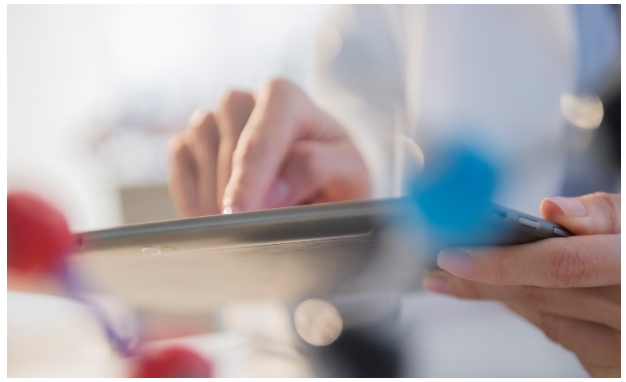

CLINERION
Real World Data Solutions

Re-Imagine Research:
An Introduction to Clinerion

Barış Erdoğan, PhD
Chief Executive Officer

Turkey – Switzerland
2022

Who We Are

CLINERION
Real World Data Solutions

OUR VISION

Imagine faster patient access to medicines and improved health outcomes with Real World Data.

OUR MISSION

We accelerate clinical research and medical access for patients using proprietary technologies for analysis of Real World Data from our global patient network.

- A global technology company headquartered in Basel, Switzerland.
- Built a global health research network.
- Working in deidentified EHR data since 2013.
- Leveraging real-time, real-patient, and real-world data for clinical research and real-world evidence.
- Working with Top 10 CROs and Top 10 pharma companies.
- Proprietary technologies for, *inter alia,* federated network of healthcare databases and re-identification of de-identified patient data.
- As of October 1, 2021, Clinerion is part of Informa Pharma Intelligence.

swiss made software

MADE SWISS

ISO 27001 TRB INTERNATIONAL TÜRKAK Bilgi Güvenliği Y.S. TS EN ISO/IEC 17021-1 AB-0140-YS

ICT CERTIFY ISO 15504-SPICE CERTIFIED

EHR DEVELOPER CODE OF CONDUCT EHRA

STRATUS 2016 AWARD FINALIST

ghp Biotechnology Awards 2020

MEDTECH BREAKTHROUGH AWARD 2020

FIERCE INNOVATION AWARDS Life Sciences Edition 2020 FINALIST Data Analytics/Business Intelligence

CorporateLiveWire SWITZERLAND PRESTIGE AWARDS Clinerion Ltd. 2020 WINNER Best in Medical Data Informatics

Today's Clinical Trials – Industry Benchmarks

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20%

of sites don't enrol any patients[1]

80%

of trials are delayed[2]

50%+

suffer a protocol amendment[3]

To improve these you need a new data-driven approach.

1 Impact Report (2013) Tufts CSDD 15(1)

2 Clinical Trial Delays: America's Patient Recruitment Dilemma (2012). Drugdevelopment-technology.com

3 Impact Report (2016) Tufts CSDD 18(1).

Clinerion Patient Network Explorer

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Clinical Research Applications

Find more patients, faster, than conventional methods, based on real-world medical data.

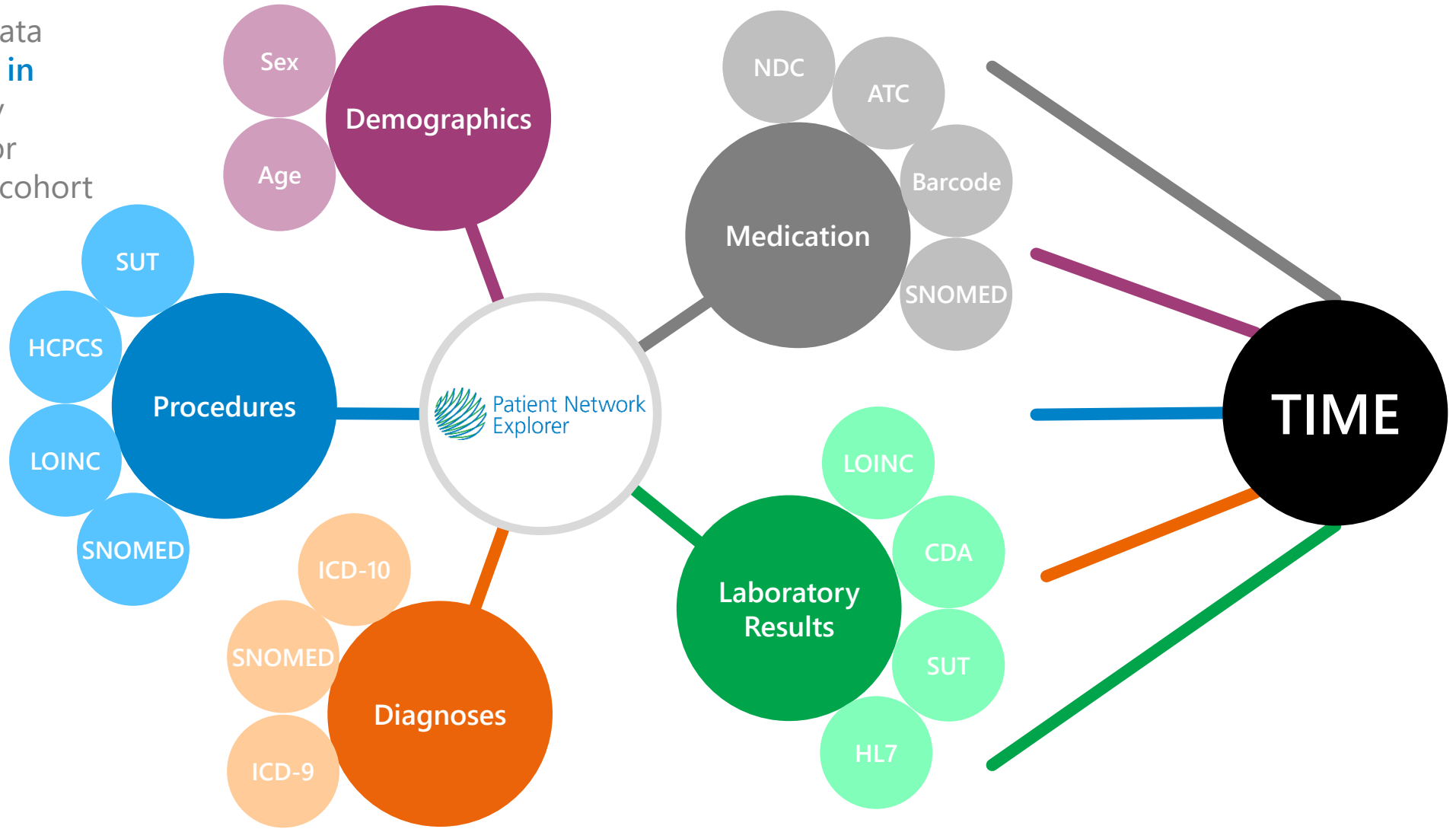
Real-world data-assisted protocol optimization.
Do it right the first time!

Data-driven feasibility evaluation and Site ID.
Select the right sites!

Patient search and re-identification, with 24/7 notification of new, eligible candidates.

Five Dimensions of EHR Data + Time

Clinerion leverages EHR data codes, **longitudinally and in real-time.** Our technology creates a data ontology for query design and patient cohort search.



… but data needs intelligence!

