

LINEAGE: VISUALIZING MULTIVARIATE CLINICAL DATA IN GENEALOGY GRAPHS

CAROLINA NOBRE, NILS GEHNLEBORG, HILARY COON, ALEXANDER LEX



visualization
design lab



HARVARD
MEDICAL SCHOOL

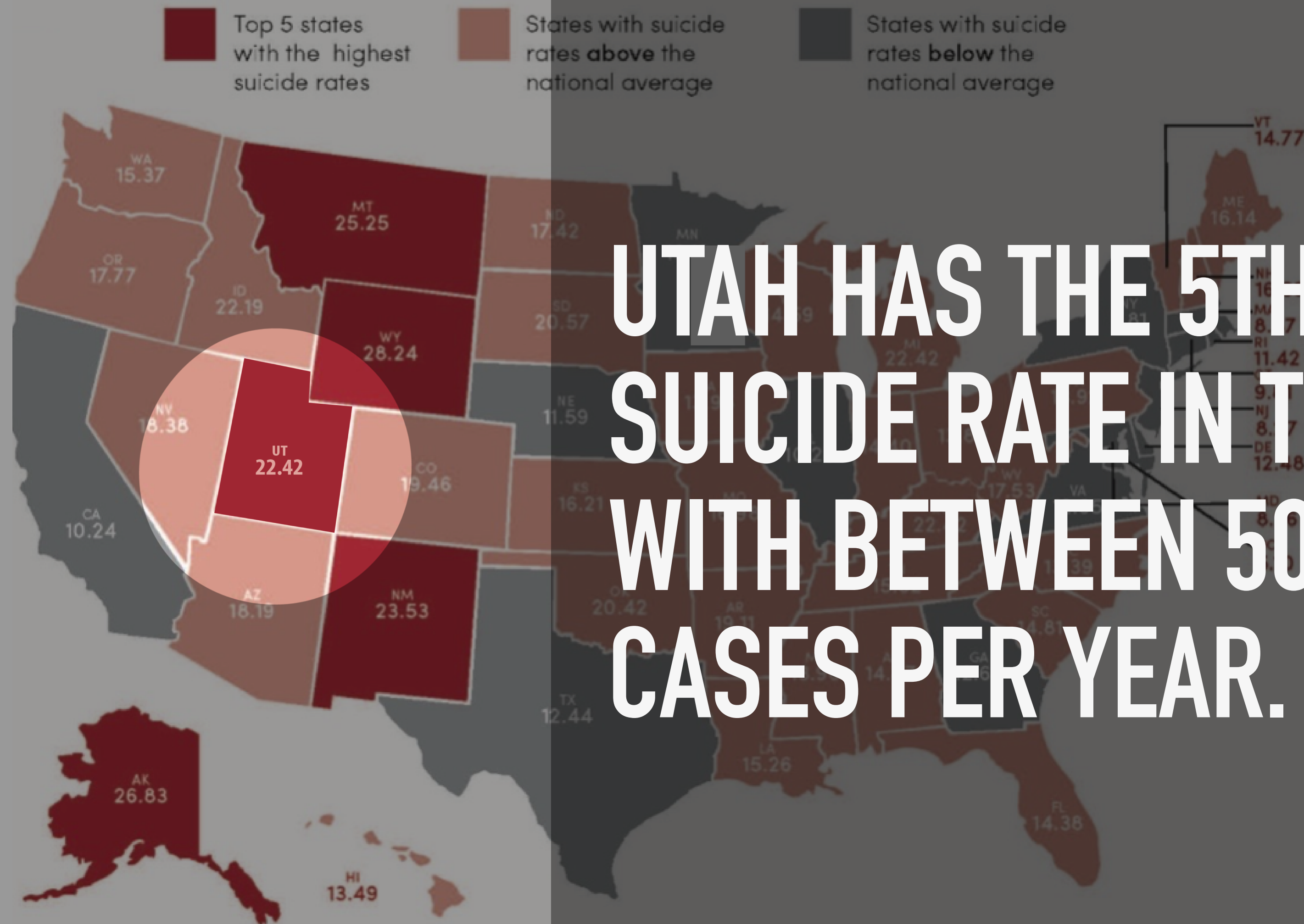


THE WORLD HEALTH
ORGANIZATION ESTIMATES

**ONE PERSON DIES OF
SUICIDE EVERY 40 SECONDS**

**SUICIDE IS THE SECOND LEADING CAUSE OF DEATH
IN YOUTHS BETWEEN 15 AND 29 YEARS OLD**

AVERAGE SUICIDE RATE BY STATE (National average **13.26** per 100,000)



UTAH HAS THE 5TH HIGHEST
SUICIDE RATE IN THE COUNTRY,
WITH BETWEEN 500–600
CASES PER YEAR.

Top 5 states with the highest suicide rates
 States with suicide rates **above** the national average
 States with suicide rates **below** the national average





What causes suicide?
WHAT CAN WE
DO TO HELP?



Original Contribution

Acute Air Pollution Exposure and Risk of Suicide Completion

OPEN

Citation: Transl Psychiatry (2013) 3, e325; doi:10.1038/tp.2013.100
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www.nature.com/tp



ORIGINAL ARTICLE

Genetic risk factors in two Utah pedigrees at high risk for suicide

H Coon¹, T Darlington¹, R Pimentel², KR Smith^{2,3}, CD Huff⁴, H Hu⁴, L Jerominski¹, J Hansen¹, M Klein⁵, WB Callor⁶, J Byrd⁶, A Bakian¹, SE Crowell^{1,7}, WM McMahon¹, V Rajamanickam⁸, NJ Camp⁸, E McGlade^{1,9}, D Yurgelun-Todd^{1,9}, T Grey⁶ and D Gray^{1,9}

We have used unique population-based data re over twice that expected from demographically two high-risk pedigrees. In the first of these (pe death was 30.95. In the second (pedigree 5), 7/ decedents in pedigree 12 and nine in pedigree analyzed using the Variant Annotation, Analysis functional impact of the DNA variation, aggreg prioritized variants that were: (1) shared across (3) ≤ 5% in genotyping data from 398 other Ut from 1358 controls and/or in dbSNP. Results inc FAM38A and HRCT1 for pedigree 5). Other gene

r, Hilary Coon, Douglas Gray, Phillip Wilson, nshaw

rtment of Psychiatry, School of Medicine, University of Utah, 650 Komas Drive, Suite 206, @hsc.utah.edu).

for publication August 11, 2014.

The Role of Social Isolation in Suicide

Deborah L. Trout M.A.

