PhenoStacks:
Cross-Sectional Cohort Phenotype Comparison Visualizations

Michael Glueck, Alina Gvozdik, Fanny Chevalier, Azam Khan, Michael Brudno, Daniel Wigdor

IEEE TRANSACTIONS ON VISUALIZATION AND COMPUTER GRAPHICS
VOL. 23, NO. 1, **JANUARY 2017**

Hooman Shariati

Or better yet:

Why you must use the task abstracts that we learned in class

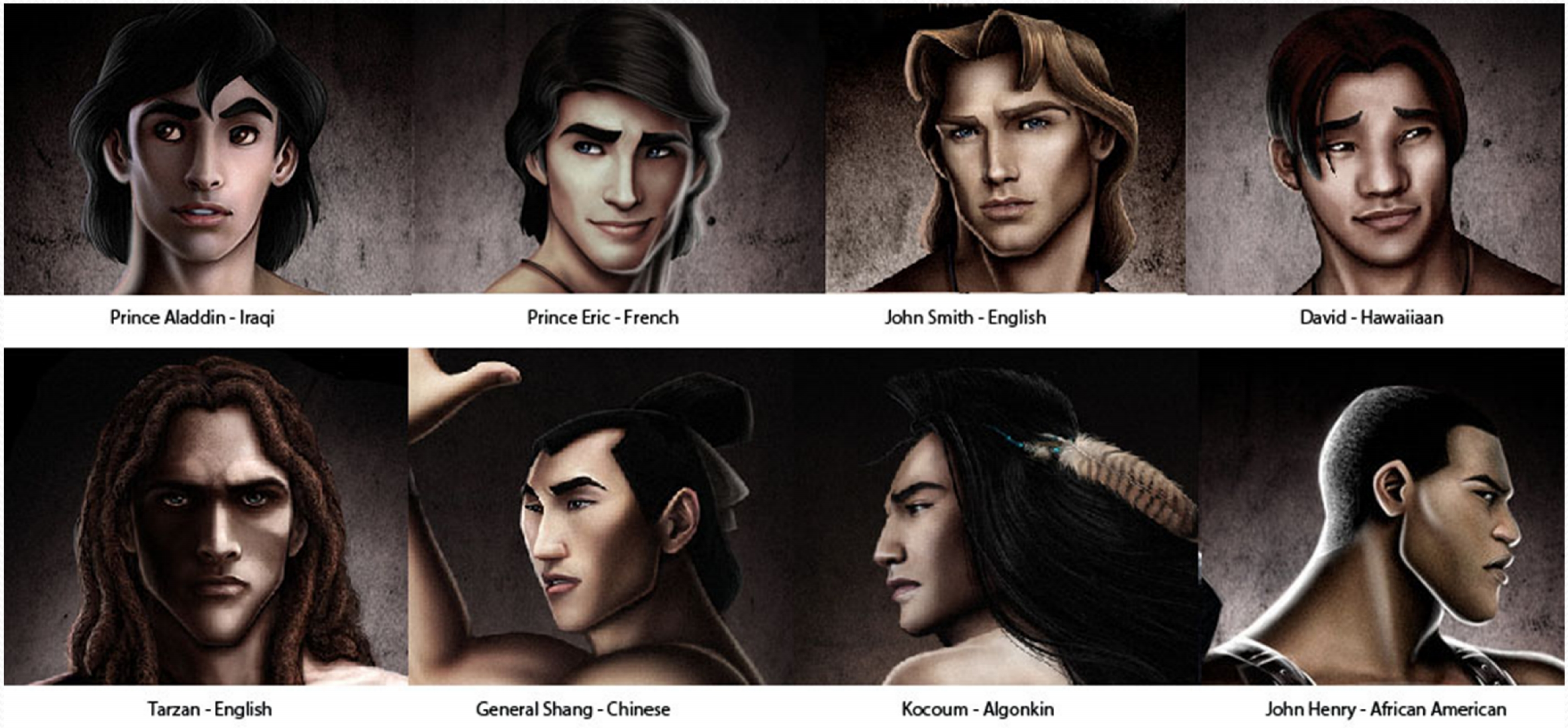
What’s a phenotype?

- A characteristic of an individual compared to the rest of its population

- Can be anything
  - Morphological, biochemical, behavioural

- Ex: the way a particular bird builds it’s nest
  - I.e. how it looks and functions

Disney Male Phenotypes:



