EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

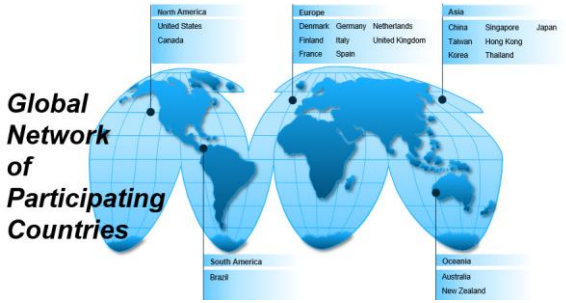
EUCOPE

HMA-EMA Data standards workshop

18th May 2021

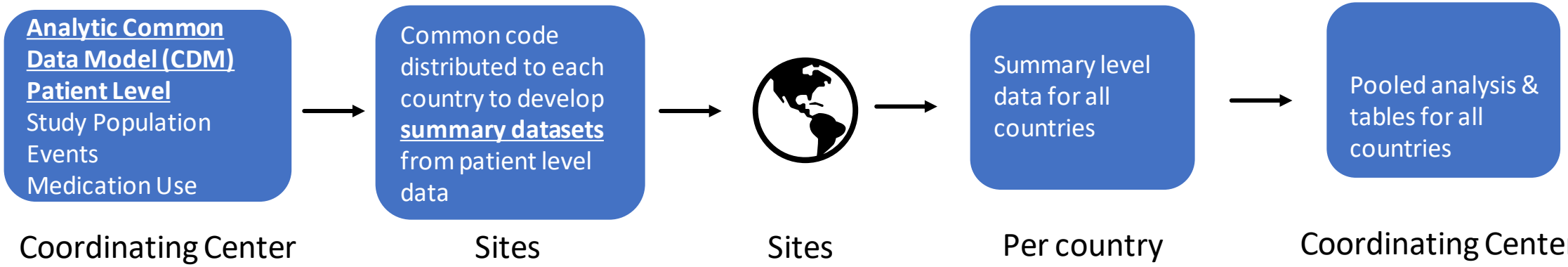
Mats Ericson (Amgen), Todd Case (Vertex)

Global Hip Fracture Study



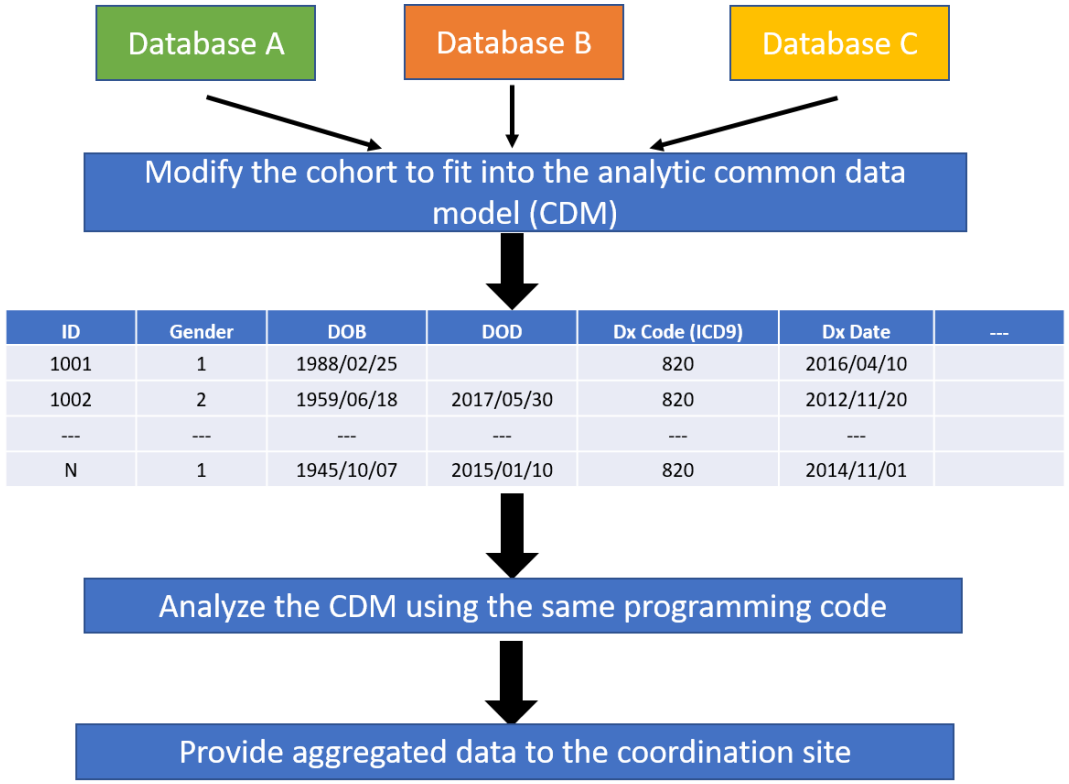
EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