First published: Spring 1980 | <https://doi-org.ezproxy.lib.utah.edu/10.1111/j.1943-278X.1980.tb00693.x>
| Cited by: 95

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We have used unique population-based data resources to identify 22 high-risk extended pedigrees that show clustering of suicide over twice that expected from demographically adjusted incidence rates. In this initial study of genetic risk factors, we focused on two high-risk pedigrees. In the first of these (pedigree 12), 10/19 (53%) of the related suicides were female, and the average age at death was 30.95. In the second (pedigree 5), 7/51 (14%) of the suicides were female and the average age at death was 36.90. Six decedents in pedigree 12 and nine in pedigree 5 were genotyped with the Illumina HumanExome BeadChip. Genotypes were analyzed using the Variant Annotation, Analysis, and Search program package that computes likelihoods of risk variants using the functional impact of the DNA variation, aggregative scoring of multiple variants across each gene and pedigree structure. We prioritized variants that were: (1) shared across pedigree members, (2) rare in other Utah suicides not related to these pedigrees, (3) $\leq 5\%$ in genotyping data from 398 other Utah population controls and (4) $\leq 5\%$ frequency in publicly available sequence data from 1358 controls and/or in dbSNP. Results included several membrane protein genes (*ANO5*, and *TMEM141* for pedigree 12 and *FAM38A* and *HRCT1* for pedigree 5). Other genes with known neuronal involvement and/or previous associations with psychiatric conditions were also identified including *NEK9*, *CACNA*, *PLXNB1* and *PRF11A* in pedigree 12, and *THOC1* and *AUTS2* in pedigree 5.

WHAT CAN WE DO TO HELP?

Select relevant cases to perform genetic analysis

Contribute to our understanding of suicide

Ultimately be able to predict and prevent suicide



WHAT MAKES UTAH UNIQUE?
The Utah Suicide Research Study (USRS) has over
6000* DNA samples from completed suicide cases...

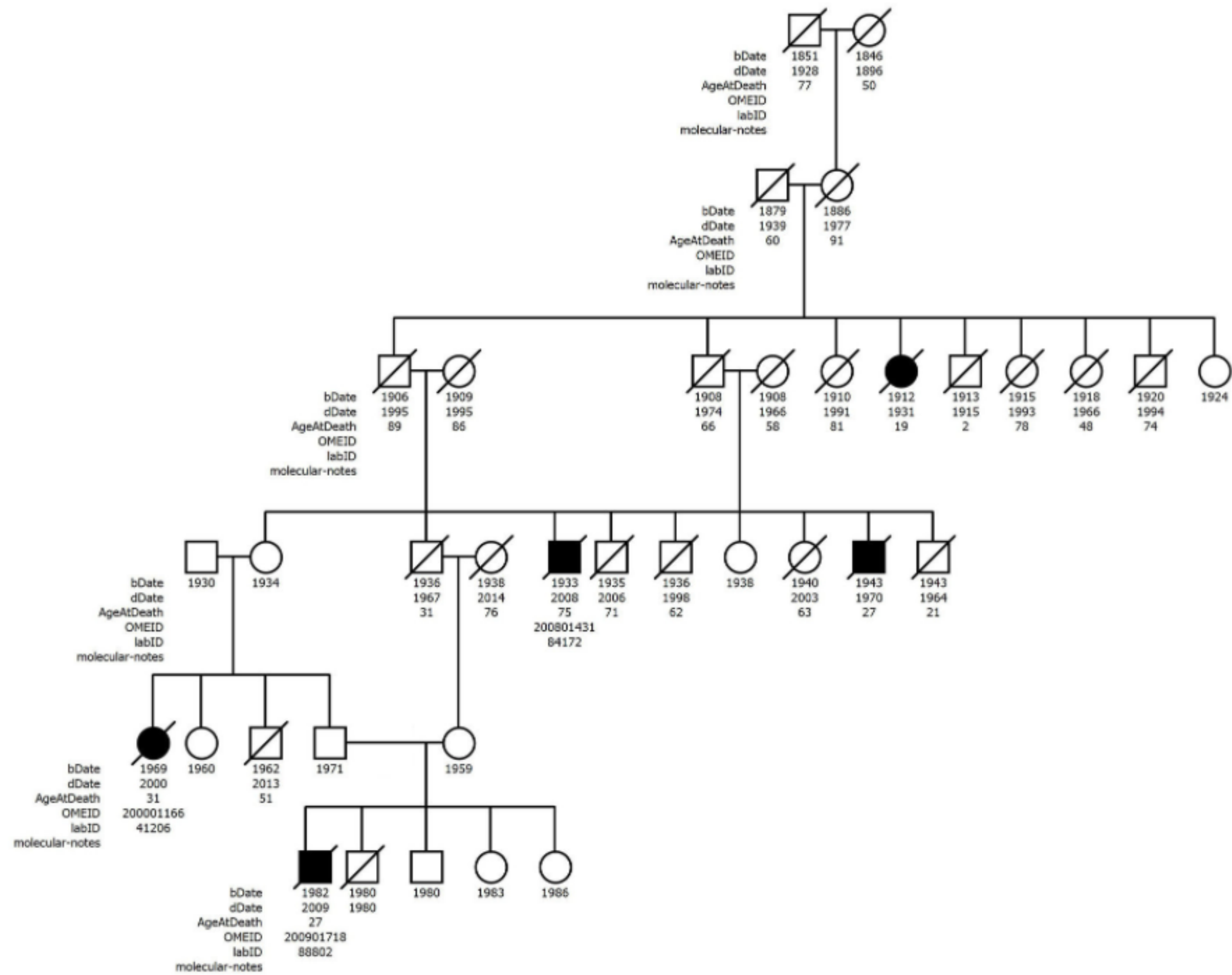
over **twice** the size of other genetic studies of completed suicides.

* 6013 as of 9/01/2018

> 19,000 CASES IN UTAH SINCE 1904

UTAH POPULATION DATABASE

- ▶ Multi-Generational Genealogies (1700s)
- ▶ Demographic Information
- ▶ Geographic/Environmental Exposure
- ▶ Clinical Information