Prince Aladdin - Iraqi

Prince Eric - French

John Smith - English

David - Hawaiiaan

Tarzan - English

General Shang - Chinese

Kocoum - Algonkin

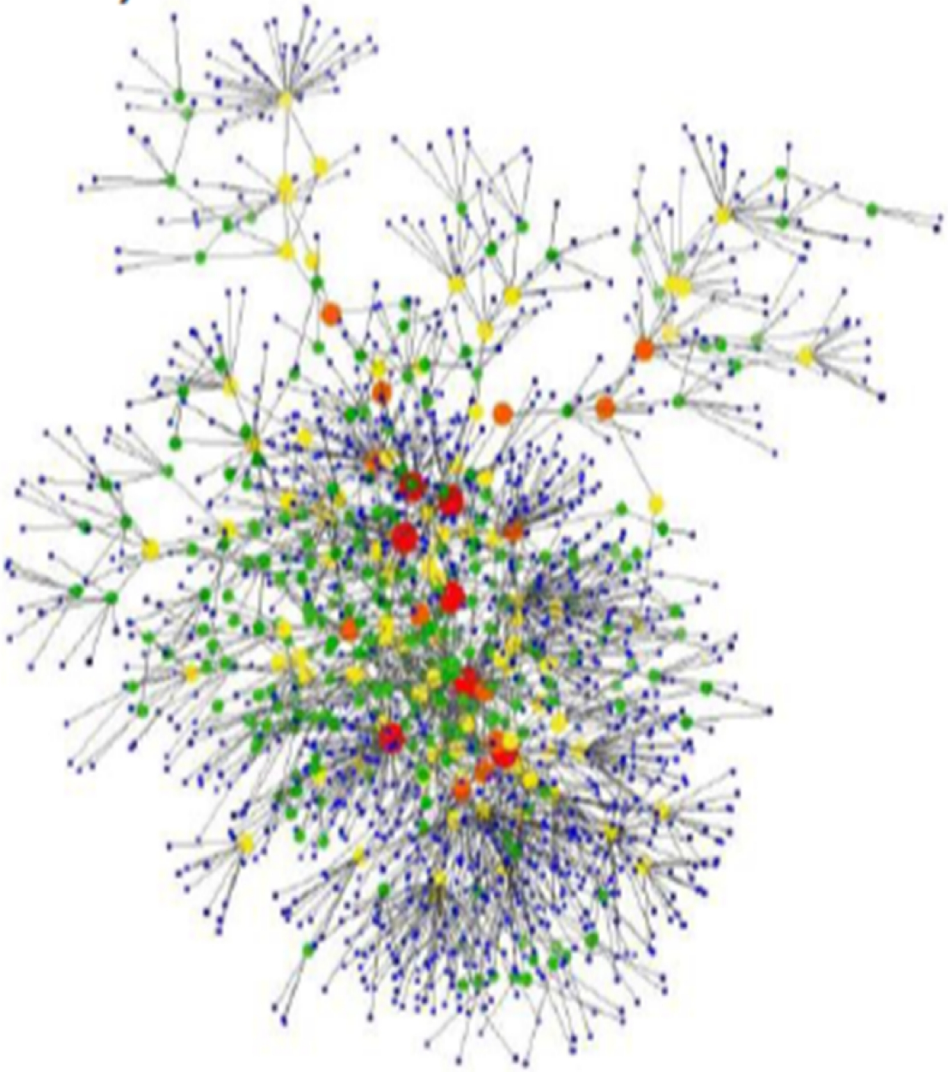
John Henry - African American

Source: Disney

Problem

- Phenotype datasets don’t match in:
  - Structure
  - Coverage
  - Granularity

Human Phenotype Ontology (HPO)



Standardized Terminology

- 11,000+ phenotype terms

Hierarchical Structure

- Abstraction of relationships
- Linked synonyms
- Multiple inheritance

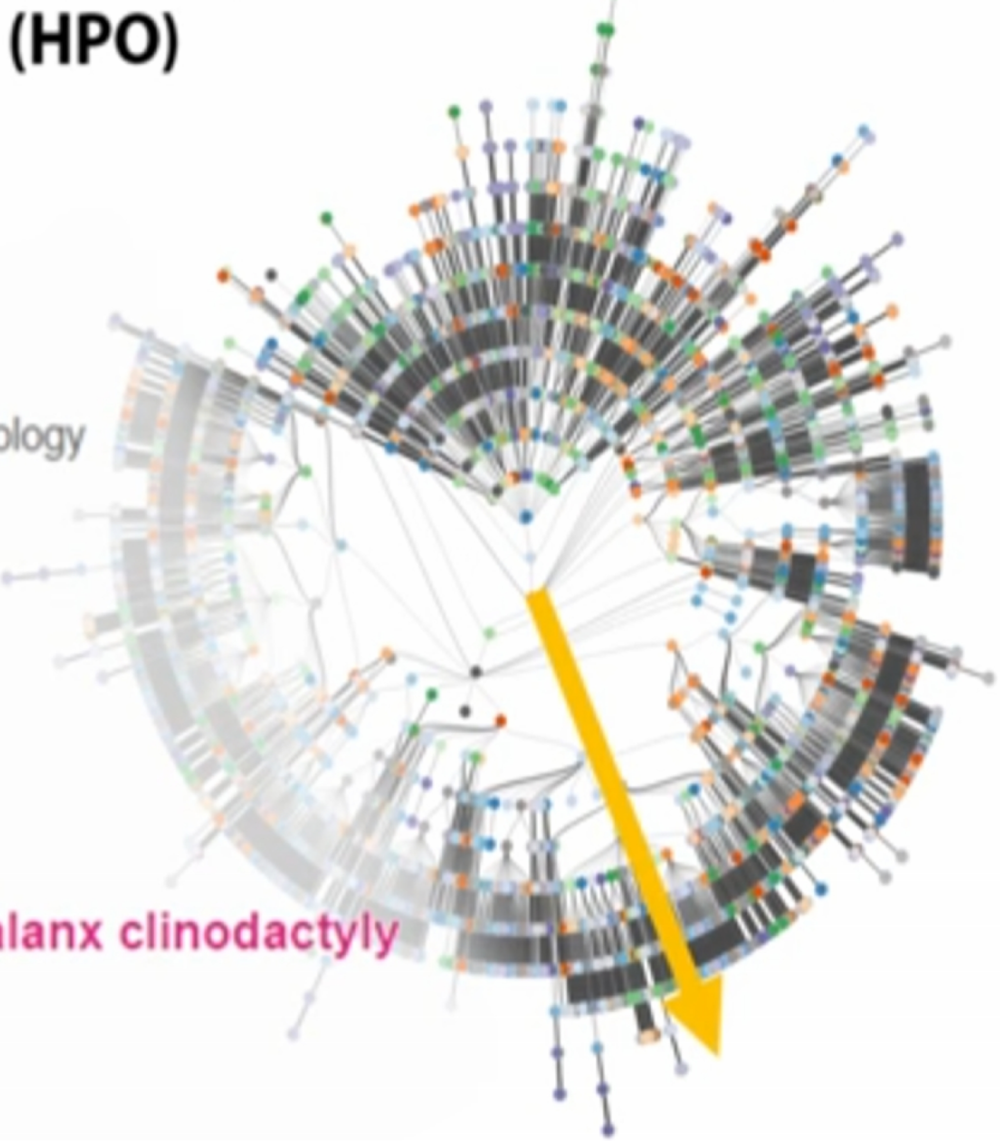
Supports Computation

- Information content

www.human-phenotype-ontology.org

Köhler et al. (2014). Nucleic Acids Research, 42, 966-974 .