“Privacy by Design” in PNEx ANID Processes

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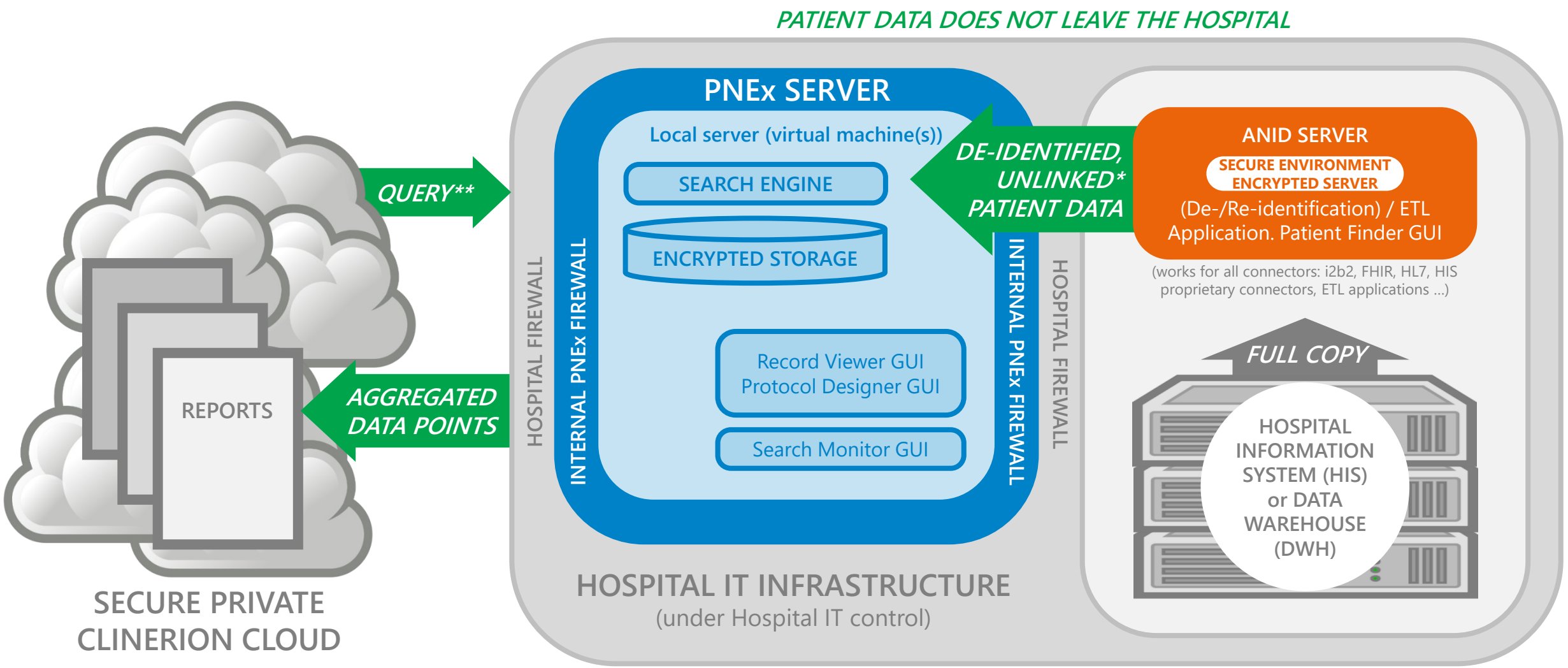
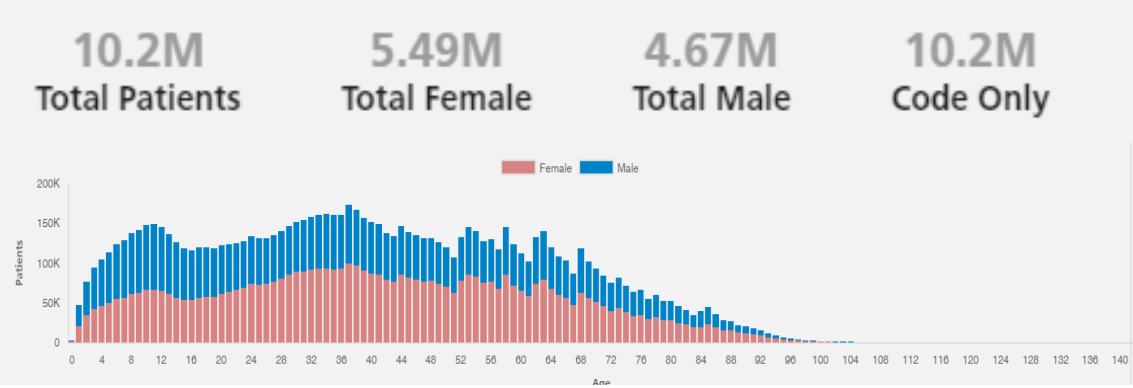


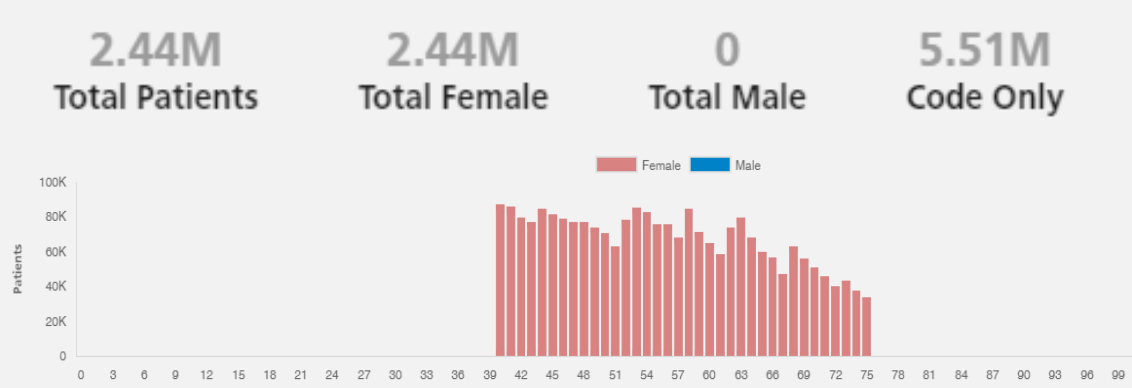
** no pseudonym, unlinked from any database and personal identifiers*
*** queries are downloaded by PNEx Server for processing (no open inbound port)*

Example: Coding a protocol with inclusion / exclusion criteria

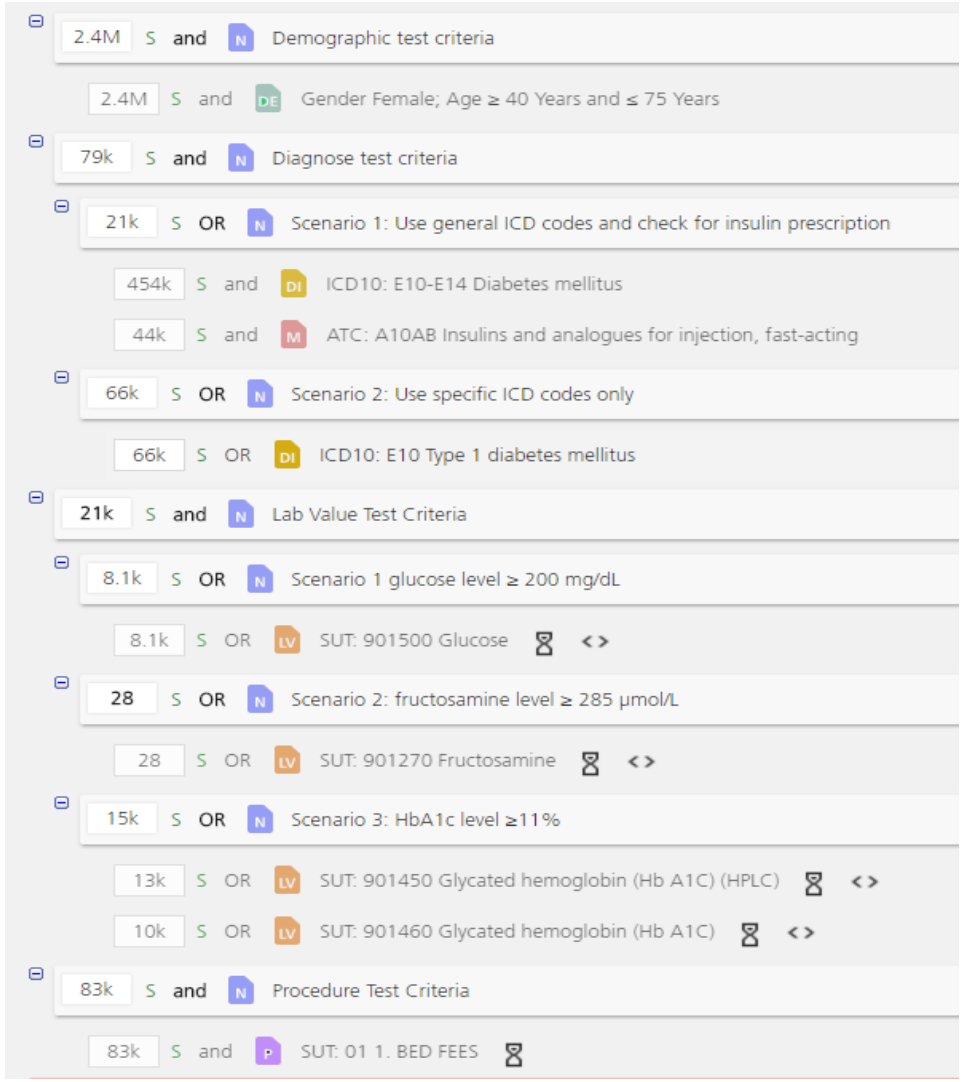
Total patients in the EHR network (16 hospitals)



