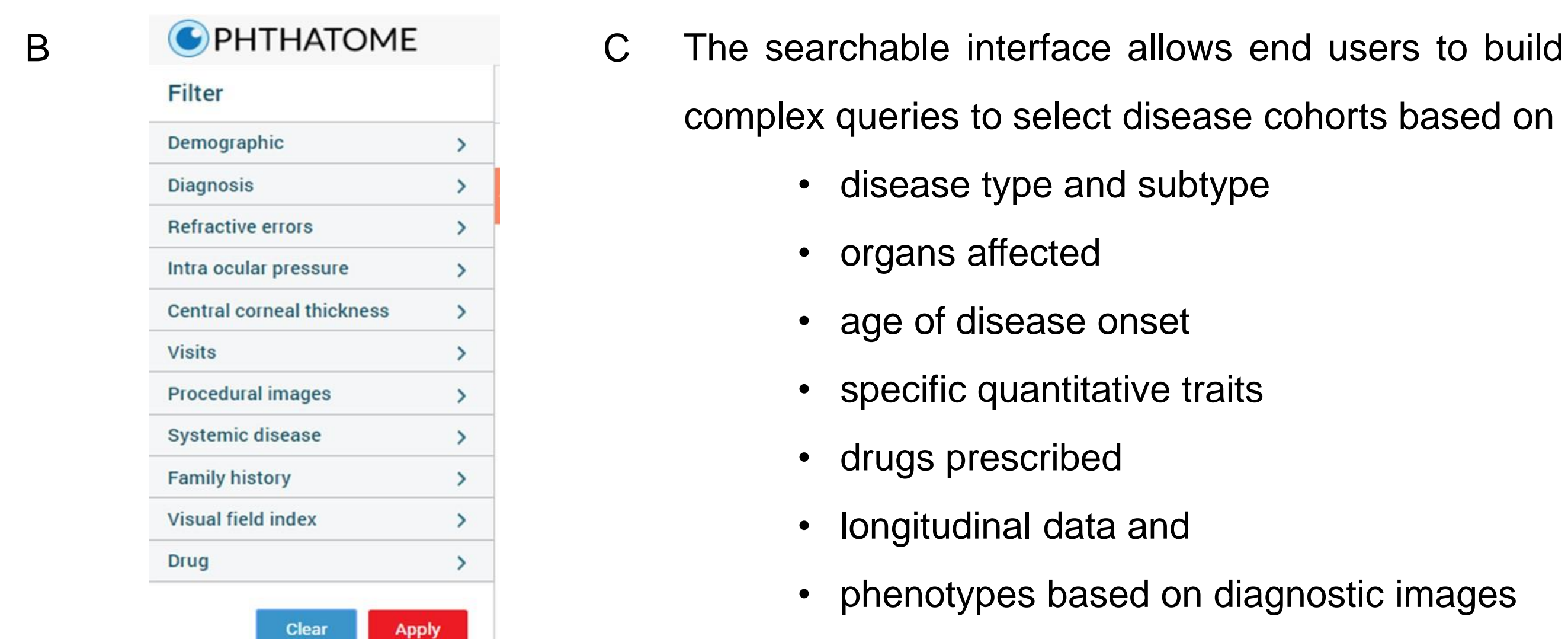
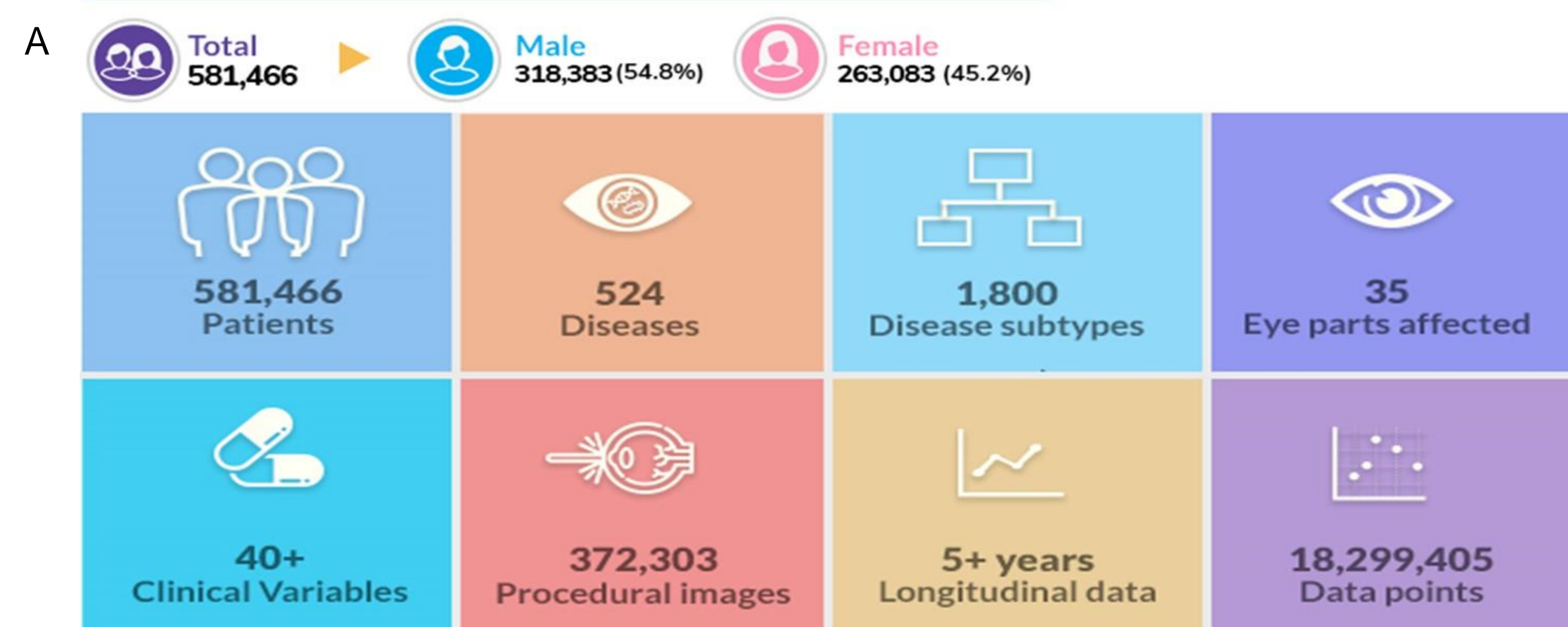