Human Phenotype Ontology (HPO)



- Phenotypic abnormality
  - Abnormality of the skeletal system
    - Abnormality of skeletal morphology
      - Abnormal appendicular skeleton morphology
        - Abnormality of limb bone morphology
          - Abnormality of the upper limb
            - Abnormality of the hand
              - Abnormality of finger
                - Deviation of finger
                  - Deviation of the 5th finger
                    - Clinodactyly of the 5th finger
                      - **Fifth finger distal phalanx clinodactyly**

www.human-phenotype-ontology.org

First attempt at visualizing HPO

- By the same authors (Jan 2016)
  - interviews with 2 clinicians identified 4 major domain tasks

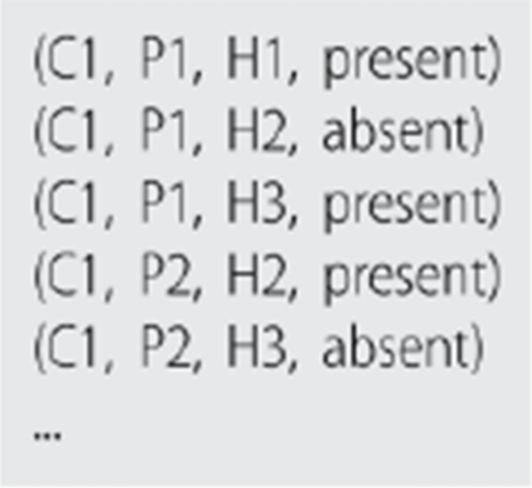
- No Task Abstraction

- Chose to: support the comparison of phenotypes between a new, undiagnosed *query* patient and a set of diagnosed *reference* patients

- Result: Algorithm for comparing an individual to a cohort

Demo:

What: Data



(C1, P1, H1, present)
(C1, P1, H2, absent)
(C1, P1, H3, present)
(C1, P2, H2, present)
(C1, P2, H3, absent)
...

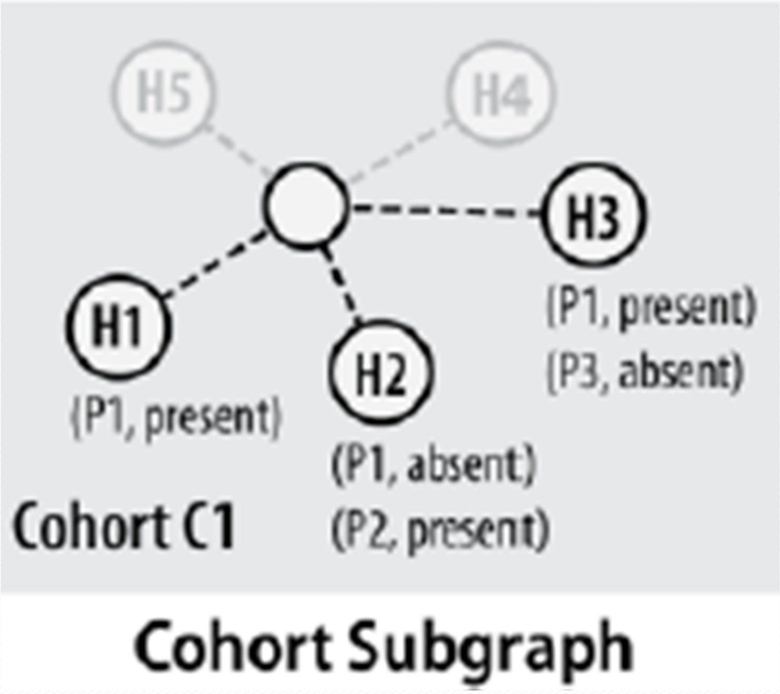
Phenotype Data
(Cohort, Patient, HPO, Observ.)

HPO Topology

Source: Paper

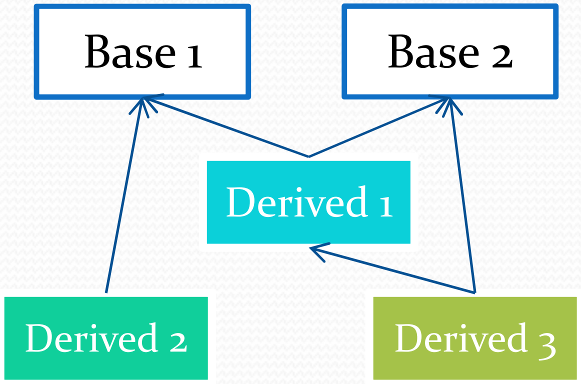
What: Derived

- **Union** of all recorded phenotypes is a cohort graph



Source: Paper

What **wasn’t** shown in their video:

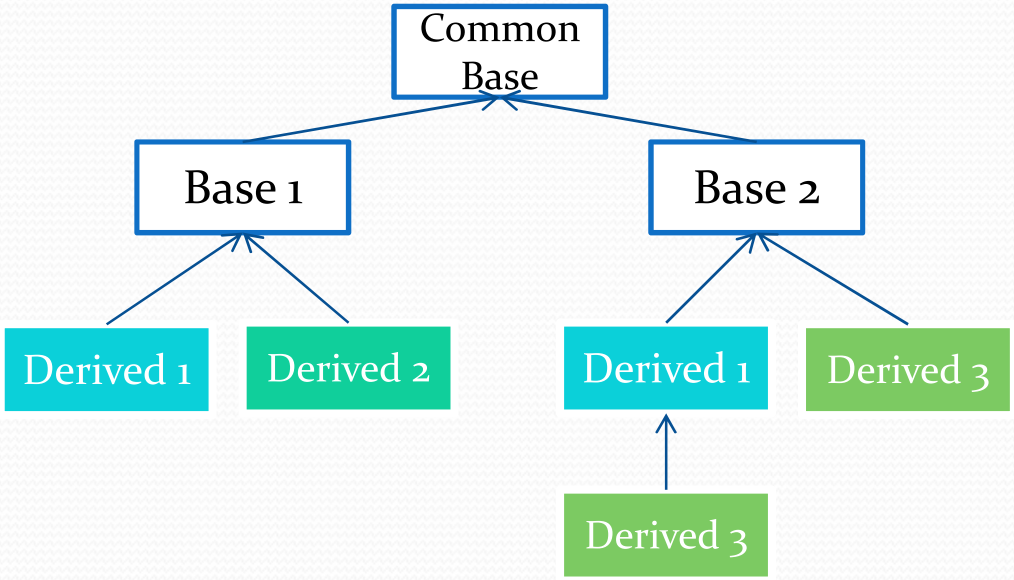

Base 1

Base 2

Derived 1

Derived 2

Derived 3


Common Base

Base 1

Base 2

Derived 1

Derived 2

Derived 1

Derived 3

Derived 3

Source: None

What **wasn't** said in their paper:

- "feedback from researchers indicated duplication of phenotypes was extremely confusing because it gave the false impression that there were more clusters."
- Oops

Second attempt at visualizing HPO

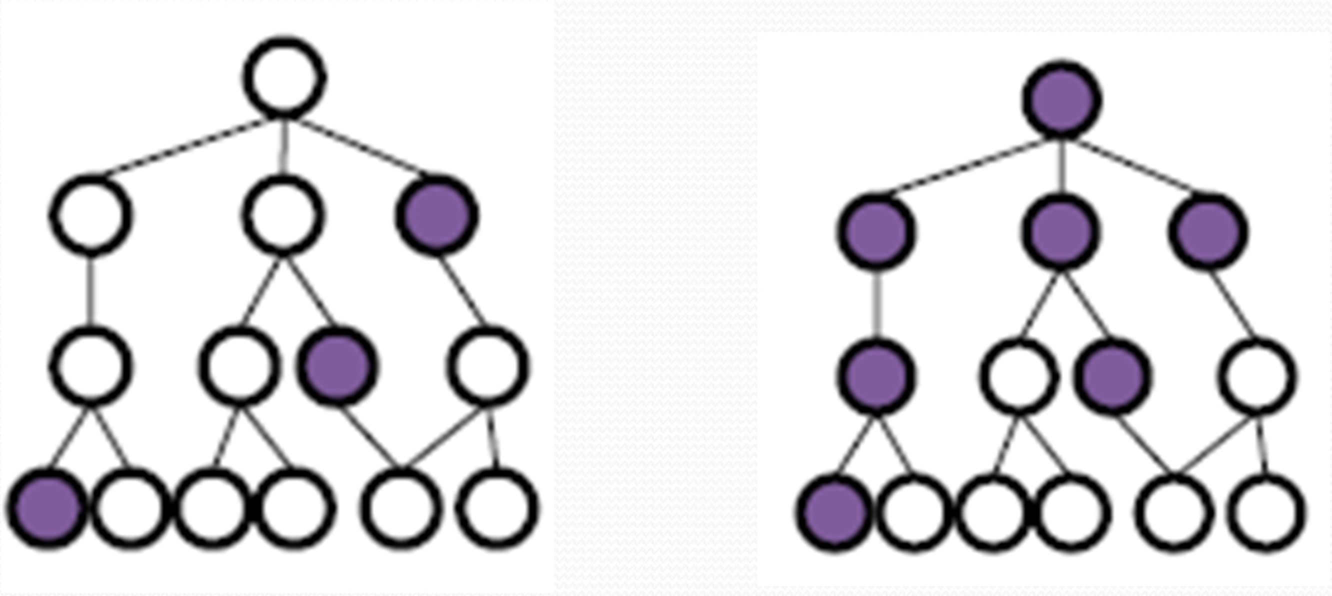
- Interviewed 6 experts
- Identified 9 domain tasks
- Synthesized them to common visualization tasks using Brehmer & Muntzner's multi-level typology
- Result: algorithm for comparing multiple cohorts
- Basically added a second view to their previous tool

Why: Tasks

- **Explore → Summarize**
  - emergent patterns (W1), disease prevalence (W5), disease characterization (W6), compare patterns across disease subtypes (B1)
- **Locate → Identify**
  - outlier patients/phenotypes (W2), subcohort discovery (W3), inform clinical practice (B3)
- **Browse → Compare**
  - audit data quality (W4), validate data quality (B2)

What: Derived

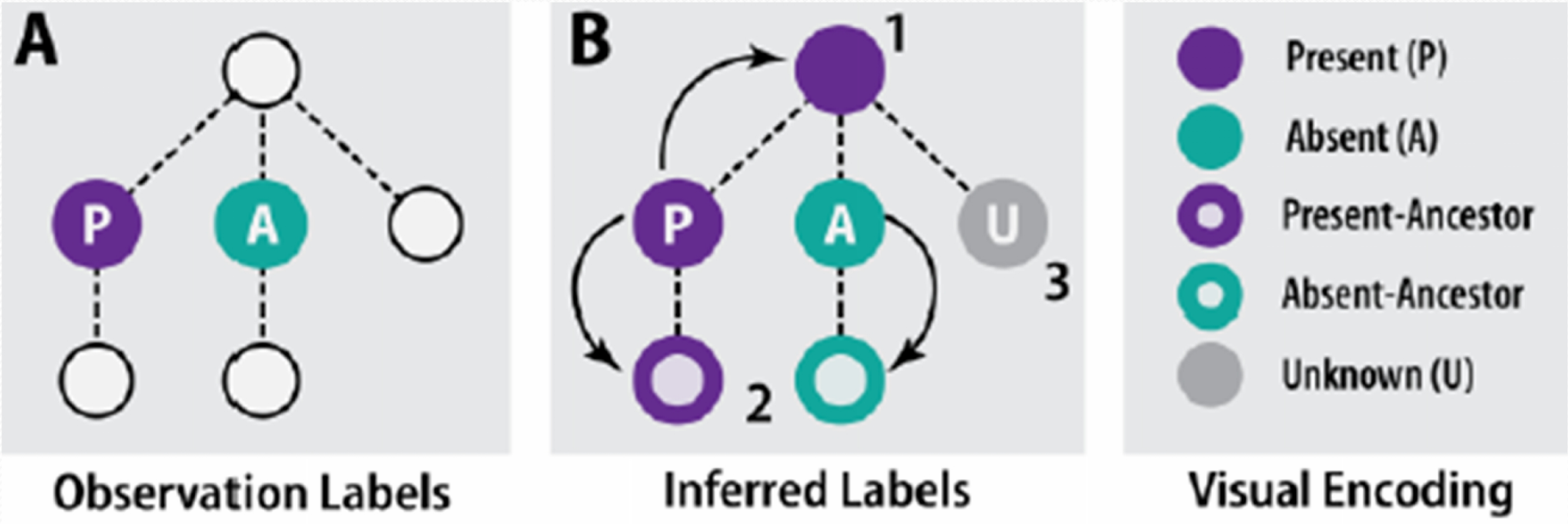
- Infer some of the HPO labels that weren't observed