Age
Gender
Race
Bipolar

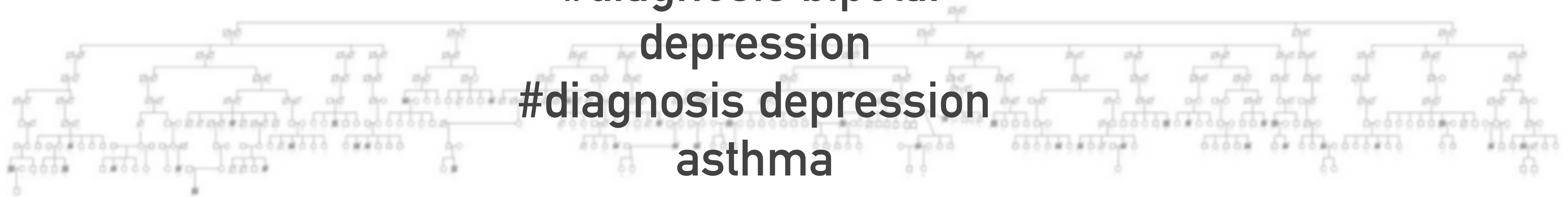
#diagnosis bipolar
depression

#diagnosis depression
asthma

#diagnosis asthma
obesity

schizophrenia
cause of death
weapon used

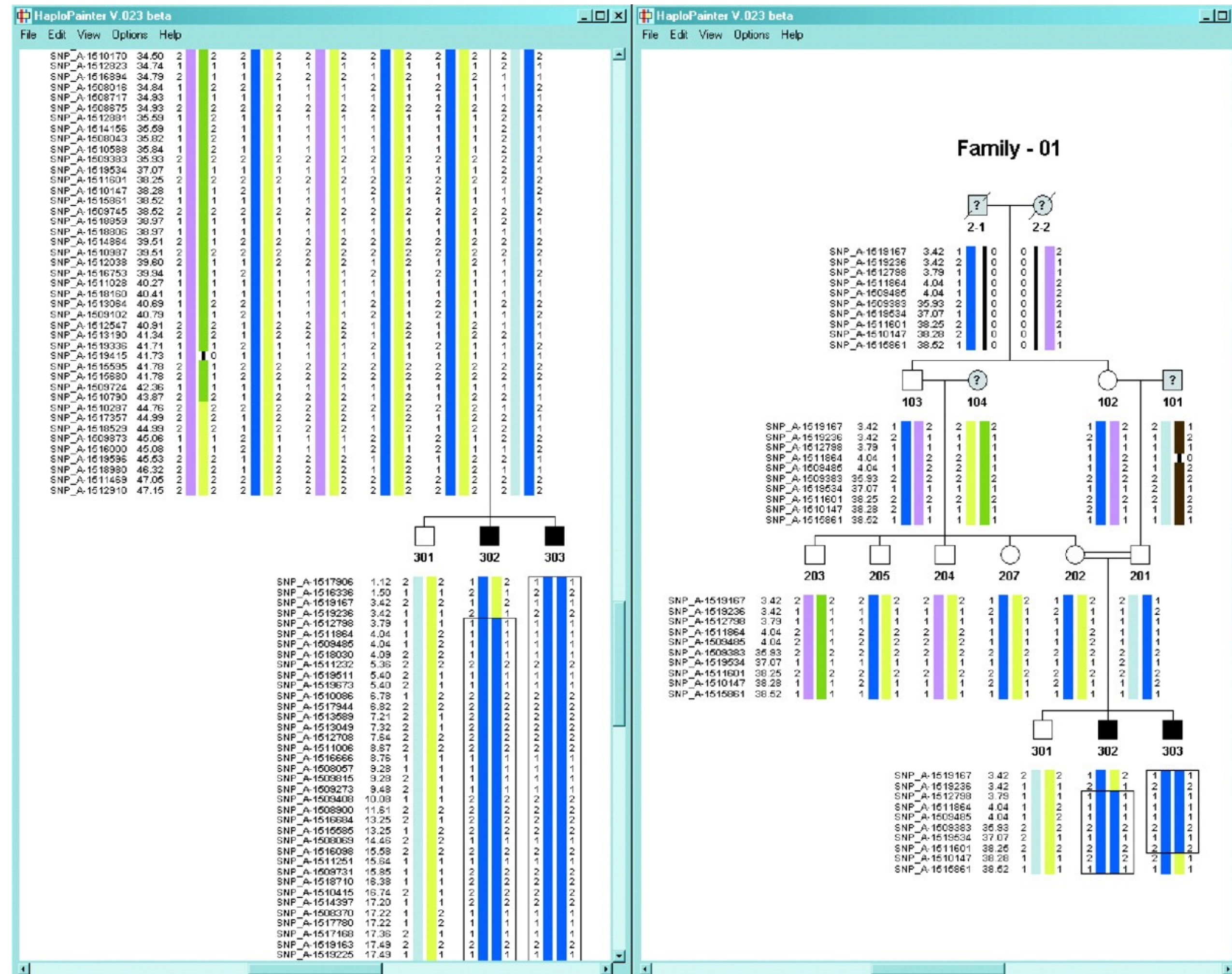
...



ATTRIBUTES CAN...

- ▶ Prioritize which genes may be of interest in a shared region in the genome.
- ▶ Attributes can also reveal co-occurring conditions
- ▶ Suggest subgroups for future target intervention and prevention studies.

HaploPainter

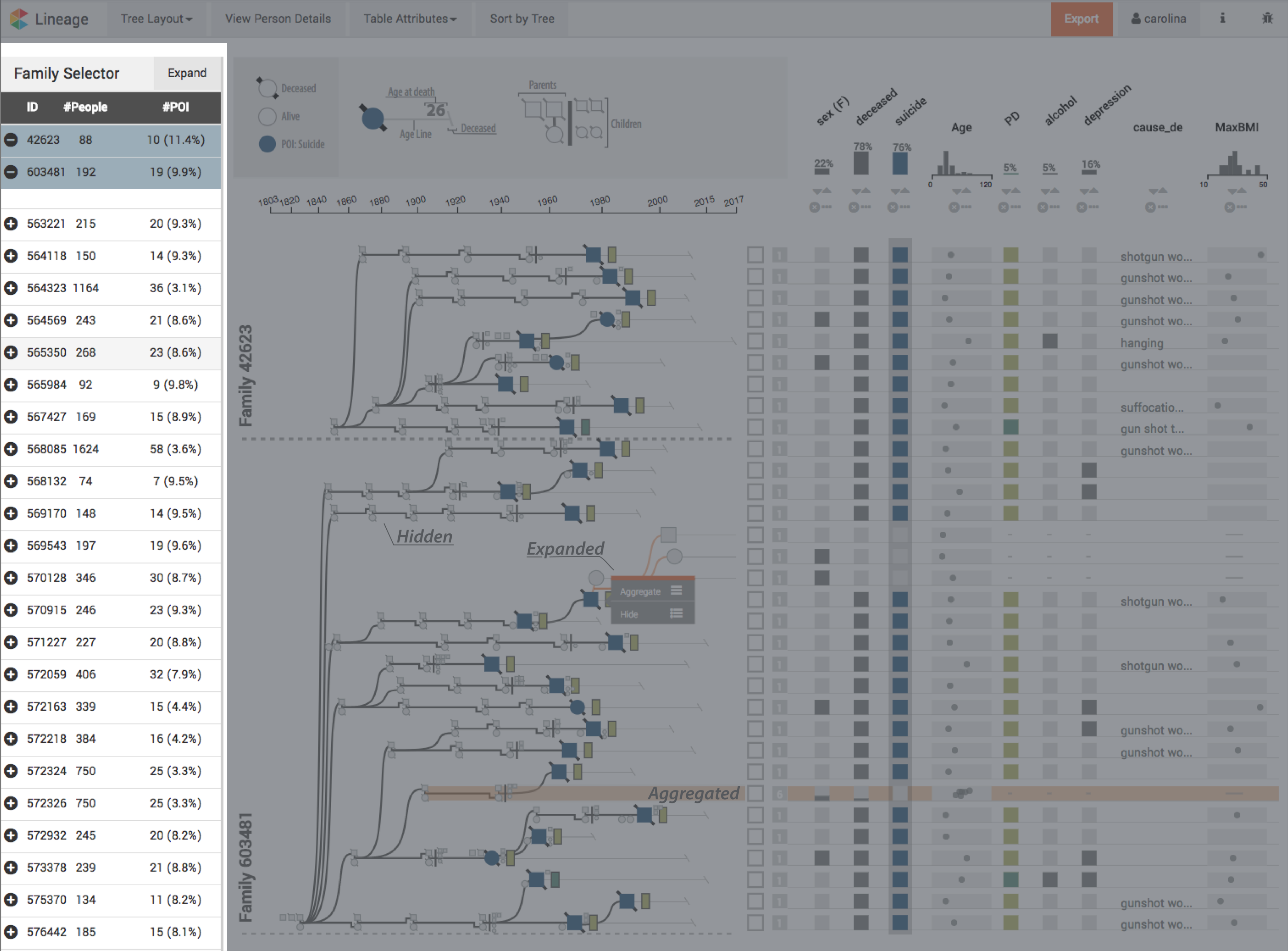


Thiele, Holger, and Peter Nürnberg. "HaploPainter: a tool for drawing pedigrees with complex haplotypes." *Bioinformatics* 21.8 (2004): 1730-1732.