Female patients aged between 40 and 75



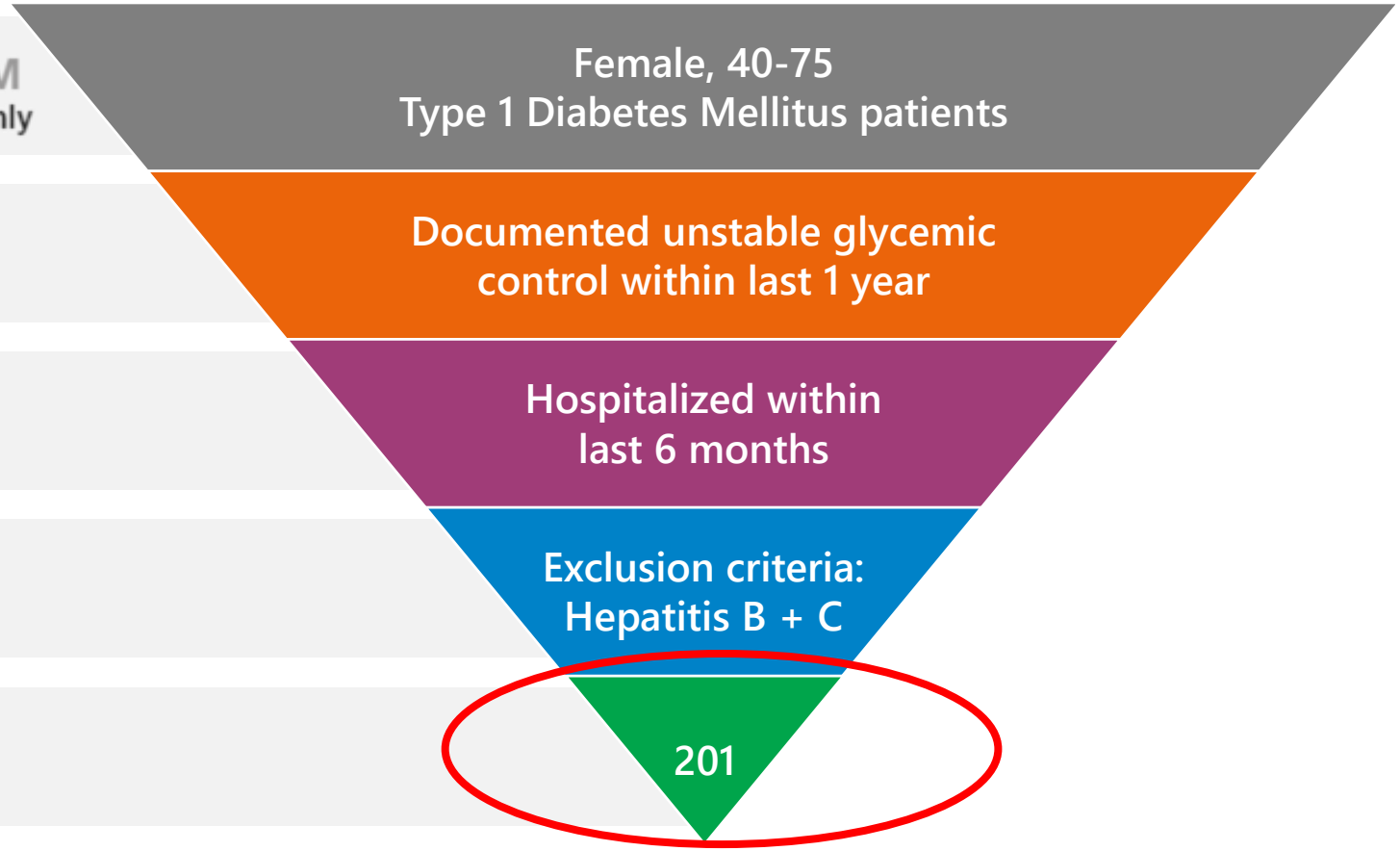
Use general ICD10 codes



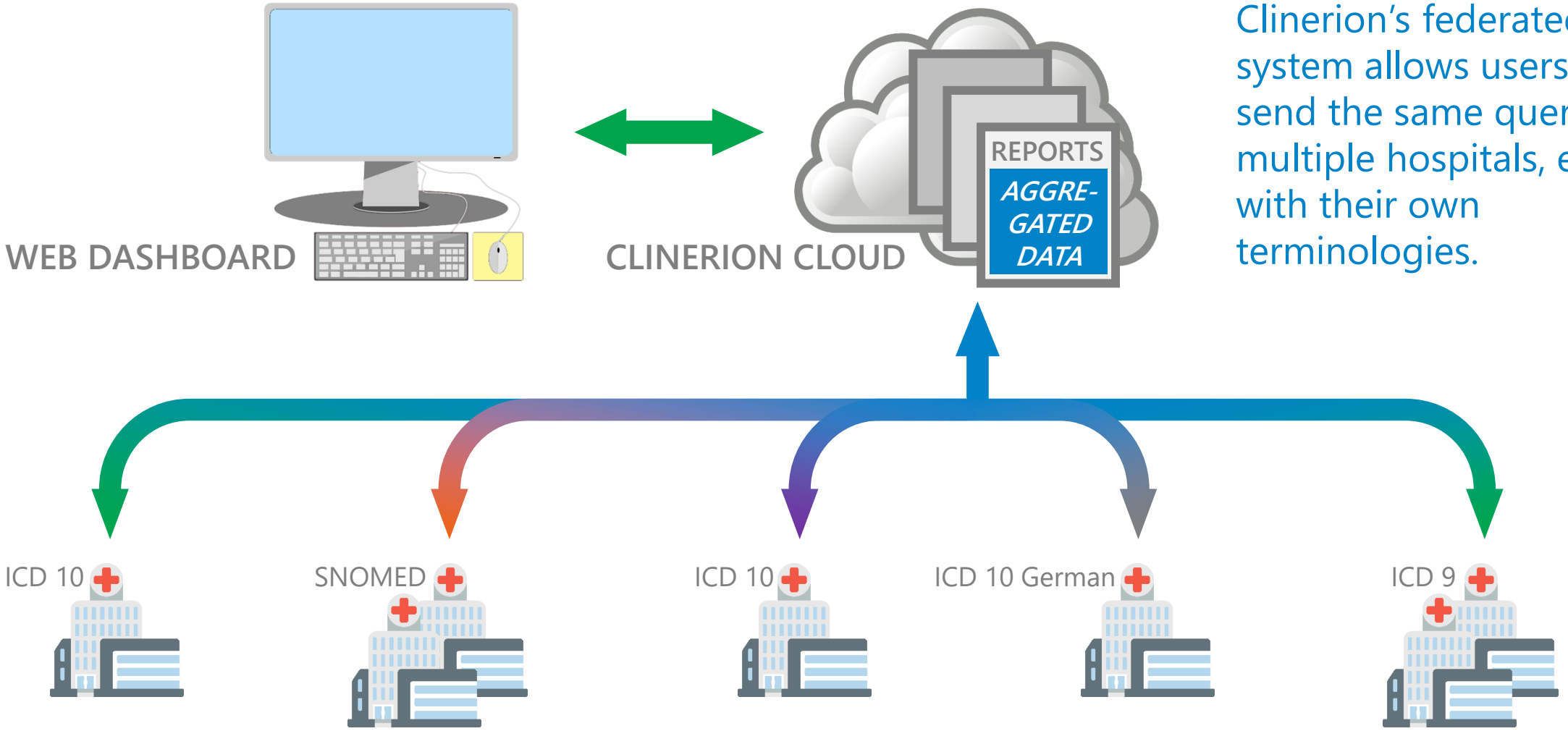
Example: Type 1 Diabetes

Optimal data driven planning and design / feasibility

10.2M Total Patients	5.49M Total Female	4.67M Total Male	10.2M Code Only
2.44M Total Patients	2.44M Total Female	0 Total Male	5.51M Code Only
25.7K Total Patients	25.7K Total Female	0 Total Male	
853 Total Patients	853 Total Female	0 Total Male	
215 Total Patients	215 Total Female	0 Total Male	
201 Total Patients	201 Total Female	0 Total Male	