Figure 1: Summary of the Ophthatome knowledgebase : A) Summary of the datasets present in the Ophthatome. B) Overview of the filters in the Ophthatome for building queries and cohorts for further analysis. C) List of all the clinical parameters that are captured in the knowledgebase.

Define cohorts in Diabetic retinopathy to study drug treatment response using the Ophthatome

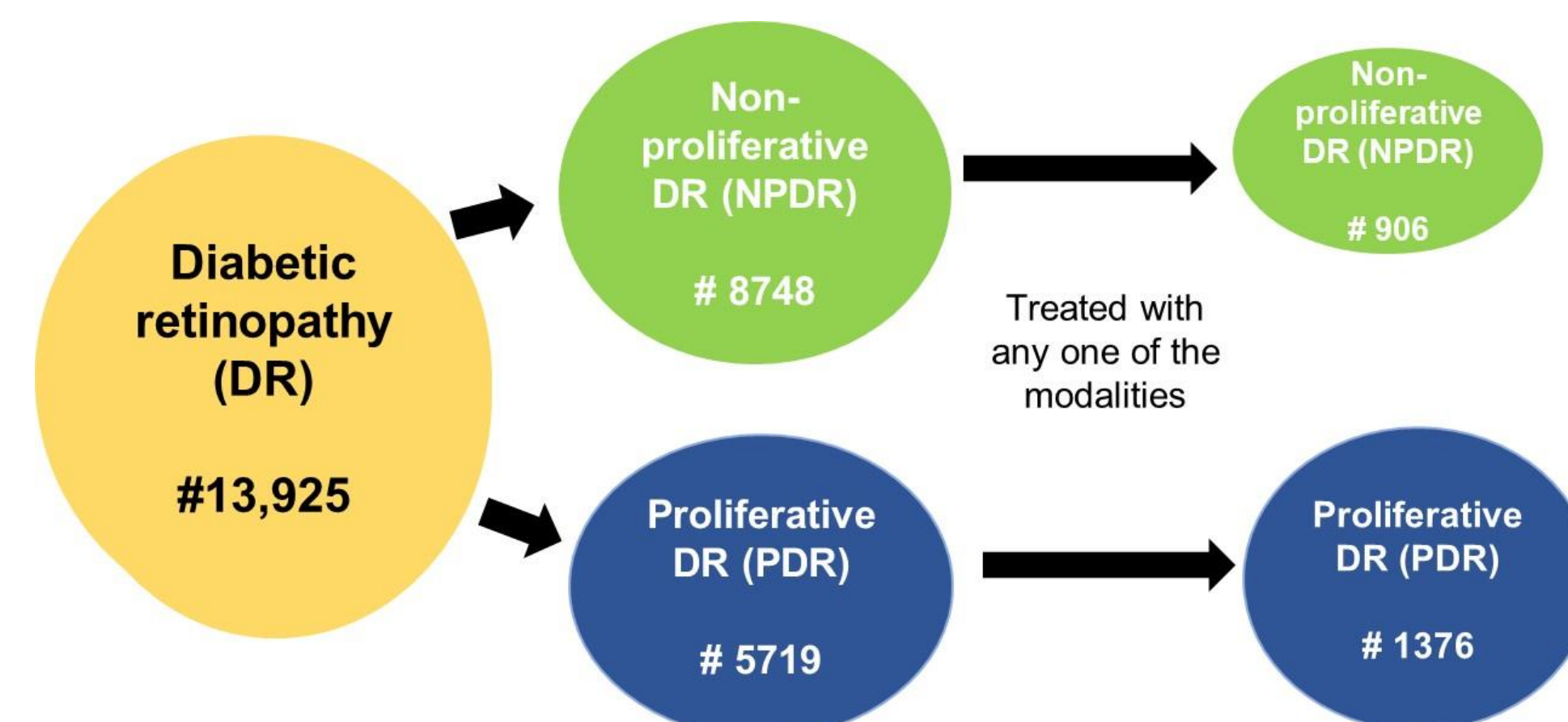


Figure 2: Schematic representation of the data distribution for Diabetic retinopathy and the subclasses for further analysis of drug response and clinical parameters