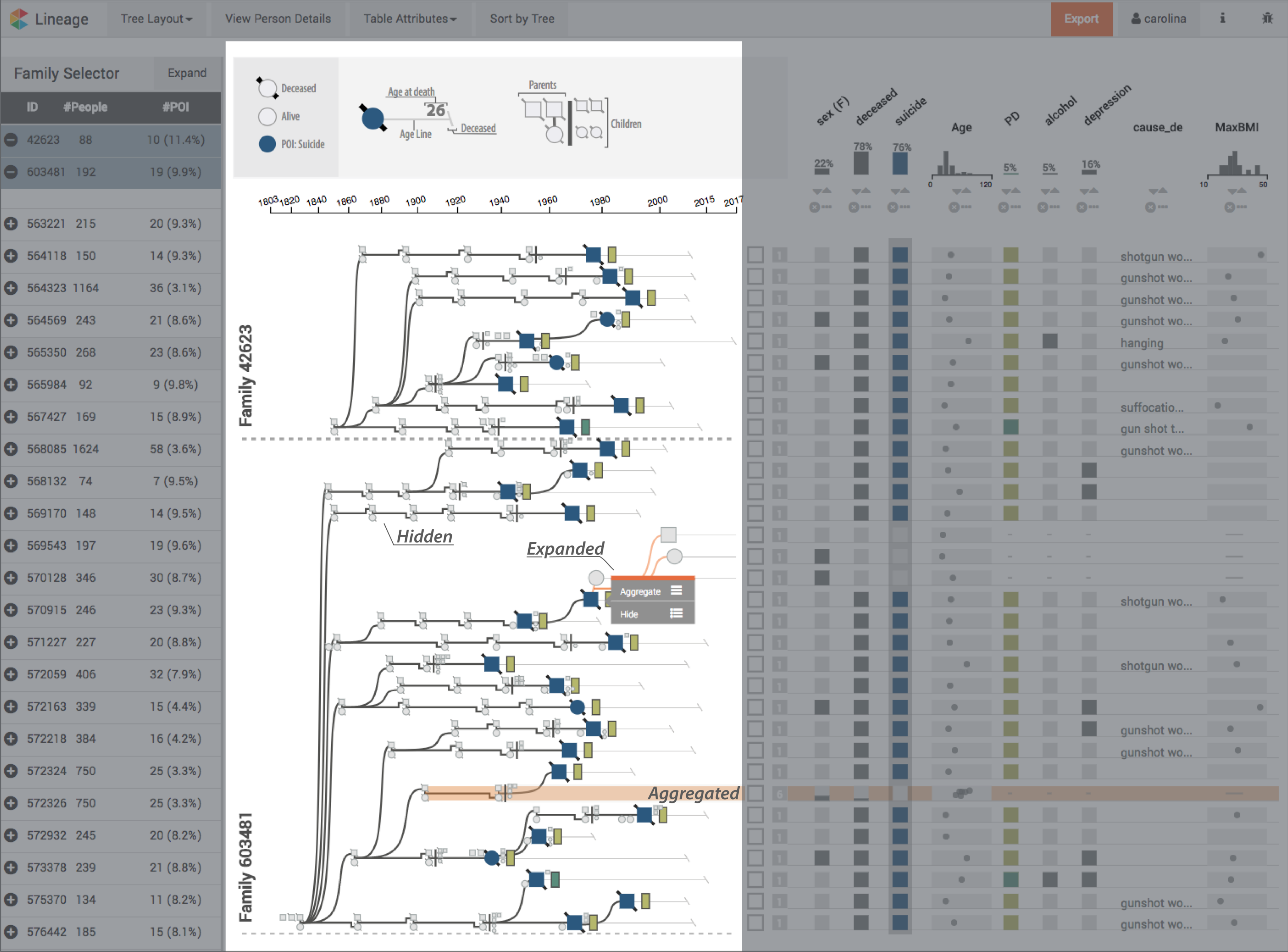
Genea Quilts

The screenshot displays a genealogical software interface with three main components:

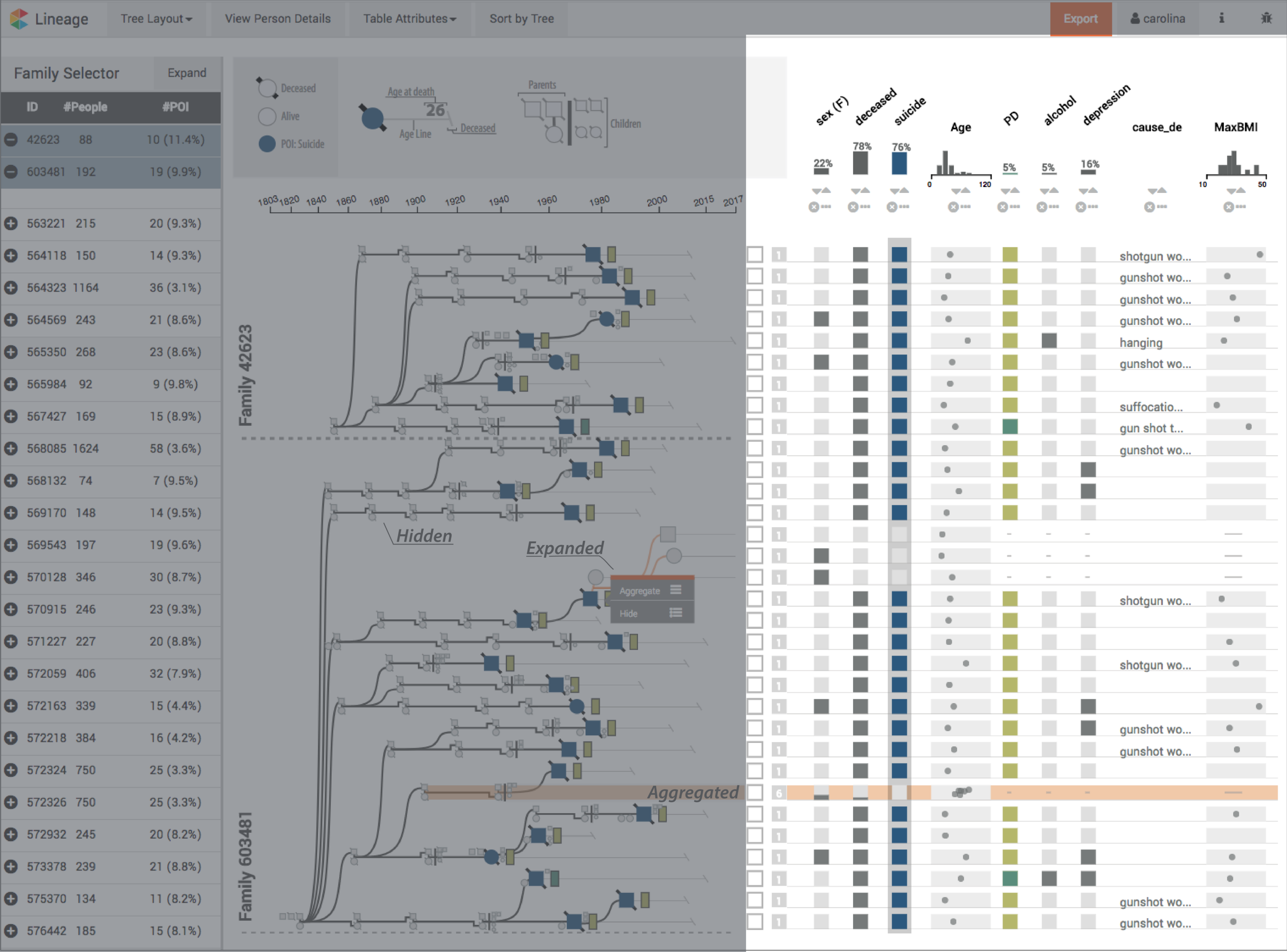
- Top Timeline:** A horizontal timeline at the top shows years 534, 1000, 1500, and 1992. A red line indicates a specific path or event over time.
- Left Panel (Pedigree Chart):** A vertical list of names, each preceded by a gender symbol (♂ for male, ♀ for female). Names include:
 - ♂ Henry IV the Great //
 - ♀ Margaret of Valois //
 - ♂ Robert /Devereux/
 - ♀ Honora /Rogers/
 - ♀ Marie Elisabeth //
 - ♂ John /Dudley/
 - ♂ Philip III //
 - ♀ Margaret of Austria //
 - ♂ Edward Beauchamp /Seymour/
 - ♂ Ferdinand II //
 - ♀ Isabel /Orley/
 - ♂ Thomas /Seymour/
 - ♂ Thomas /Howard/
 - ♀ Aletheia /Talbot/
 - ♂ William of Newcastle /Cavendish/
 - ♀ Elizabeth /Basset/
 - ♂ Henry /Howard/
 - ♂ Theophilus /Howard/
 - ♀ Elizabeth /Dunbar/
 - ♀ Catherine /Howard/
 - ♂ William of Berkshire /Cecil/
 - ♂ Robert /Devereux/
 - ♀ Frances /Howard/
 - ♂ Robert /Carr/
 - ♂ Thomas of Berkshire /Howard/
 - ♀ Elizabeth /Cecil/
 - ♂ Ivan /Rayevski/
 - ♂ Constantine /Volkonski/
 - ♂ Ivan of Shestov //
 - ♂ William /Hill/
 - ♀ Eleanor /Boyle/
- Right Panel (Search Results):** A search results window showing details for a specific individual:
 - Search:** * (with a dropdown arrow)
 - Attribute | Value**
 - BIRT DATE: 13 DEC 1553
 - BIRT PLAC: Pau, Navarre, France
 - BURI PLAC: St. Denis, France
 - COMP: 0
 - DEAT DATE: 14 MAY 1610
 - DEAT PLAC: Paris, France
 - ID: 1740
 - LAYER: 128
 - NAME: Henry IV the Great
 - SEX: M
 - TITL: King of France