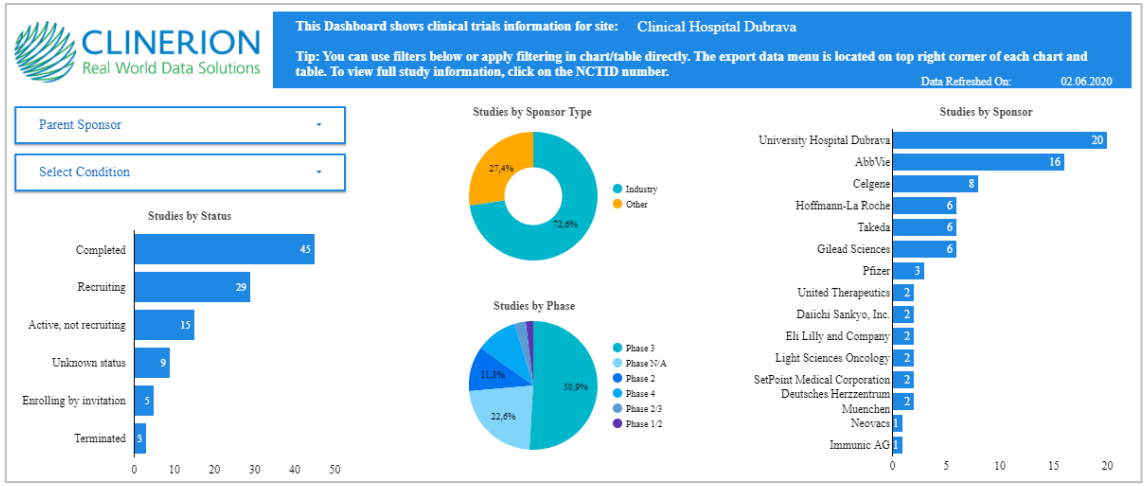
Clinerion Patient Network Explorer Architecture



Clinerion's federated system allows users to send the same query to multiple hospitals, each with their own terminologies.

Site Clinical Trial Performance Data

Current and historical clinical trial performance data for all partner hospitals and trial sites in Clinerion's worldwide patient network, in collaboration with LongTaal.

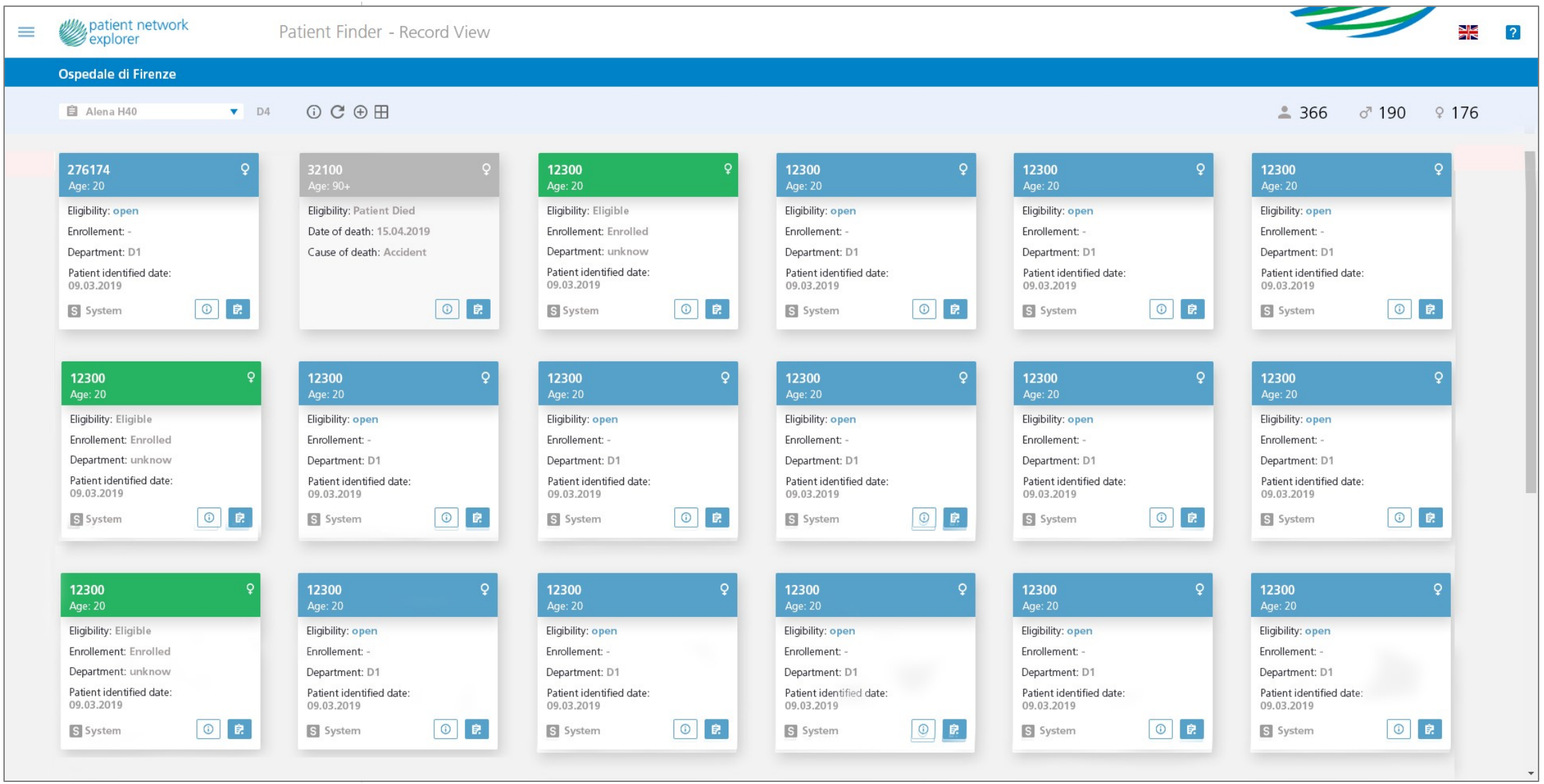


NCTID (link)	Brief Title	Parent Sponsor	Study Status	Conditions (MESH)	Interventions (MESH)	Study Phase	Global Countries / Sites / Enrollment	Start Date	Completion Date
NCT04191408	Predictive Ability of PEEP Induced Changes in CVP to Predict Volume Responsiveness in Mechanically Ventilated Patients After Major Abdominal Surgery	University Hospital Dubrava	Recruiting	Cardiac Output, Low | Critical Illness | Surgery	PEEP increase	Phase N/A	1 / 1 / 60	2019-11-01	2020-02-01
NCT03683186	A Study Evaluating the Long-Term Efficacy and Safety of Ralinepag in Subjects With PAH Via an Open-Label Extension	United Therapeutics	Enrolling by invitation	Cardiovascular Diseases | Connective Tissue Diseases | Familial Primary Pulmonary Hypertension | Hypertension | Hypertension, Pulmonary | Lung Diseases | PAH | Respiratory Tract Diseases | Vascular Diseases	Ralinepag	Phase 3	20 / 115 / 1000	2019-09-23	2024-09-01
NCT03843125	A Study of Baricitinib in Participants With Systemic Lupus Erythematosus (SLE)	Eli Lilly and Company	Recruiting	Lupus Erythematosus, Discoid	Baricitinib	Phase 3	32 / 363 / 1100	2019-09-09	2024-06-30
NCT04032158	Study of Evobrutinib in Participants With Relapsing Multiple Sclerosis (RMS)	EMD Serono	Recruiting	Multiple Sclerosis	Avonex® | Evobrutinib | Placebo	Phase 3	26 / 206 / 950	2019-08-26	2026-10-26
NCT03945188	Etrasimod Versus Placebo for the Treatment of Moderately to Severely Active Ulcerative Colitis	Arena Pharmaceuticals	Recruiting	Colitis, Ulcerative	Etrasimod | Placebo	Phase 3	36 / 302 / 372	2019-06-13	2021-11-01
NCT04004156	Safety Study for An Artificial Disc Replacement to Treat Chronic Low Back Pain	Spinal Stabilization Technologies	Recruiting	Degenerative Disc Disease | Low Back Pain	PerQdisc® Nucleus Replacement Device.	Phase N/A	4 / 4 / 15	2019-03-01	2021-12-31
NCT04083313	Analysis of Endoloops, Endostaples and Endoclips for Closing the Appendiceal Stump During Laparoscopic Appendectomy	University Hospital Dubrava	Completed	Appendicitis | Surgery	Technique used for closing the appendiceal stump	Phase N/A	1 / 1 / 300	2019-01-01	2020-03-15

1 - 106 / 106

- Allows for browsing, filtering, reviewing, and comparing site trial performance statistics.
- Breakdowns on studies by sponsor, by condition, by trial phase and by recruitment status.
- Filter by study status, sponsor, phase, or condition to obtain a list of the respective studies.
- Provides more information, such as on other locations where the study is being conducted
- Derived and mapped from multiple public sources.

