

CRITICAL PATH INSTITUTE

BIOMARKERS PROGRAM WORKSHOP 2019

Solutions to Drug Development Challenges: Utilizing Quantitative Approaches, Data Sharing, and Novel Biomarkers





Converting Data Into Knowledge

Bridging the Gap – Amanda Borens

Bridging the Gap



- How do we transform data → information?
Especially when we have **minimal data**?
Or when we are **inundated with data**?
- Two Case Studies:
Alzheimer's Disease, biomarkers, and longitudinal data
Tuberculosis, ReSeqWHO, and genomics data



Alzheimer's Disease– *AD Interoperability*

➤ **Research Question:**

“Which longitudinal biomarkers are related to specific clinically-relevant measures of progression and drug effects, at specific disease stages?”

➤ **Data challenge:**

- Combine data from **disparate platforms** to answer question
- No common **data dictionary** or data model
- Create **data marts on demand**

Combining Disparate Data Sets

Combining data from different studies is *more than mapping variables*

Clinical Trial #1

SUBJID	SEX
0001	M
0002	F
0003	F
0004	M
0005	F

Observational Study

ID	GENDER
A1	Male
A2	Male
A3	Female
A4	Female
A5	Male

Pre-clinical Trial #2

USUBID	SEX
00011	0
00012	1
00013	1
00014	0
00015	1

EHR records

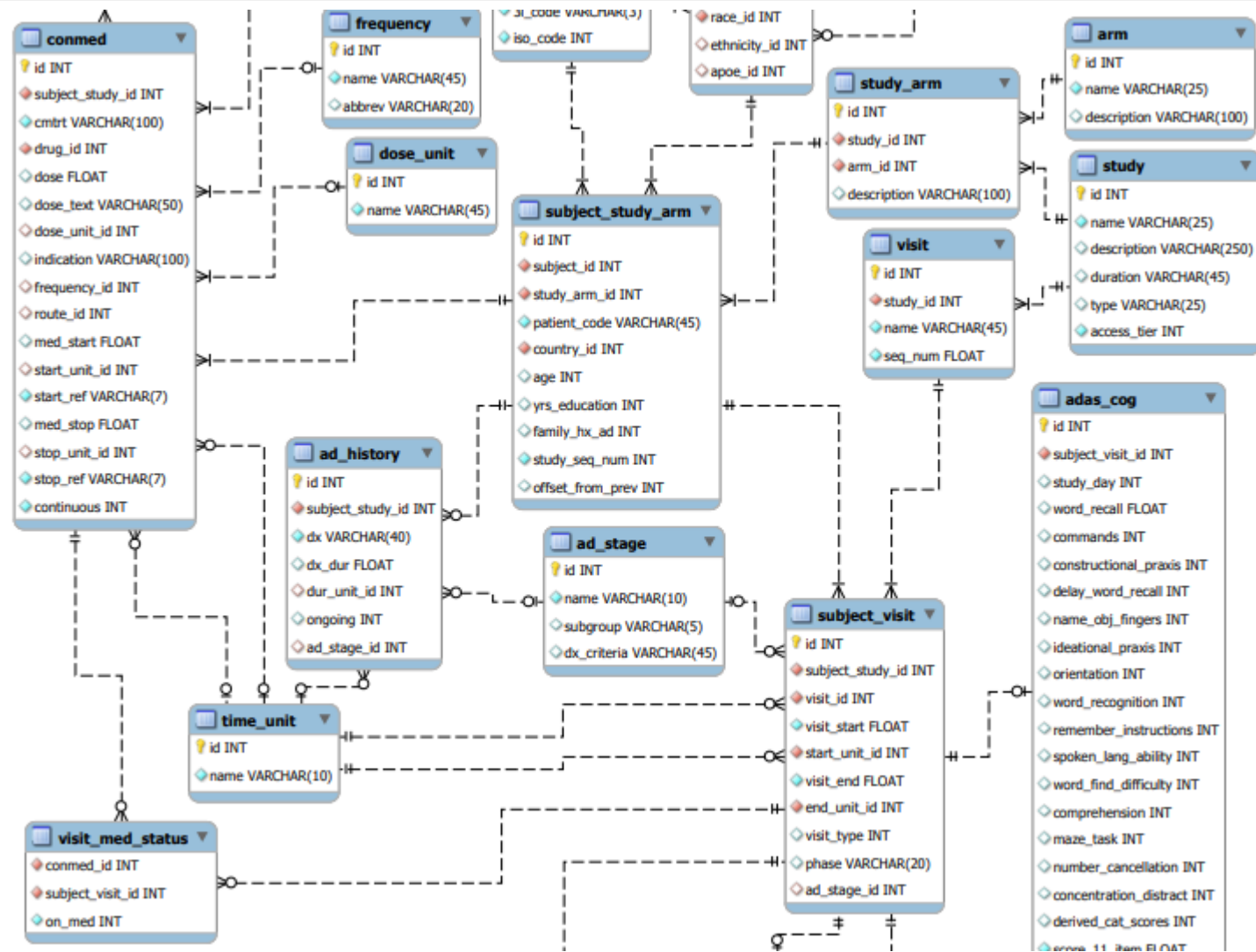
PTID	GENDER
0001	1
0002	1
0003	2
0004	2
0005	1