- **Conducted by Amgen 2015-2018 (publication pending; citation can be shared once available)**
- **Hip fractures surrogate for disease burden;** loss of functional independence (30-50%); mortality (20-40%)
  - Generally undertreated but global incidence variation and divergent temporal trends
  - Cross-geographical comparisons of longitudinal data – insights to aetiology, risk factors, effectiveness of healthcare practices
- **Choice of distributed model for network analysis**
  - Standardised methodology applied to large EHR databases, one master protocol, one coordinating centre
  - Single program was used to create summary data in an analytic common data model from patient level data per country



Common Data Model

- **Sources of Heterogeneity**
  - *Coding to identify hip fractures (ICD-9 vs. ICD-10 vs county-specific)*
  - *Coding to identify pharmacological treatments (country specific vs WHO Anatomical Therapeutic Chemical Classification System)*
  - *Practice of medicine (e.g., criteria for admission, available therapies, how reimbursed that can affect coding)*
- **Approach to address Heterogeneity**
  - More limited study scope – Hip fracture only
  - Use of common protocol
  - Use of analytic common data model (CDM)
  - **Sites used their expertise to populate the same data template and follow standard instructions across all sites for how to check for completeness, handle impossible values, and how to report missing values (standardization)**
  - Single analytical program provided by the coordinating center (quality control)



Challenges & Lessons Learnt

- **Have an Statistical Analysis Plan (SAP) with complete, accurate and clear diagnosis/medication codes available as early as possible**
  - Develop the SAP in tandem with the study protocol
  - Table shells are very important to have so programmers can interpret language provided in the SAP
  - **Clearly defined concepts, e.g. what is a hospitalization for hip fracture? Since care settings and definitions can vary by country, clarity on what defines a concept is critical.**

- **Multi-site studies**
  - Data collection methods vary by country (i.e., some countries will have only population level denominator data, not individual level)
  - Site-specific SAP is necessary as data structure, data elements..etc can be different across sites
  - Phased approach: US, EU, and Hong Kong had known data to work with, JAPAC & other countries do not (logistical reasons).
  - Provide programs in different programming languages

Use of Natural History Studies as a Reference arm for Late Phase Clinical Trials

Historical control: not a new concept

Compared to a different group of people with similar situation treated in a different manner – **Historical Control**

Or compared to the same group of people previously untreated – **Self-control**

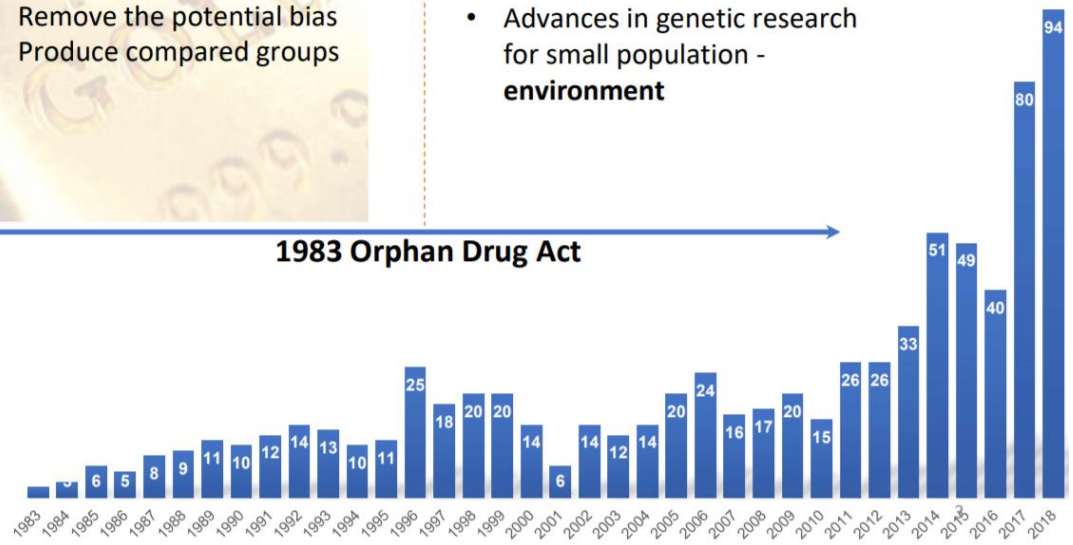
Randomized clinical trial was widely recognized.