Patient Finder – Record Viewer View



Record Viewer behind the Firewall: secure and confidential

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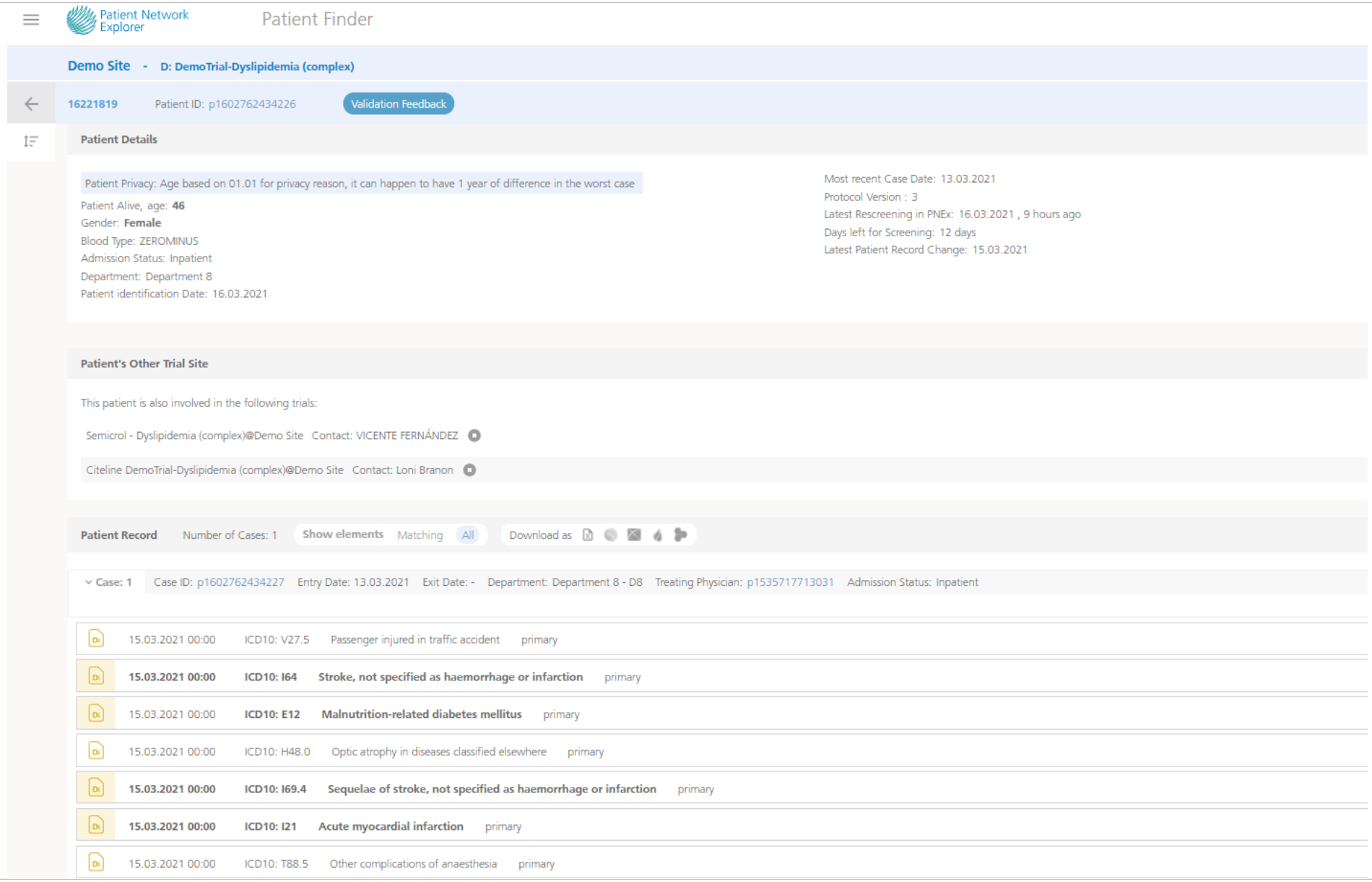
Authorized hospital staff retrieve records corresponding to query matches.

Downloads are enabled either from identified or de-identified patient records (*depending on staff access privileges and patient consent*).

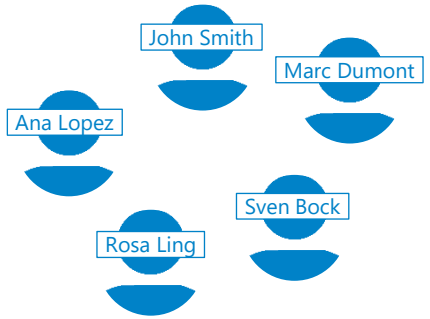


NEW Anonymized Identification (ANID) Technology

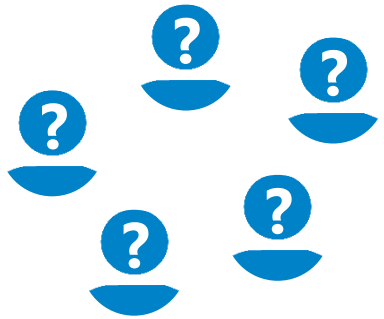
How does it work?

1. **Patient records are anonymized and then synchronized to a separate server inside hospital's infrastructure.**

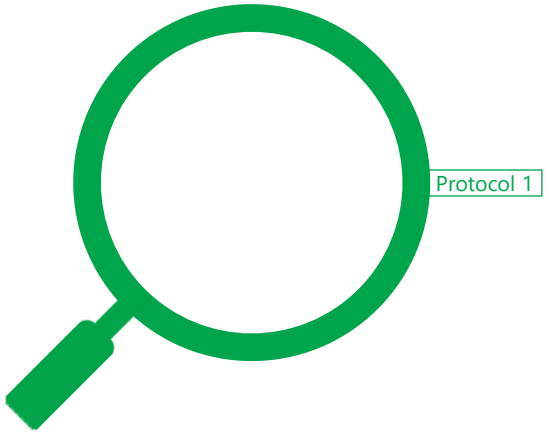
Original hospital patient records



Anonymized patient records



2. **Query is created in Clinerion cloud based on protocol parameters**

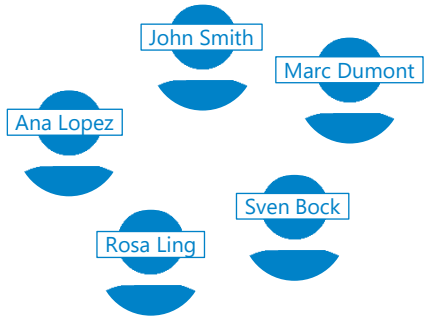


NEW Anonymized Identification (ANID) Technology

How does it work?