Standardizing **dates** (eg. medications) **can be a quagmire**

Ranges, start only, month only, year only....

Alzheimer's Disease

- CPAD clinical trials
- Observational studies
- Future expansion to include **EHR data**



Alzheimer's Disease

TABLE_NAME	COLUMN_NAME	DATA_TYPE	COLUMN_KEY	COLUMN_COMMENT	VALUES
ad_history	ad_stage_id	INT	MUL	(FK: ad_stage.id) The standardized AD stage term for the diagnosis	
ad_stage	subgroup	VARCHAR		The subgroup within the disease stage. Primarily used for MCI to indicate whether it is "early" or "late" stage MCI.	e.g., "Early MCI", "Late MCI"
ad_stage	name	VARCHAR		The name of the Alzheimer's related disease stage	Normal, MCI, AD
ad_stage	id	INT	PRI	Database assigned numeric ID	
ad_stage	dx_criteria	VARCHAR		The criteria used to make the AD stage diagnosis	
adas_cog	word_recognition	INT		The number of incorrectly recognized words	Score Range: 0 - 12; Not Done Codes: -4 = cognitive impairment reasons, -3 = physical reasons, -2 = subject refused, -1 = other reasons
adas_cog	word_recall	FLOAT		The mean number of words not recalled on the 3 word recall trials	Score Range: 0.0 - 10.0; Not Done Codes: -4 = cognitive impairment reasons, -3 = physical reasons, -2 = subject refused, -1 = other reasons
adas_cog	word_find_difficulty	INT		Rating of the word finding difficulty in spontaneous speech	Score Range: 0 - 5; Not Done Codes: -4 = cognitive impairment reasons, -3 = physical reasons, -2 = subject refused, -1 = other reasons
adas_cog	subject_visit_id	INT	MUL	(FK: subject_visit.id) The visit during which the subject performed the assessment	
adas_cog	study_day	INT		The study day the assessment occurred on	