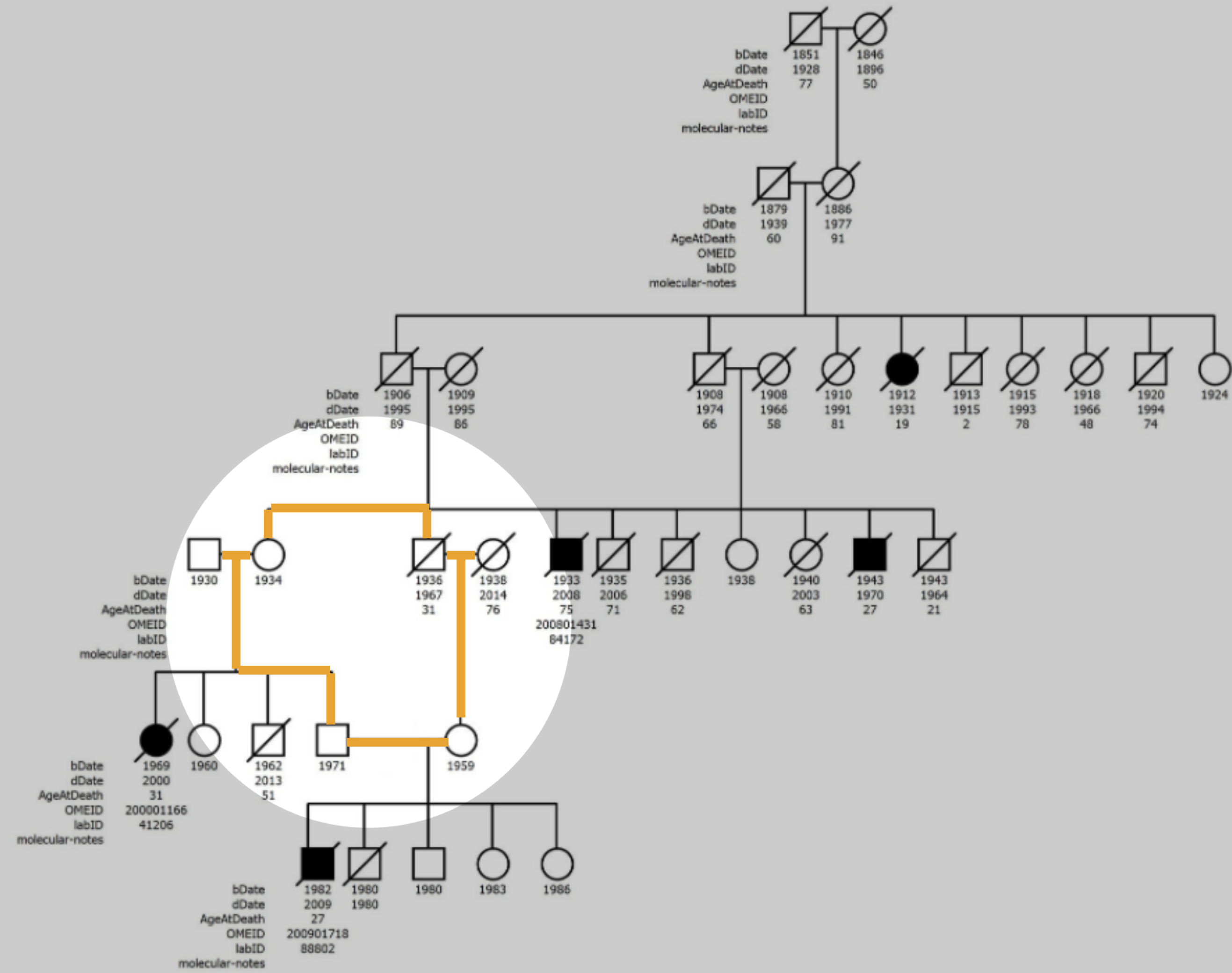
1. Select Families of Interest



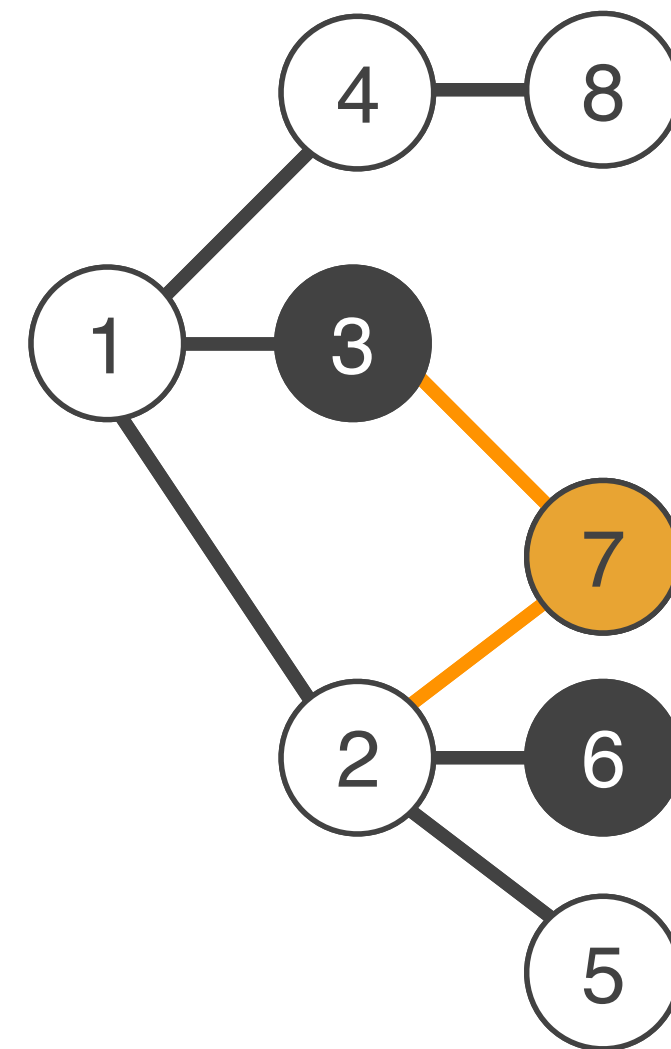
- 1. Select Families of Interest
- 2. De-cycle and linearize graph