Gold standard of clinical trial
- Remove the potential bias
- Produce compared groups

Back to "historical control" ?
- Accessibility to massive historical data - **resources**
- Advances in genetic research for small population - **environment**

1950 **1983 Orphan Drug Act**

Number of Orphan Indications Approved in the United States 1983–2018:



Source: FDA. Search Orphan Drug Designations and Approvals. Available from: https://www.accessdata.fda.gov/scripts/opdlisting/oopd/

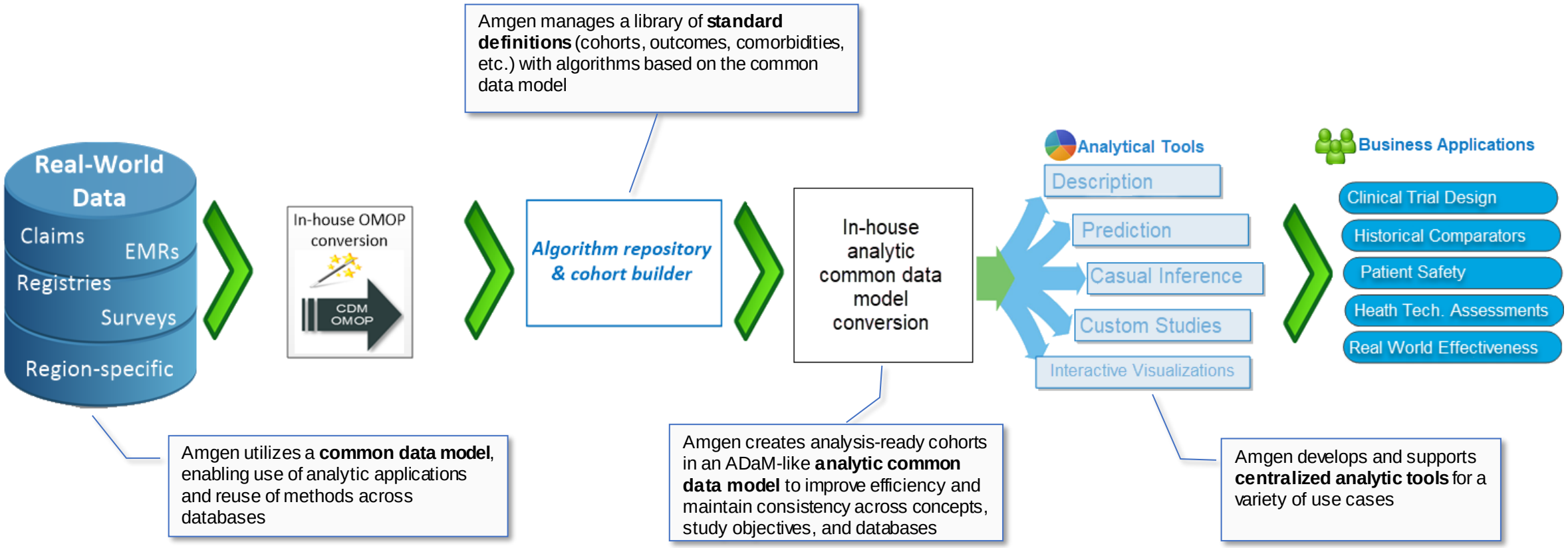
In ultra rare populations where the data from every single patient is highly valued, use of placebo/control is a high luxury, particularly when the course of the disease is predictable and the expected treatment effect is transformative. However, the use of standard data is often not possible and thus the need to find acceptable formats for regulatory required data is critical.

2020 ASA Biopharmaceutical Section Regulatory-Industry Statistics Workshop Ziliang Li, Chenkun Wang Vertex Pharmaceuticals Inc.

Back-Up

A Platform Connects Data Ingestion, Evaluation and Curation to Suite of Analytics

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL



Standardized ingestion and curation process enables a platform that can support enterprise RWE generation