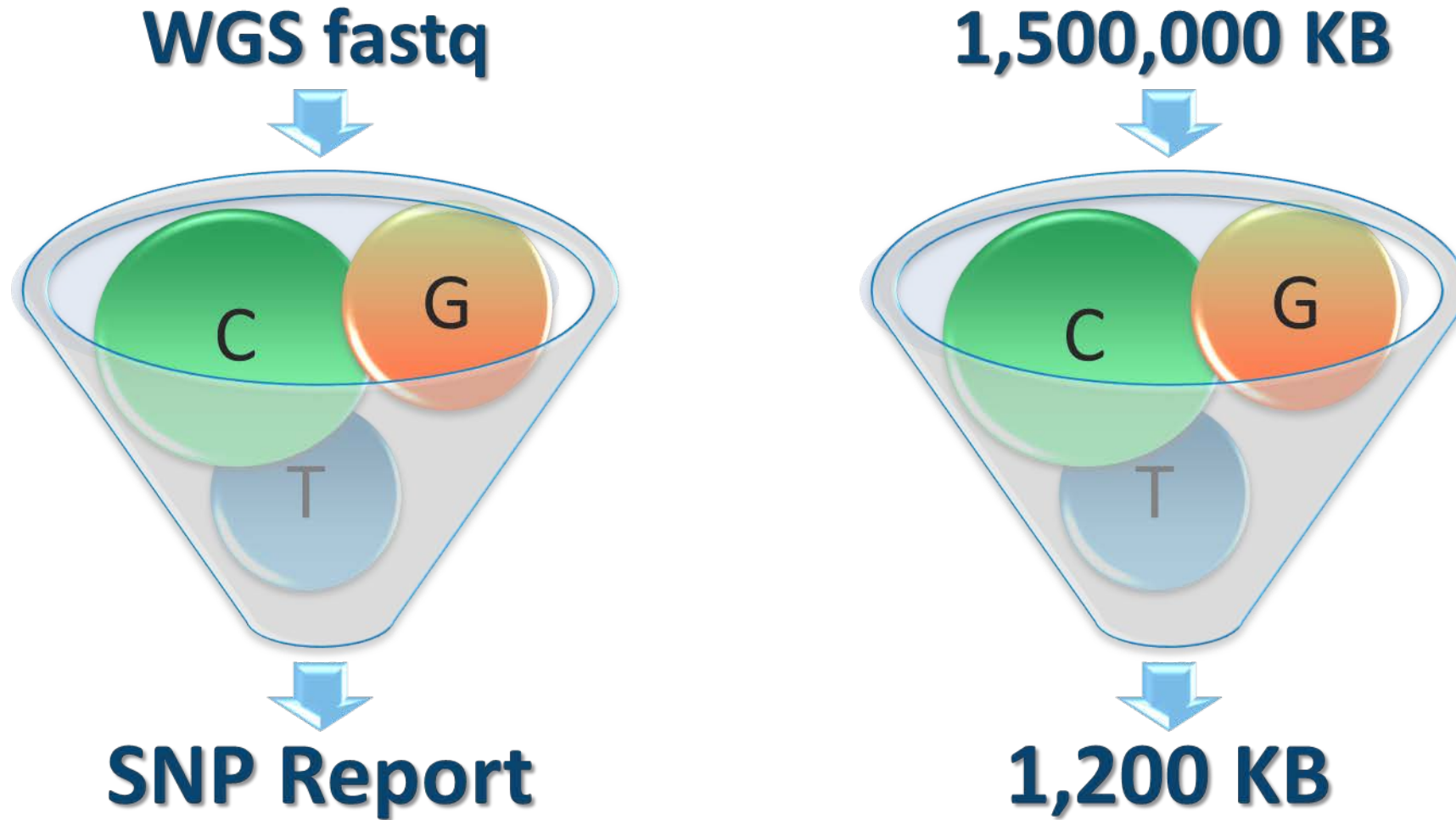
Tuberculosis – *Critical Path to TB Drug Regimens*

➤ Data challenge:

- Combine drug sensitivity testing results with genomic variants
- This enables statistical analyses to identify mutations that confer resistance
- Requires **terabytes** of data to elucidate relationships
- Epidemiologists and policy-makers may not have Big Data skills, making information inaccessible

- Combining statistical resistance reports with global surveillance reports **could guide first-line drug recommendations**
- **C-Path's role:**
 - **Reduce the data burden** by providing tools that give scientists manageable output reports
 - **Communicate** the usefulness of the data with 'stories' in reports