Source: Author Presentation

What: Derived

- Add new labels in addition to HPO labels



Source: Paper

What: Derived

- Information Content
  - Lower for common phenotypes higher for rare ones
  - Corresponds to Diagnostic Significance
  - Calculated for each phenotype independent of study

Demo:

How: Encode

- Matrix: phenotypes as rows patients as columns
- Matrix Cells: Shape and Color for observations

- Dendrogram / categories/ clusters: Grouping of related phenotype rows

- Vertical position: Ranking in the sorted list

How: Facet

- Juxtapose and Coordinate Multiple Side-by-Side Views
  - Histograms aligned to common baseline
  - Dendrograms top-aligned with observation plot

- Linked Highlighting

- Shared data (Subset)

- Shared Sorting and filtering

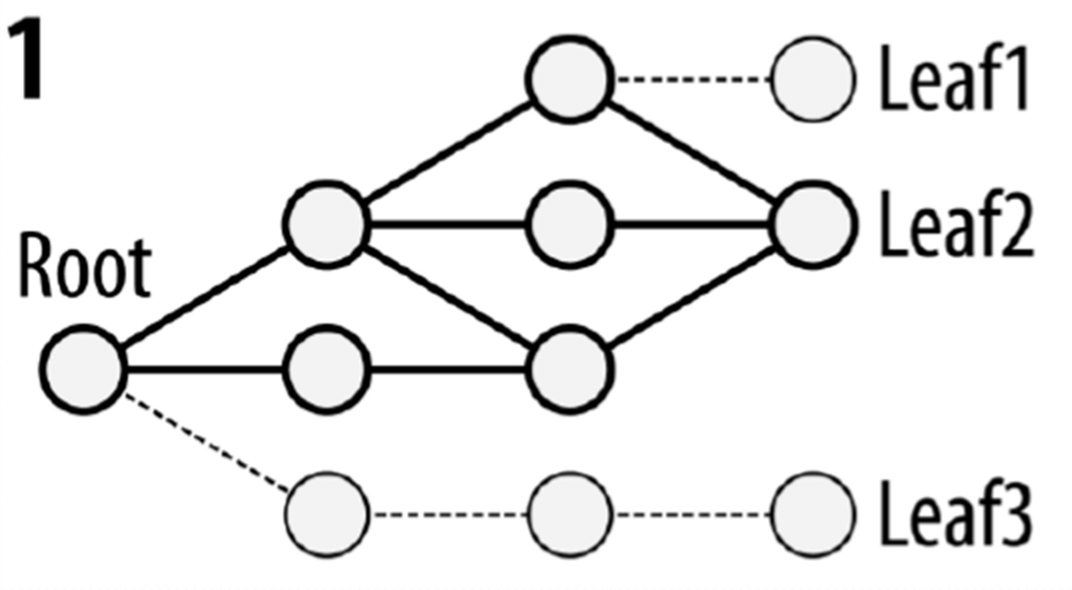
How: Manipulate

- Select the sort criteria for phenotypes and cohorts
- Select the Grouping of Phenotypes in layout view
- Collapse and Expand nodes in the Tree layout
  - Users saw this one as too much intractability

How: Reduce

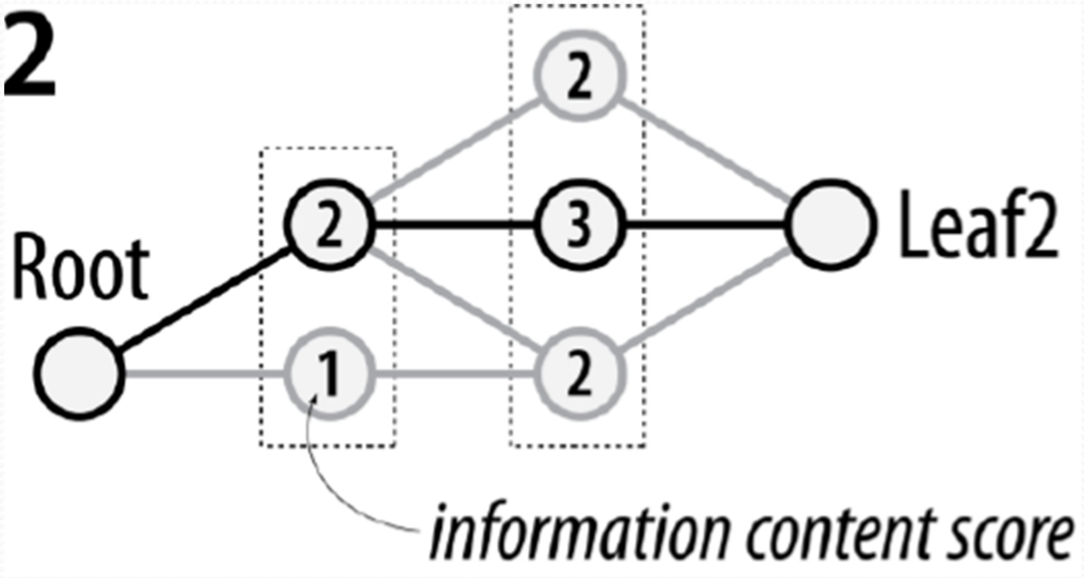
- Aggregation: by grouping rows according to categories and their hierarchy
- Filtering by information content using novel algorithm