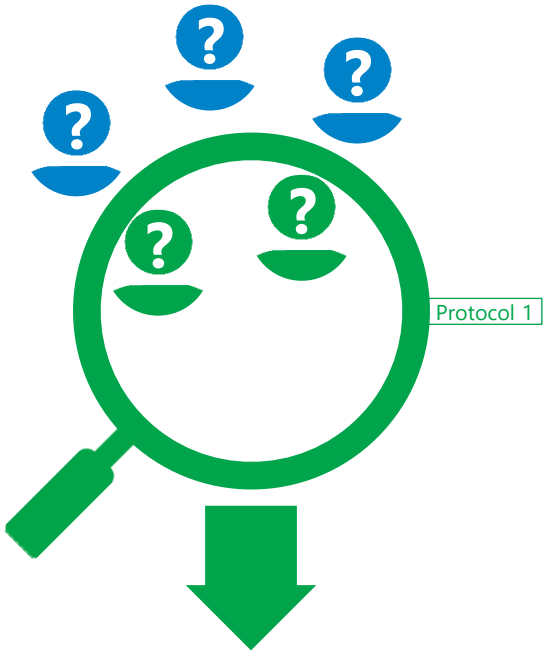
3. Clinerion user sends query to all local sites which allow queries. Query runs on the anonymized patient data to evaluate number and location of eligible candidates.

Original hospital patient records



ANONYMIZED

Anonymized patient records



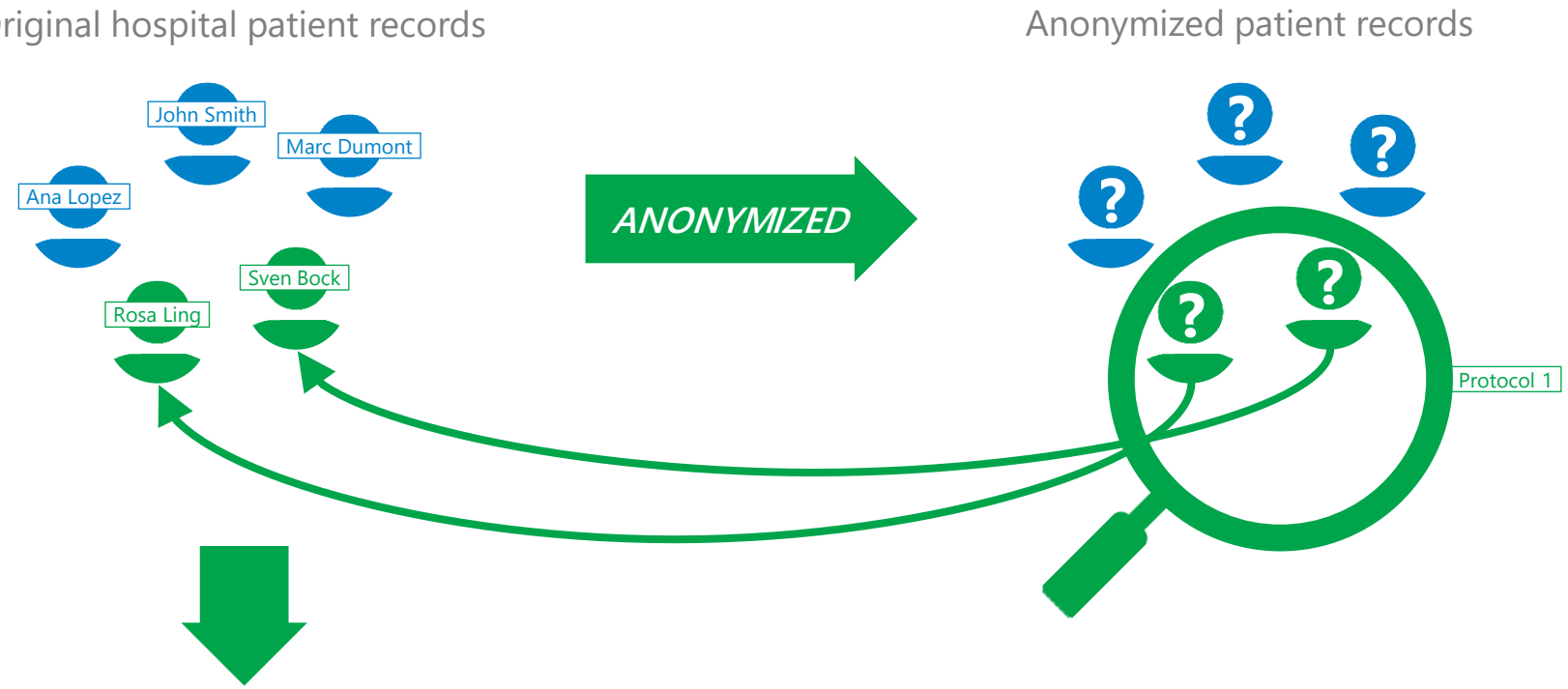
4. Query returns a COUNT of patients matching the protocol criteria at each site which has allowed its database to be queried.

Two matches seen by Clinerion user

NEW Anonymized Identification (ANID) Technology

How does it work?

5. Query is sent back to the individual hospital. Authorized hospital staff at the hospital run the query again on their own local anonymized database.



Two matching patients are IDENTIFIED.

6. Query results are matched locally by authorized hospital staff.

Clinerion Patient Network Explorer

Real-World Evidence Applications

You give us your questions, we give you real-world answers

Late phase studies. Prospective and retrospective.

Post-marketing surveillance – monitor efficacy, safety and personalized outcomes.

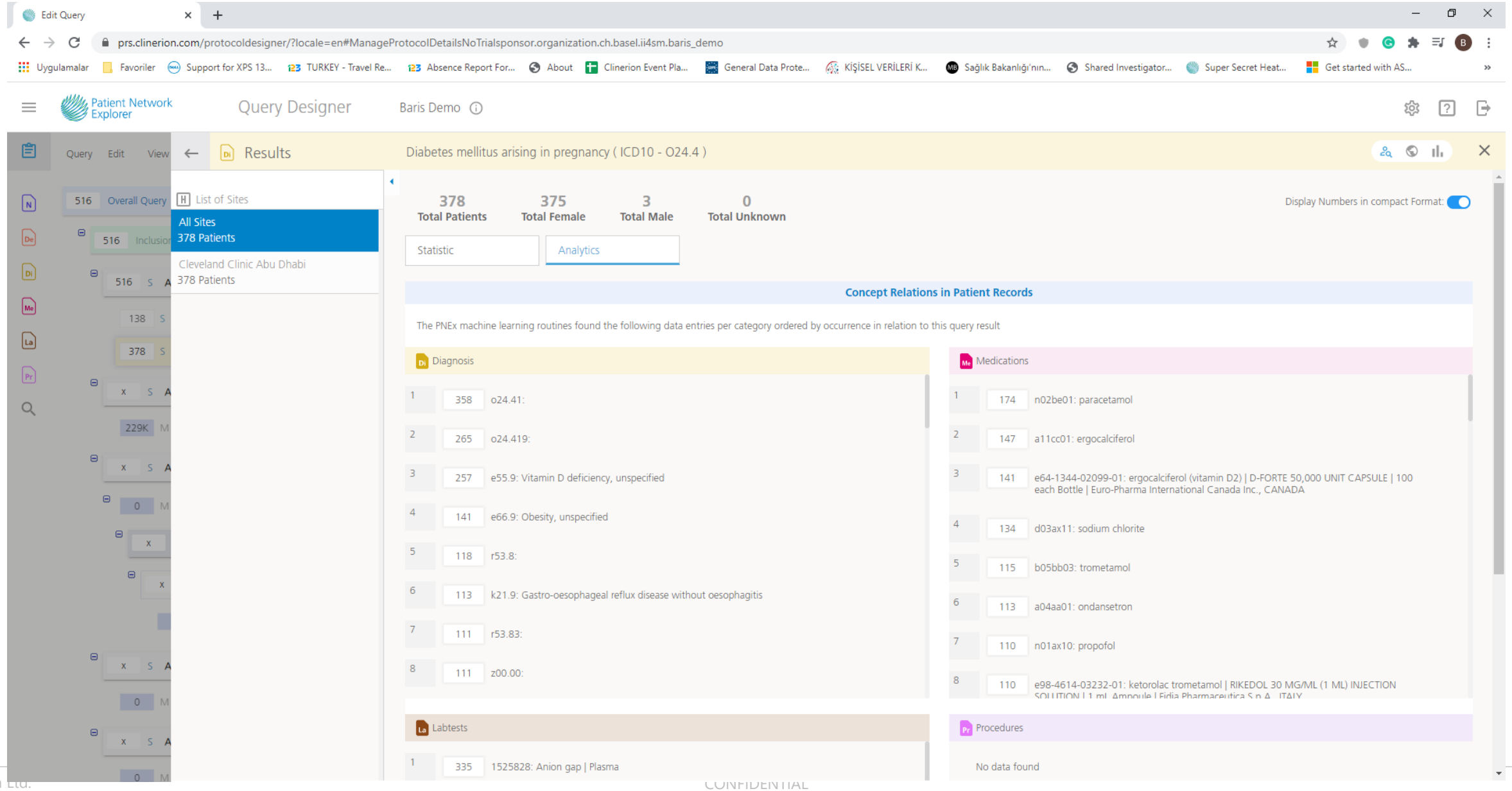
Prevalence queries and patient journey analysis

Ensures that all patients who could benefit get access to a drug at the right price.