Reduce the Data Burden

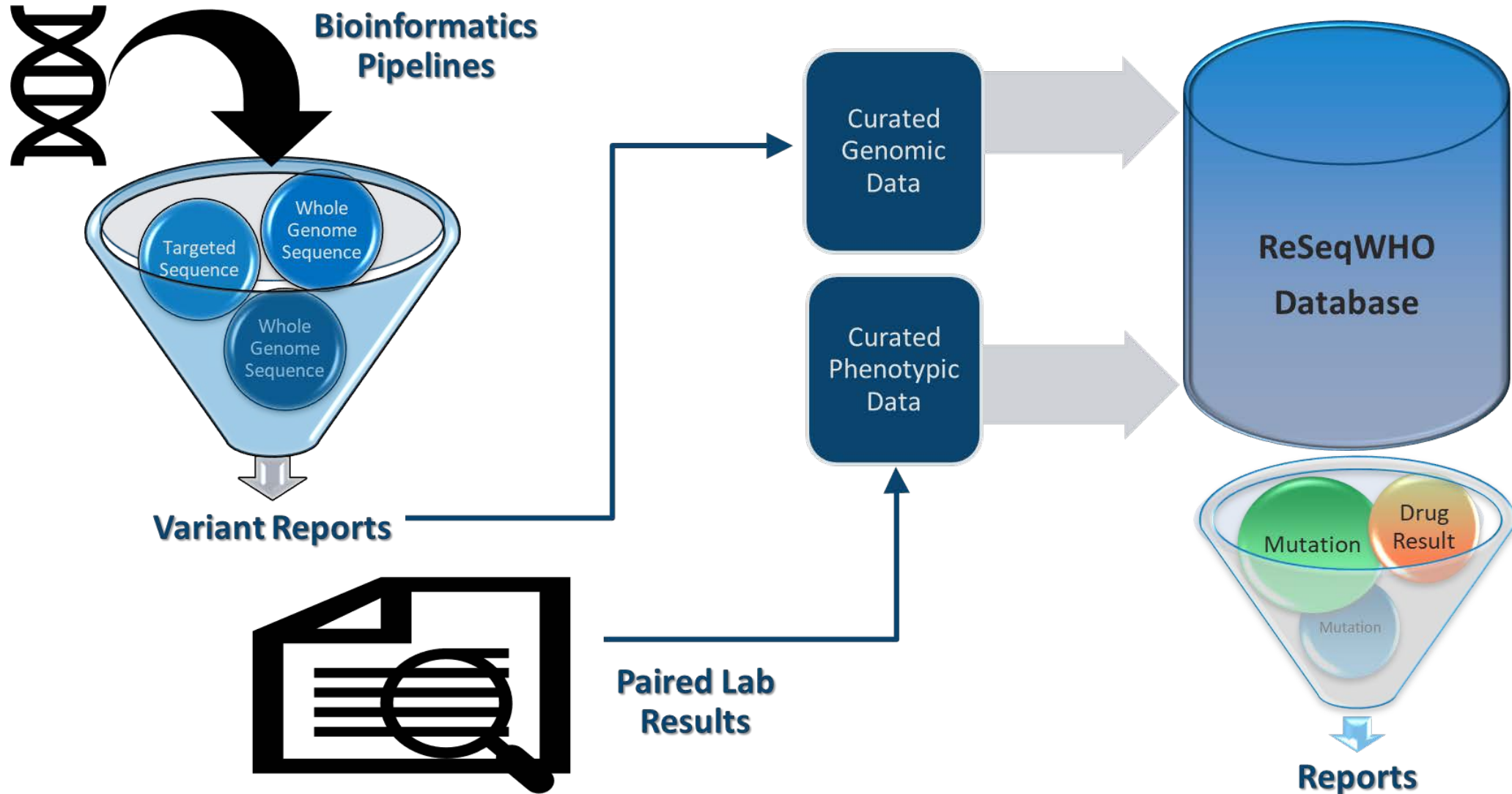


- ReSeqTB in CODR platform – not yet optimized for analytics
 - SQL algorithm for reporting SNPs that are associated with resistance **ran in 3-8 hours**

- ReSeqWHO with redesigned database schema, relations, and indexes
 - SQL algorithm for reporting SNPs that are associated with resistance **ran in about 8 seconds**

- Combining statistical resistance reports with global surveillance reports **could guide first-line drug recommendations**
- **C-Path's role:**
 - **Reduce the data burden** by providing tools that give scientists manageable output reports
 - **Communicate** the usefulness of the data with 'stories' in reports

Communicate with Reports



Bridging the Gap



THANK YOU

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Data Collaboration Center

<https://c-path.org/programs/dcc/>