How: Reduce



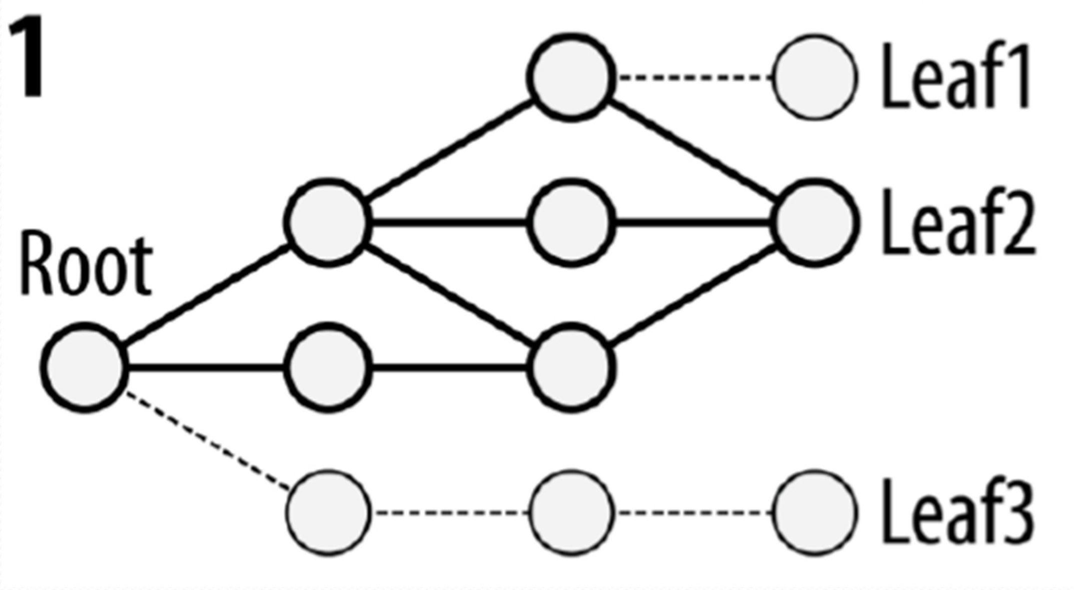
Source: Author Presentation

How: Reduce



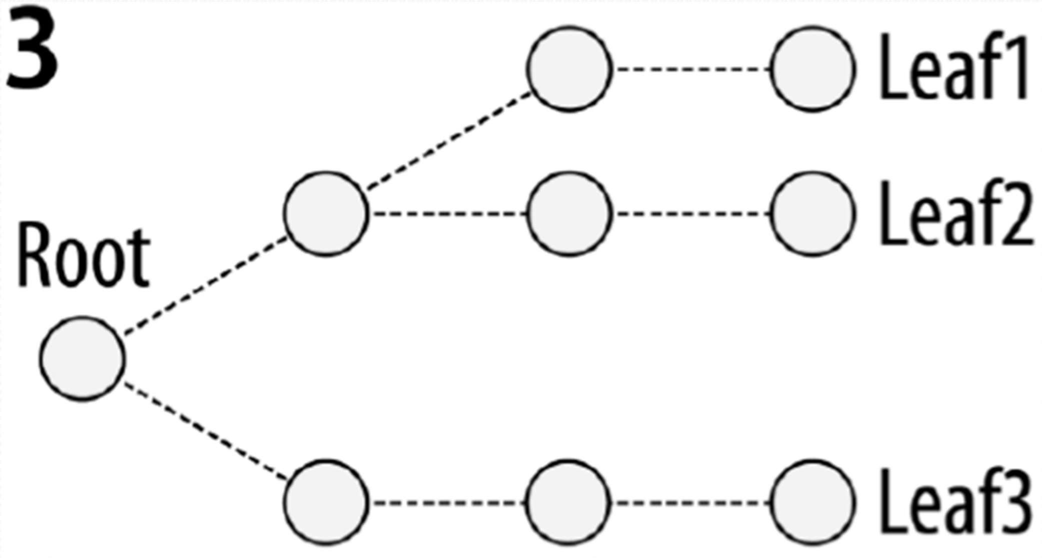
Source: Author Presentation

How: Reduce



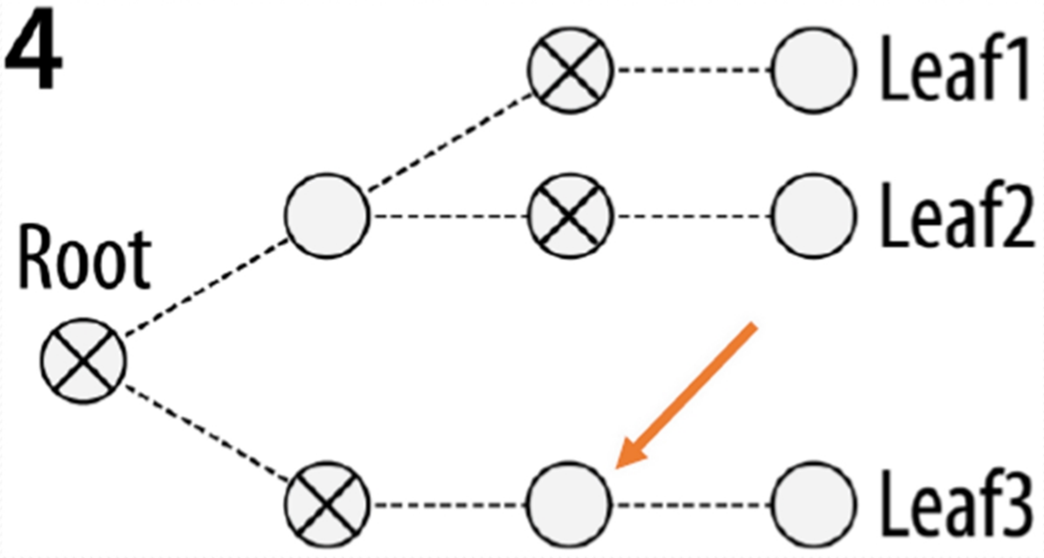
Source: Author Presentation

How: Reduce



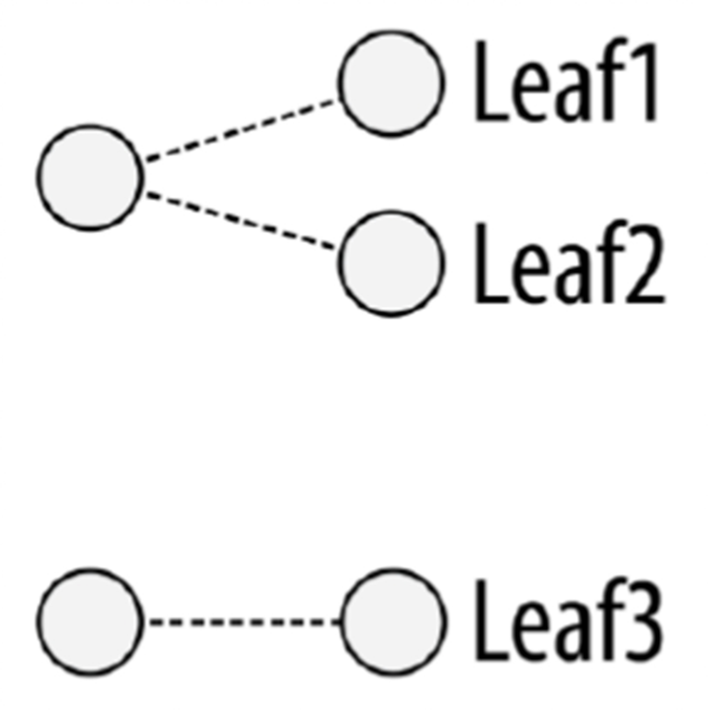
Source: Author Presentation

How: Reduce



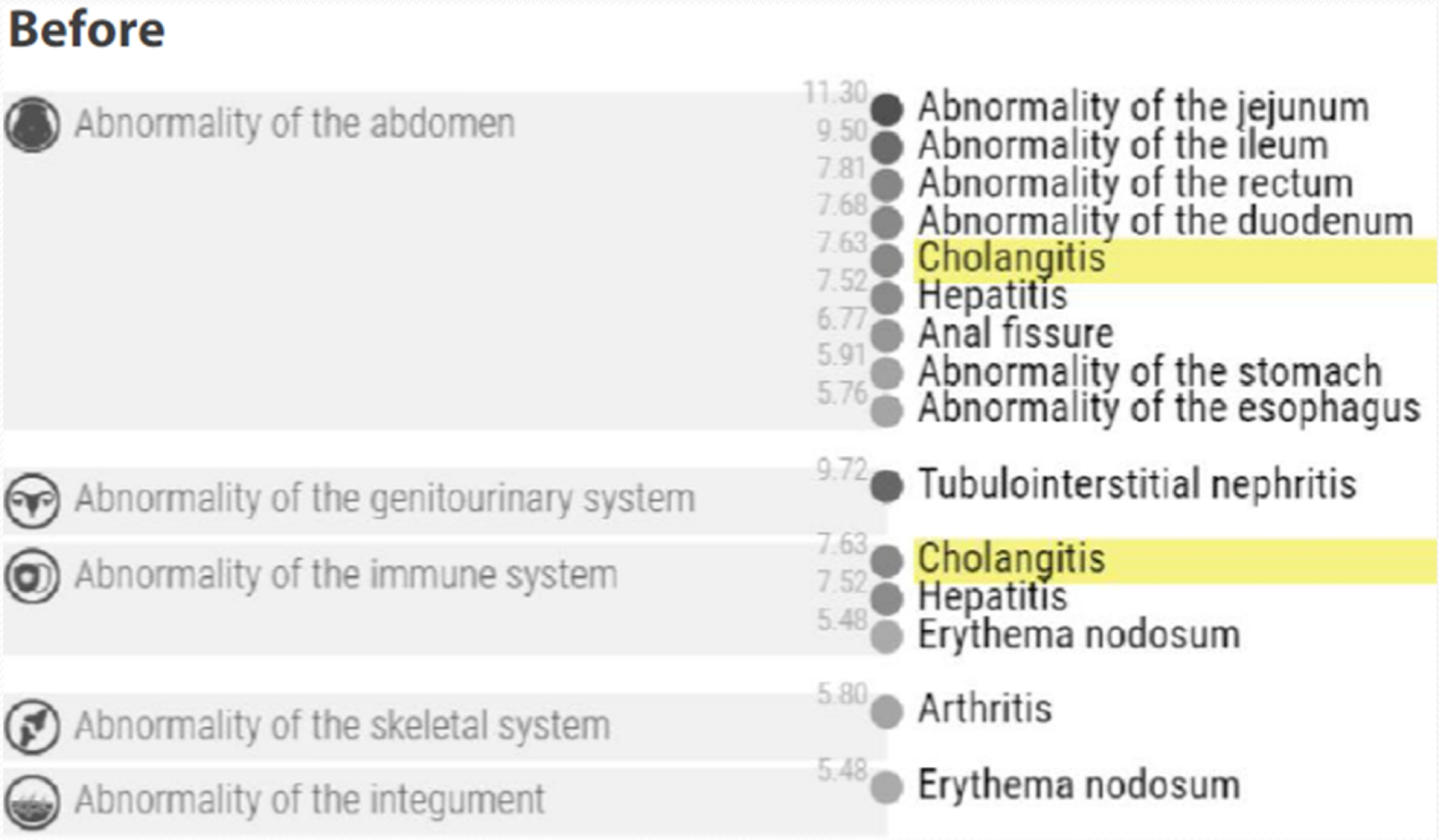
Source: Author Presentation

How: Reduce



Source: Author Presentation

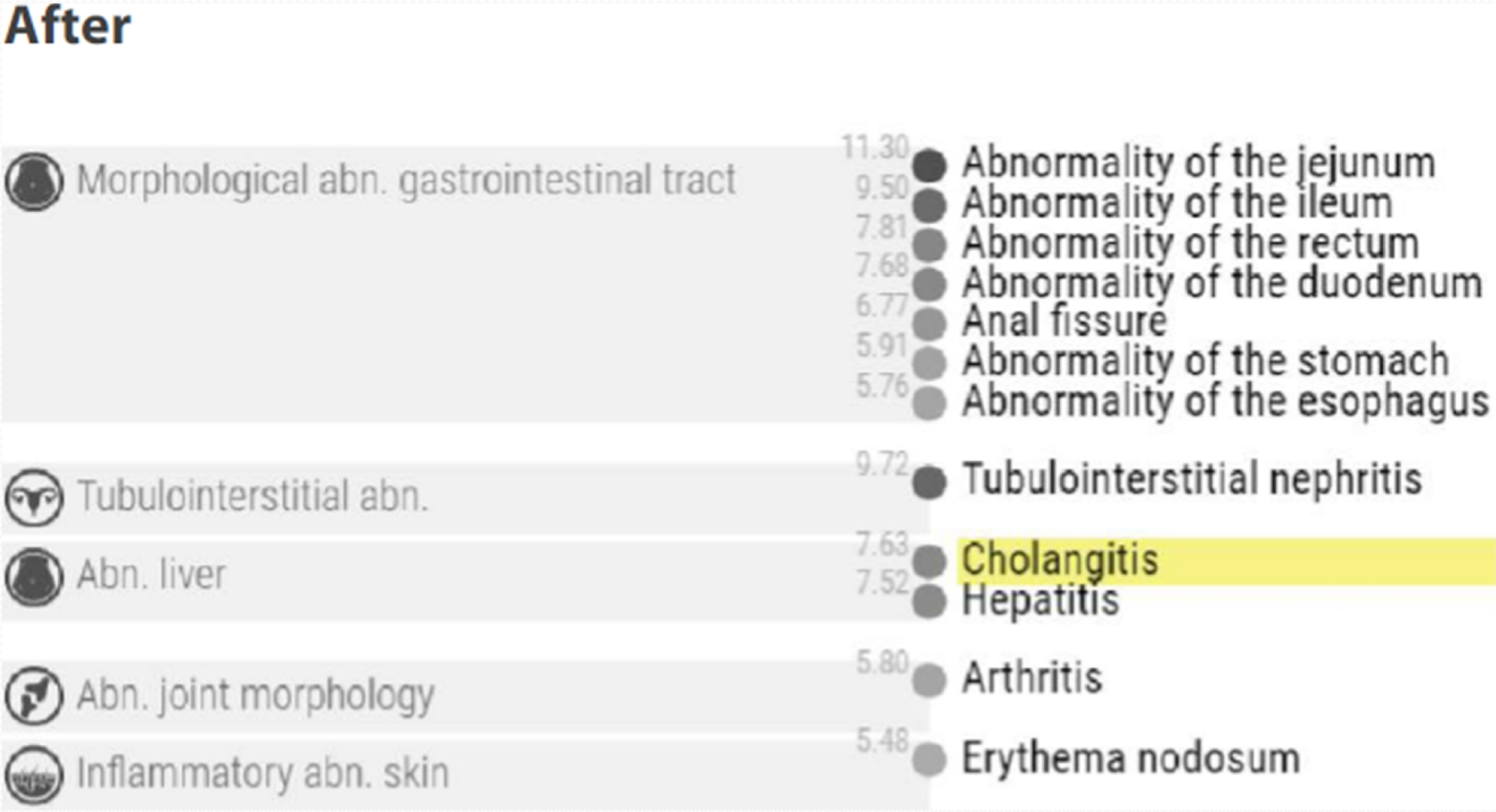
How: Reduce



Before

Abnormality of the abdomen	11.30	Abnormality of the jejunum
	9.50	Abnormality of the ileum
	7.81	Abnormality of the rectum