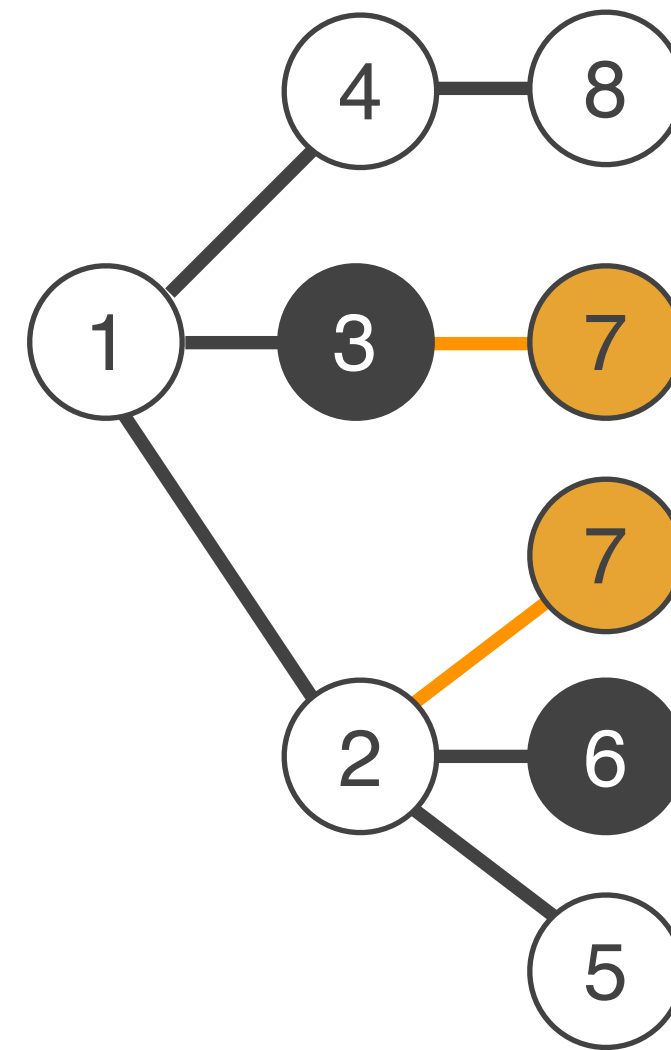
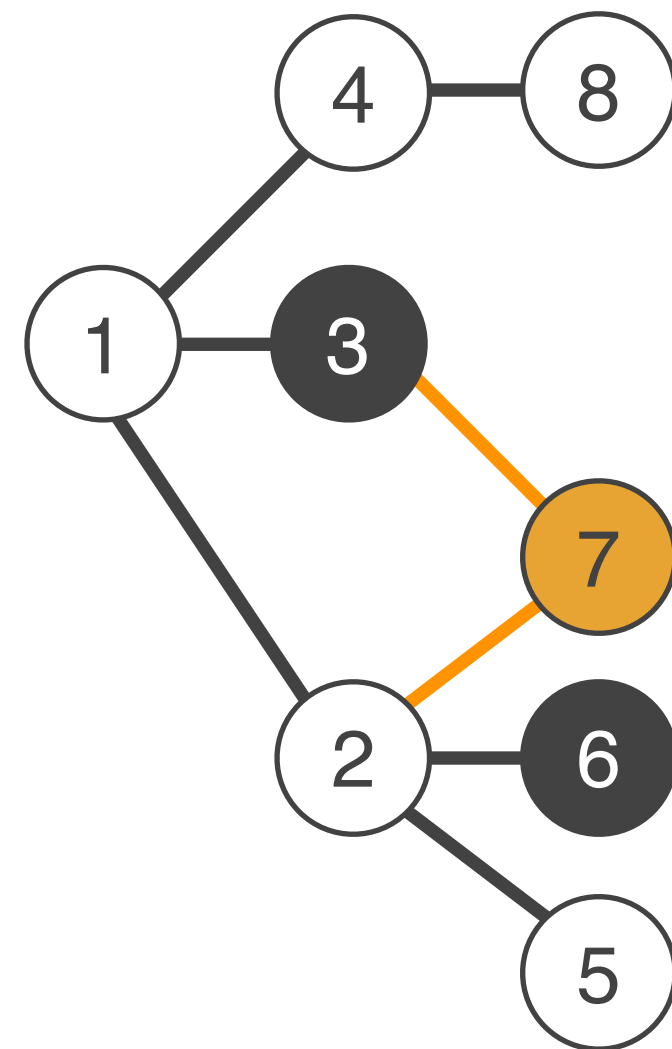
- 1. Select Families of Interest
- 2. De-cycle and linearize graph
- 3. Plot attributes in table