Planning of how the drug fits into the market.

PNEx Analytics

CLINERION
Real World Data Solutions



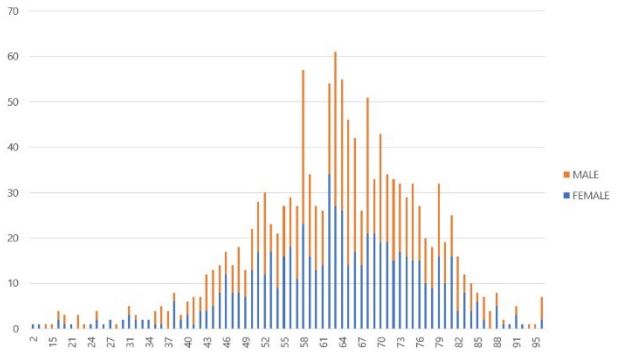
Real World Insights – Example

Turkey 2018 Multiple Myeloma

Clinerion's Patient Network Explorer offers indication-agnostic access to live, real-world, anonymized, aggregate EMR data of its partner hospitals.

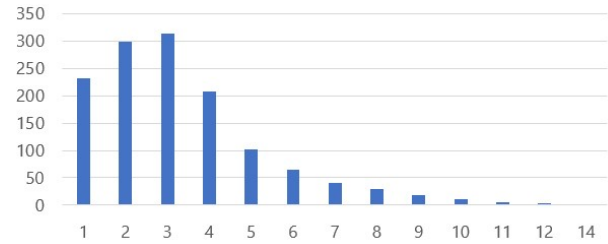
In this example, the Patient Network Explorer was used to develop multiple myeloma Charlson comorbidity scores and co-treatment regime models.

Identified patients in Turkey with multiple myeloma with first diagnosis in 2018 were evaluated on:	
Query Date:	17-Jan-2020
Query Type:	– ICD10: C90.0 – Multiple myeloma – First diagnosis in 2018
Sample Size:	1,330 patients matching query
Country incidence 2018:	2,331
5-year prevalence:	5,432 Patients (prop. 6,63)*
# of Clinics:	13
Clinic Types:	Teaching Hospitals
Total Patients:	13,286,251
Turkey 2018 population:	81,916,866



At baseline event (first diagnosis with multiple myeloma):

Patients ≤65 years	751
Patients 65–75 years	355
Patients >75 years	217
Median Age	66
Standard Deviation	13



Charlson Score	# of Patients
1 Point	231
2 Points	299
3 Points	314
4 Points	207
5 Points	102
6 Points	65
7 Points	41
8 Points	30
9 Points	19
10 Points	12
11 Points	6
12 Points	3
14 Points	1

Real World Insights – Example

CLINERION
Real World Data Solutions

Turkey 2018 Multiple Myeloma

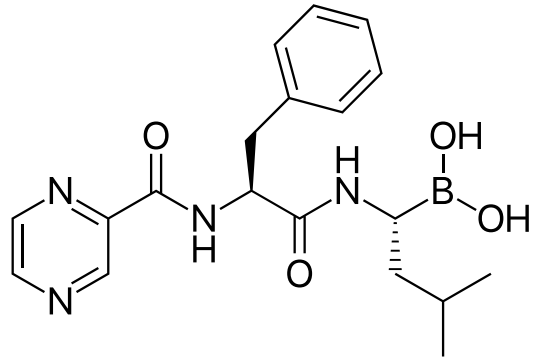
Clinerion's Patient Network Explorer offers indication-agnostic access to live, real-world, anonymized, aggregate EMR data of its partner hospitals.

In this example, the Patient Network Explorer was used to develop multiple myeloma Charlson comorbidity scores and co-treatment regimen models.

Administered Therapeutics

Sodium Chloride	400	30.23%
Bortezomib	393	29.71%
Paracetamol	273	20.63%
Pantoprazole	267	20.18%
Dexamethasone	241	18.22%
Methylprednisolone	224	16.93%
Pheniramine	207	15.65%
Carbohydrates	189	14.29%
Granisetron	189	14.29%
Prilocaine	188	14.21%
Ranitidine	175	13.23%
Cyclophosphamide	171	12.93%
Potassium Chloride	144	10.88%
Zoledronic Acid	143	10.81%
Enoxaparin	131	9.90%
Electrolytes With Carbohydrates	130	9.83%
Furosemide	122	9.22%
Piperacillin And Beta-Lactamase Inhibitor	119	8.99%
Fluconazole	115	8.69%
Heparin	107	8.09%
Tramadol	106	8.01%
Ondansetron	106	8.01%
Meropenem	103	7.79%
Valaciclovir	99	7.48%
Allopurinol	94	7.11%
Sulfamethoxazole And Trimethoprim	92	6.95%
Magnesium Sulfate	92	6.95%
Benzydamine	87	6.58%
Salbutamol And Ipratropium Bromide	87	6.58%
Ceftriaxone	85	6.42%

Bortezomib Treatment Regimens



Criteria	#patients	%patients
Patients In Cohort	1330	
Regimen 0 // Bortezomib	393	29.55%
Regimen 1 // Bortezomib AND Dexamethasone +/- (additional)	341	25.64%
Regimen 1.1 // Bortezomib AND Dexamethasone	66	4.96%
Regimen 2 // Bortezomib AND Dexamethasone AND Cyclophosphamide	225	16.92%
Regimen 3 // Bortezomib AND Dexamethasone AND Doxorubicine	17	1.28%
Regimen 4 // Bortezomib AND Dexamethasone AND Revlimid (Lenalidomide)	33	2.48%
Regimen 5 // Bortezomib AND Prednisone AND Melphalan	2	0.15%
Regimen 6 // Bortezomib AND Prednisone AND Thalidomide	3	0.23%
Regimen 7 // Bortezomib AND Prednisone AND Thalidomid AND Daratumumab	0	0.00%
Regimen 8 // Bortezomib AND Bendamustin	7	0.53%

Clinerion Patient Network Explorer on Rare Diseases

Using Patient Network Explorer for rare disease patient enrichment

Multiple projects use Patient Network Explorer to identify potential rare disease patients and flag them for hospital outreach, testing and appropriate treatment. (Turkey) ⇨ Enrichment at 10 to 15%.

- POMPE
- Gaucher
- Fabry
- MPS1
- Rare Disease Top N treatments and co-conditions

- Phase 1: Adapting existing cohort model inclusion and exclusion parameters into PNEx query builder and refining query with sponsor for multiple sites, multiple diseases
- Phase 2: Study implementation at multiple sites, patient identification, outreach, recruitment, testing and diagnosis

Ongoing Developments at Clinerion: AI/ML

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Swiss Confederation

Innosuisse – Swiss Innovation Agency

Online Application

Application Number: 42089.1 IP-LS

Application Title: PPML-Health: A Privacy-Preserving Machine Learning Infrastructure for Health Research

Main partners and project manager

Project manager	Dr Bernhard Bodenmann Clinerion LTD
Main research partner	Dr Ulrich Fiedler Berner Fachhochschule, BFH
Main implementation partner	Dr Bernhard Bodenmann Clinerion LTD