	7.68	Abnormality of the duodenum
	7.63	Cholangitis
	7.52	Hepatitis
	6.77	Anal fissure
	5.91	Abnormality of the stomach
	5.76	Abnormality of the esophagus
Abnormality of the genitourinary system	9.72	Tubulointerstitial nephritis
Abnormality of the immune system	7.63	Cholangitis
	7.52	Hepatitis
	5.48	Erythema nodosum
Abnormality of the skeletal system	5.80	Arthritis
Abnormality of the integument	5.48	Erythema nodosum

How: Reduce



After

Morphological abn. gastrointestinal tract	11.30	Abnormality of the jejunum
	9.50	Abnormality of the ileum
	7.81	Abnormality of the rectum
	7.68	Abnormality of the duodenum
	6.77	Anal fissure
	5.91	Abnormality of the stomach
	5.76	Abnormality of the esophagus
Tubulointerstitial abn.	9.72	Tubulointerstitial nephritis
Abn. liver	7.63	Cholangitis
	7.52	Hepatitis
Abn. joint morphology	5.80	Arthritis
Inflammatory abn. skin	5.48	Erythema nodosum

Paper's Major Limitation

- Longer more robust evaluation of the simplification algorithm

- Give user's control over the aggressiveness of intermediate phenotype removal
    - Ie. control over granularity of computed categories

- My suggestion: At the very least, give user's more information about the quality of the categories as well

How: Scale

- Patients or Patient Cohorts: One dozen
- Phenotypes: About a 100
- HPO Graph Nodes: several thousands