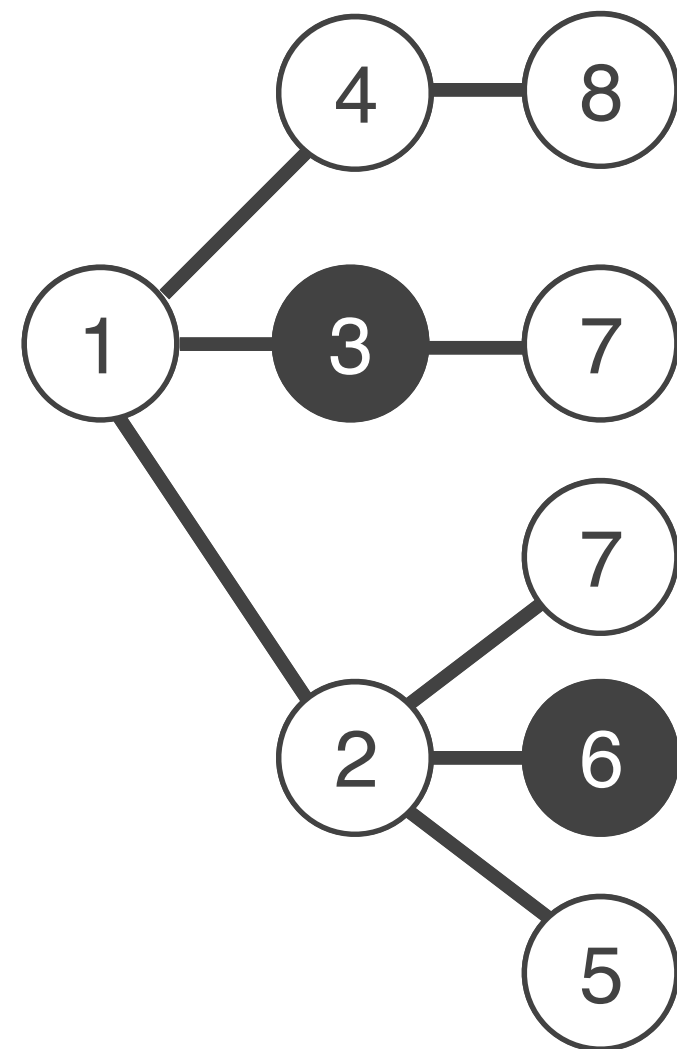
De-Cycling



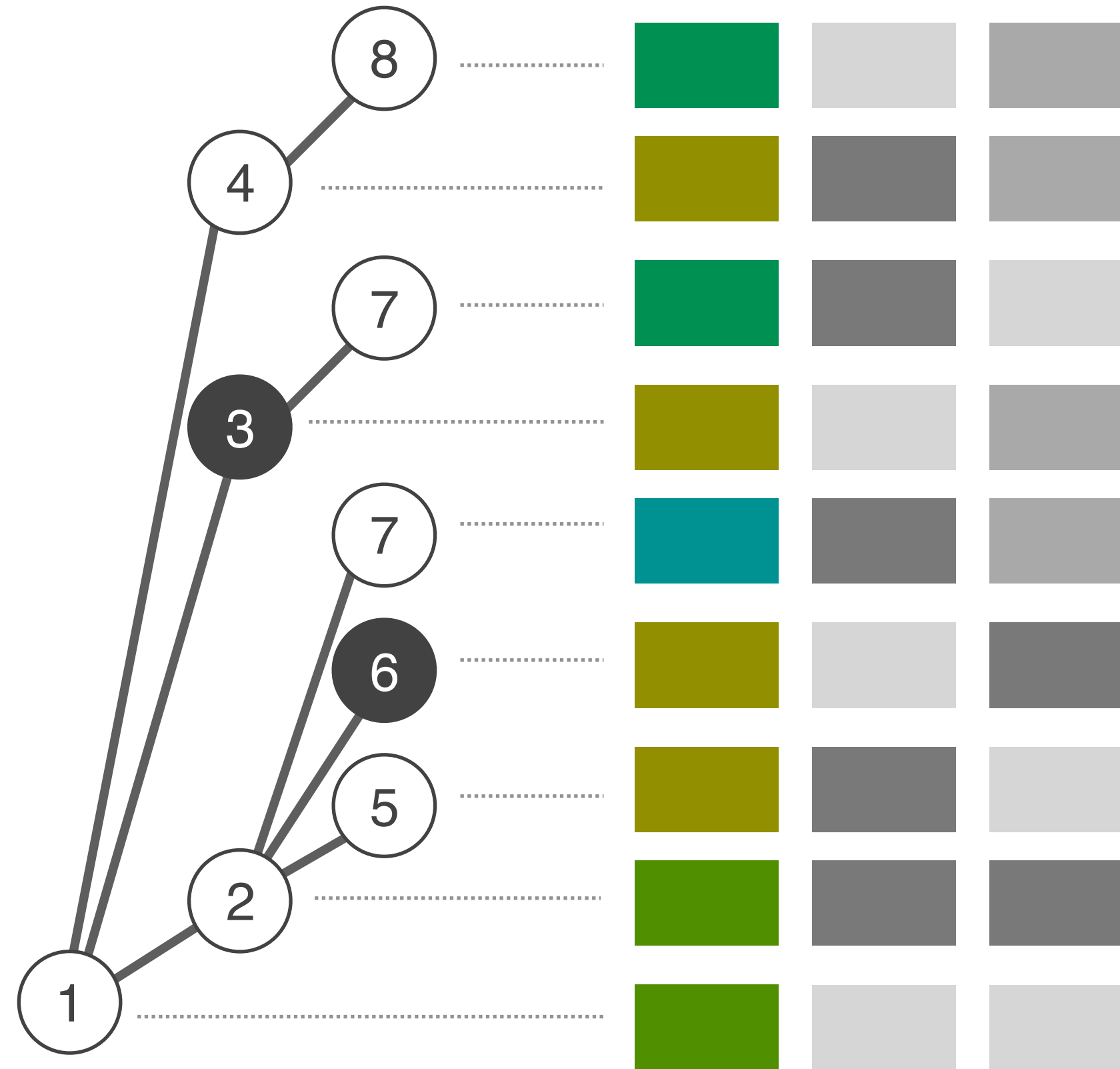
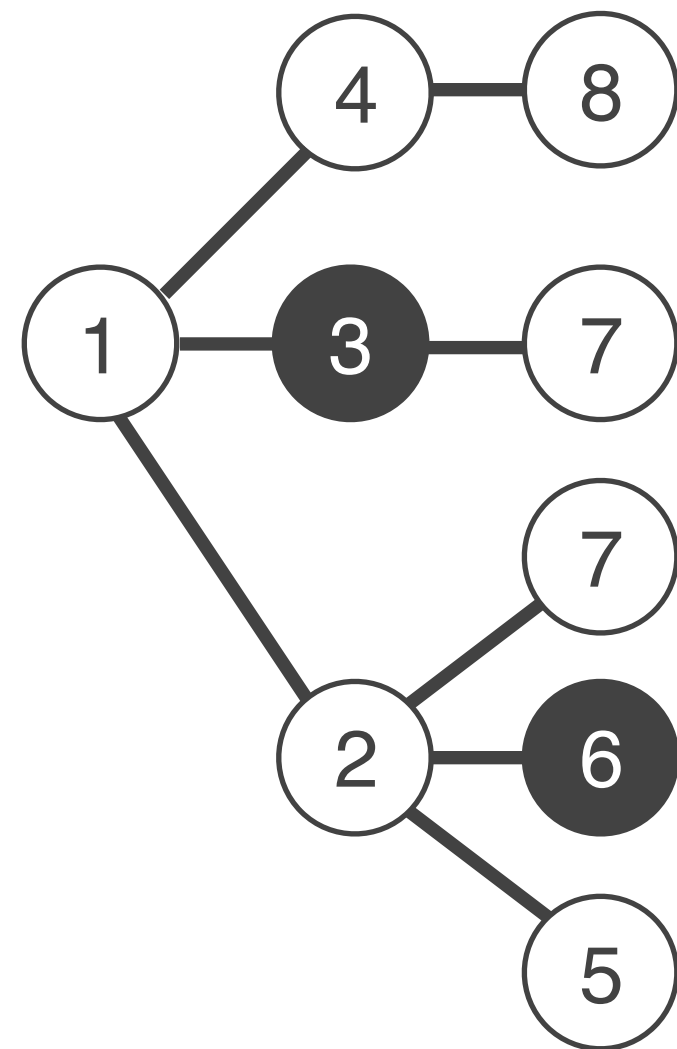
De-Cycling