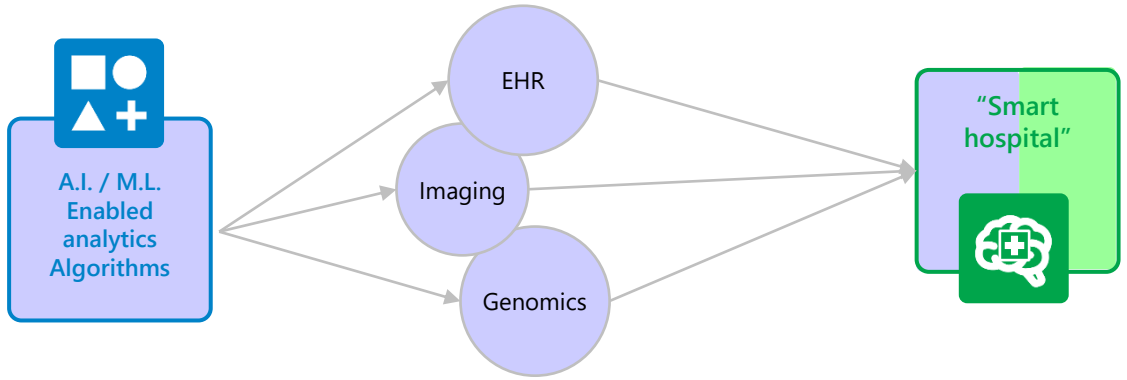
General information

Application title	PPML-Health: A Privacy-Preserving Machine Learning Infrastructure for Health Research
Application title EN	PPML-Health: A Privacy-Preserving Machine Learning Infrastructure for Health Research
Abstract	Clinerion's Patient Network Explorer (PNEX) is a global health record system allowing for the privacy-preserving aggregation of patient information across hospitals. This proposal extends PNEX's capabilities beyond information aggregation towards cutting-edge federated machine-learning capabilities.
Planned project start	01.11.2020
Duration in months	18
Planned project end	01.05.2022
Subgroup of Innovation Council	Life Sciences

Artificial Intelligence Infrastructure:

Together with an academic consortia, Clinerion has been recently been awarded an grant from Innosuisse (Swiss Innovation Agency) to implement the infrastructure for deployment of A.I./M.L algorithms for the analysis of clinical data without the need for the extraction of the underlying record or data kind.

Clinerion is creating a consortia of hospitals for the deployment of this technology and you are welcome to join us and design your specific needs (e.g. AI assisted patient diagnosis) and other bespoke use cases.



Patient Network Explorer (PNEx) Architecture

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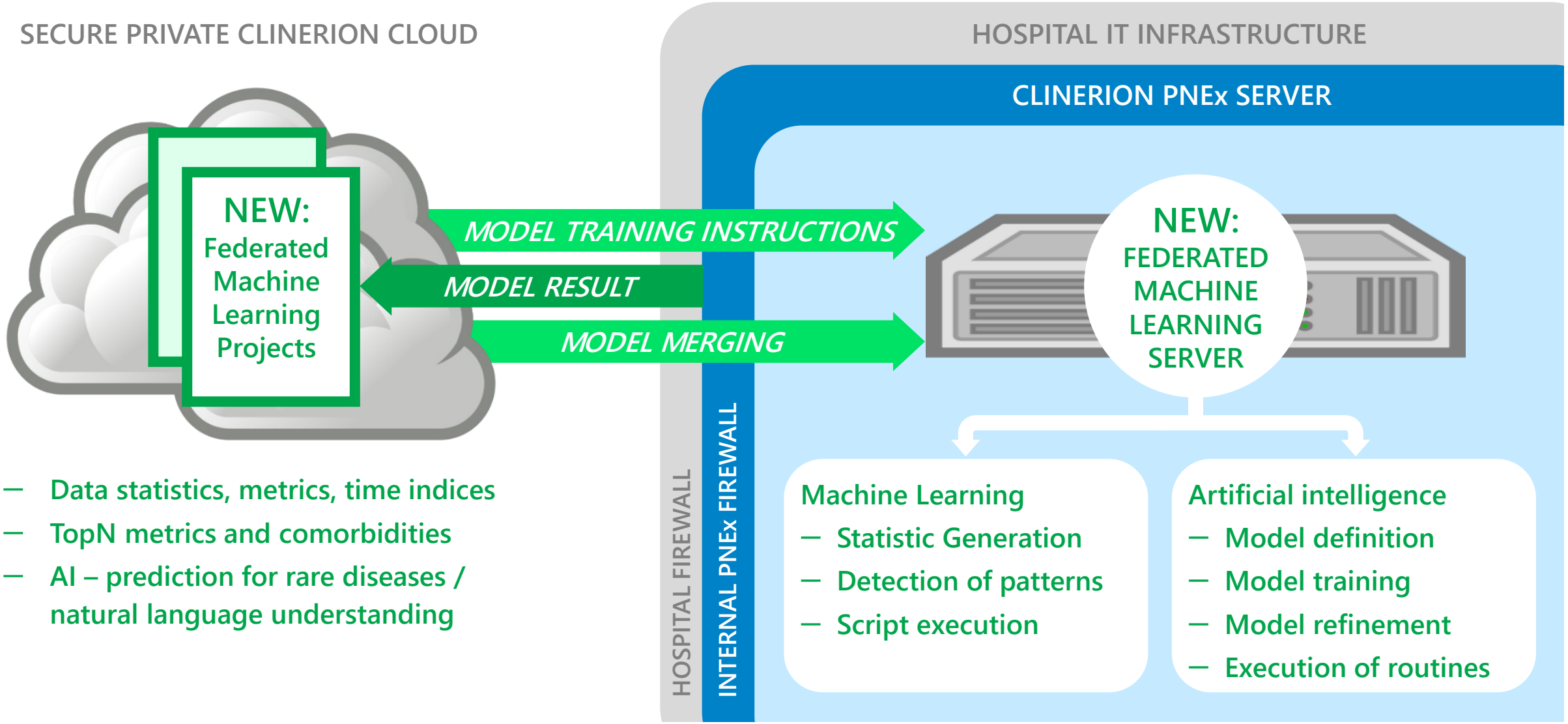

- Data statistics, metrics, time indices
- TopN metrics and comorbidities
- AI – prediction for rare diseases / natural language understanding

Patient Network Explorer: the Ultimate Solution for Hospitals

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- Manage and visualize EHR data
- Access a global network
- de-identified cohort data extracts for RWD analytics
- Gain sponsor / academic awareness of expertise & care standards.
- Cohort search & patient identification
- Development of new data analytics technologies

→ Better patient care

→ Align expectations with incoming clinical trials

→ More research collaboration

→ More efficient performance of site

→ More Scientific Publications

→ "Smart hospital"

Clinerion Global Research Network

CLINERION
Real World Data Solutions

LIVE
(online, in real-time):
248.8 M
Patients

TOTAL CONTRACTED:
264.3 M Patients
@ 300+ Sites

PLUS
est. 200 M Patients
via external
data partners

Europe, Middle East and Africa

35.6 M

Hospitals

FRANCE	SWITZERLAND	SWITZERLAND	GREECE	GREECE	GREECE	GREECE	SPAIN	ARMENIA	
BULGARIA	CROATIA	CROATIA	CROATIA	ESTONIA	ESTONIA	GEORGIA	GEORGIA	GEORGIA	
GEORGIA	HUNGARY	HUNGARY	HUNGARY	HUNGARY	HUNGARY	POLAND	POLAND	ROMANIA	
SAUDI ARABIA	SAUDI ARABIA	SAUDI ARABIA	SAUDI ARABIA	SAUDI ARABIA	SAUDI ARABIA	SAUDI ARABIA	SERBIA	SERBIA	
TURKEY	TURKEY	TURKEY	TURKEY	TURKEY	TURKEY	UKRAINE	UKRAINE	U.A.E.	

External Data Sources

GERMANY
FRANCE
FRANCE
EUROPE
EUROPE

Americas

213.1 M

Hospitals

ARGENTINA	BRAZIL	BRAZIL	BRAZIL	BRAZIL	BRAZIL
BRAZIL	BRAZIL	BRAZIL	BRAZIL	BRAZIL	BRAZIL
BRAZIL	BRAZIL	BRAZIL	BRAZIL	BRAZIL	BRAZIL
BRAZIL	BRAZIL	BRAZIL	BRAZIL	BRAZIL	BRAZIL
BRAZIL	BRAZIL	BRAZIL	BRAZIL	BRAZIL	BRAZIL
BRAZIL	BRAZIL	BRAZIL	COLOMBIA	COLOMBIA	URUGUAY

External Data Sources

BRAZIL
BRAZIL
BRAZIL
BRAZIL
BRAZIL

Asia-Pacific

0.1 M

Hospitals

INDIA
INDIA
TAIWAN R.O.C.
SOUTH KOREA

External Data Sources

INDIA
JAPAN
SOUTH KOREA
SOUTH KOREA

Thank you

CLINERION
Real World Data Solutions

www.clinerion.com

Baris.Erdogan@clinerion.com