Cases in Ophthatome with different treatment modalities for Proliferative vs non-proliferative diabetic retinopathy

Table 1 : Treatment and management modalities for Diabetic retinopathy

Different treatment/management modalities for NPDR and PDR
1. Anti-VEGF molecules – Avastin, Lucentis, Accentrix, Razumab
2. Antiinflammatory – Dexamethasone implant (Ozurdex)
3. Corticosteroids – Intra-vitreous triamcinolone acetonide (IVTA)
4. Laser - Pan-retinal photocoagulation (PRP laser)
5. Vitreoretinal (VR) surgery

Table 2 : Number of cases with combination therapy

Combination therapy	No. of cases
Anti-VEGF therapy	178
Ozurdex	80
IVTA	119
PRP laser	8
Vitreoretinal (VR) surgery	55

Table 3 : Number of cases with monotherapy

Mono therapy	No. of cases
Anti-VEGF therapy	581
Ozurdex	34
IVTA	88
PRP laser	18

Table 4 : Number of cases with combination therapy

Combinations of treatments given	No. of cases
Anti-VEGF and IVTA	112
Anti-VEGF and Ozurdex	74
Ozurdex and IVTA	20
Anti-VEGF and PRP laser	7
IVTA and PRP laser	2
Anti-VEGF, Ozurdex, IVTA	14
Anti-VEGF, IVTA, PRP laser	1
Anti-VEGF and VR surgery	46
Ozurdex and VR Surgery	9
IVTA and VR surgery	11
Laser and VR Surgery	3

Table 5: Number of cases with different generics of Anti-VEGF therapeutics

Different generics of Anti-VEGF	No. of cases
Bevacizumab (Avastin)	529
Ranibizumab (Lucentis)	100
Ranibizumab (Accentrix)	86
Ranibizumab biosimilar (Razumab)	27
Anti-VEGF not specified	26

Cohorts of Diabetic retinopathy with various treatment modalities and Other clinical parameters

Combination therapy	No. of cases
Anti-VEGF therapy	231
Ozurdex	44
IVTA	142
PRP laser	78
Vitreoretinal (VR) surgery	379

Combinations of treatments given	No. of cases	Combinations of different anti-VEGF generics	No. of cases
Anti-VEGF and IVTA	132	Avastin and Lucentis	36
Anti-VEGF and Ozurdex	40	Avastin and Accentrix	31
Anti-VEGF and PRP laser	72	Avastin and Razumab	11
Ozurdex and IVTA	11	Avastin and anti-VEGF not specified	17
IVTA and PRP laser	13	Lucentis and Accentrix	15
Anti-VEGF, Ozurdex, IVTA	7	Lucentis and anti-VEGF not specified	7
Anti-VEGF, IVTA, PRP laser	7	Accentrix and Razumab	2
Anti-VEGF and VR surgery	311	Accentrix and anti-VEGF not specified	5
Ozurdex and VR Surgery	12	Razumab and anti-VEGF not specified	3
IVTA and VR surgery	70		
Laser and VR Surgery	65		

Methods

- Data captured from the EMR between September 2012 and January 2018 from two centres of Narayana Nethralaya
- The dataset is from the Indian population and has complete clinical records related to patient demography, disease-specific attributes and treatment information collected during each patient visit.
- The captured data was manually curated, missing data and ambiguities were resolved to preserve data integrity and accuracy by working with the clinician.
- The unstructured diseases diagnosis was reclassified and grouped as per the ICD10 codes.
- The range of expected values for quantitative traits was defined and errors associated with outliers were either rectified or flagged and removed.
- Unstructured data such as personal and family history of systemic diseases and family history of ophthalmic diseases were annotated with structured terminologies.
- These processes have enabled presentation of the data in a web-based portal that allows basic and advanced search functions.

Summary and conclusions

- The Ophthatome™, presents a comprehensive knowledgebase for ophthalmic disease research with manually curated and cleaned clinical and diagnostic images data of over 500,000 cases
- Comprehensive and longitudinal clinical, phenotype and treatment (pharmacological and surgical) data is the key to understand disease phenotypes, sub-phenotypes, progression and prognostics information
- Specific cohort with defined criteria and phenotype details help perform basic and advanced analytics
- The Ophthatome knowledgebase can be used to design genomics and pharmacogenomics and clinical studies to address the unmet needs in this disease space.