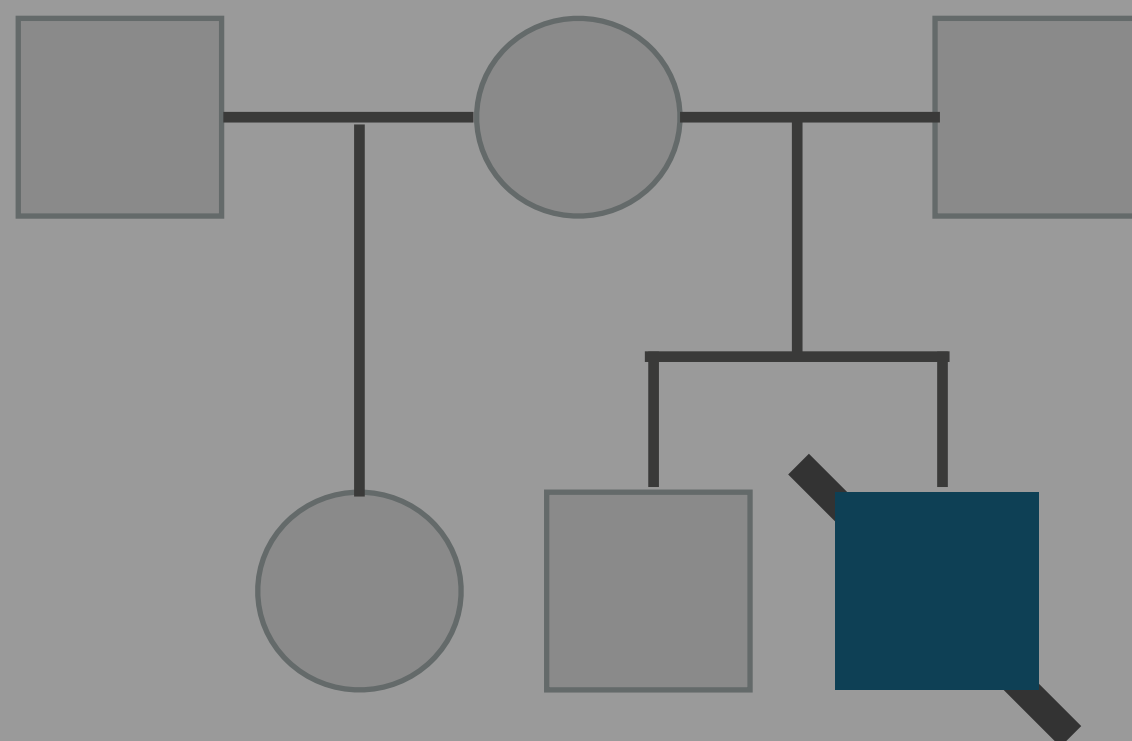
Linearizing



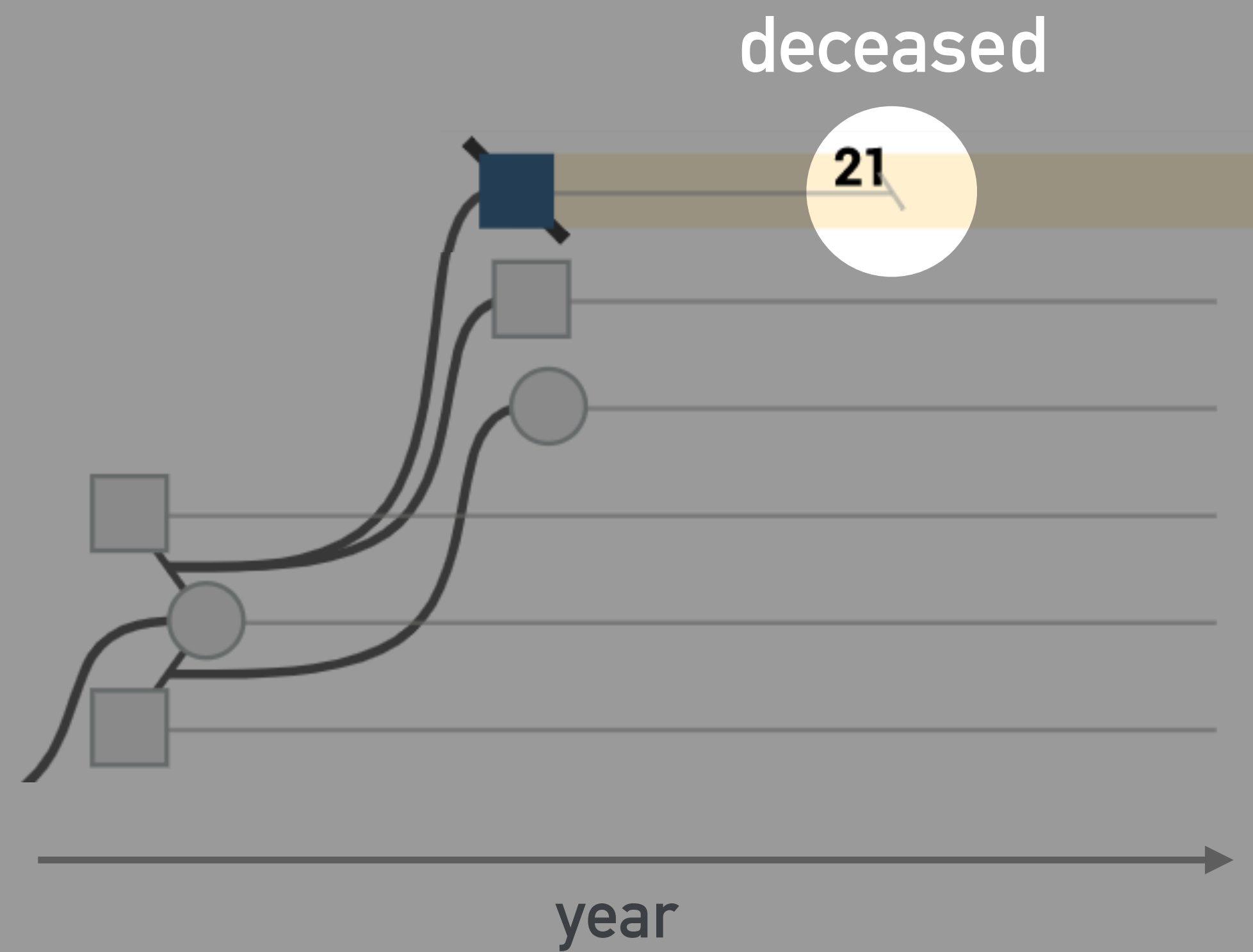
Linearizing




Traditional Pedigree Chart

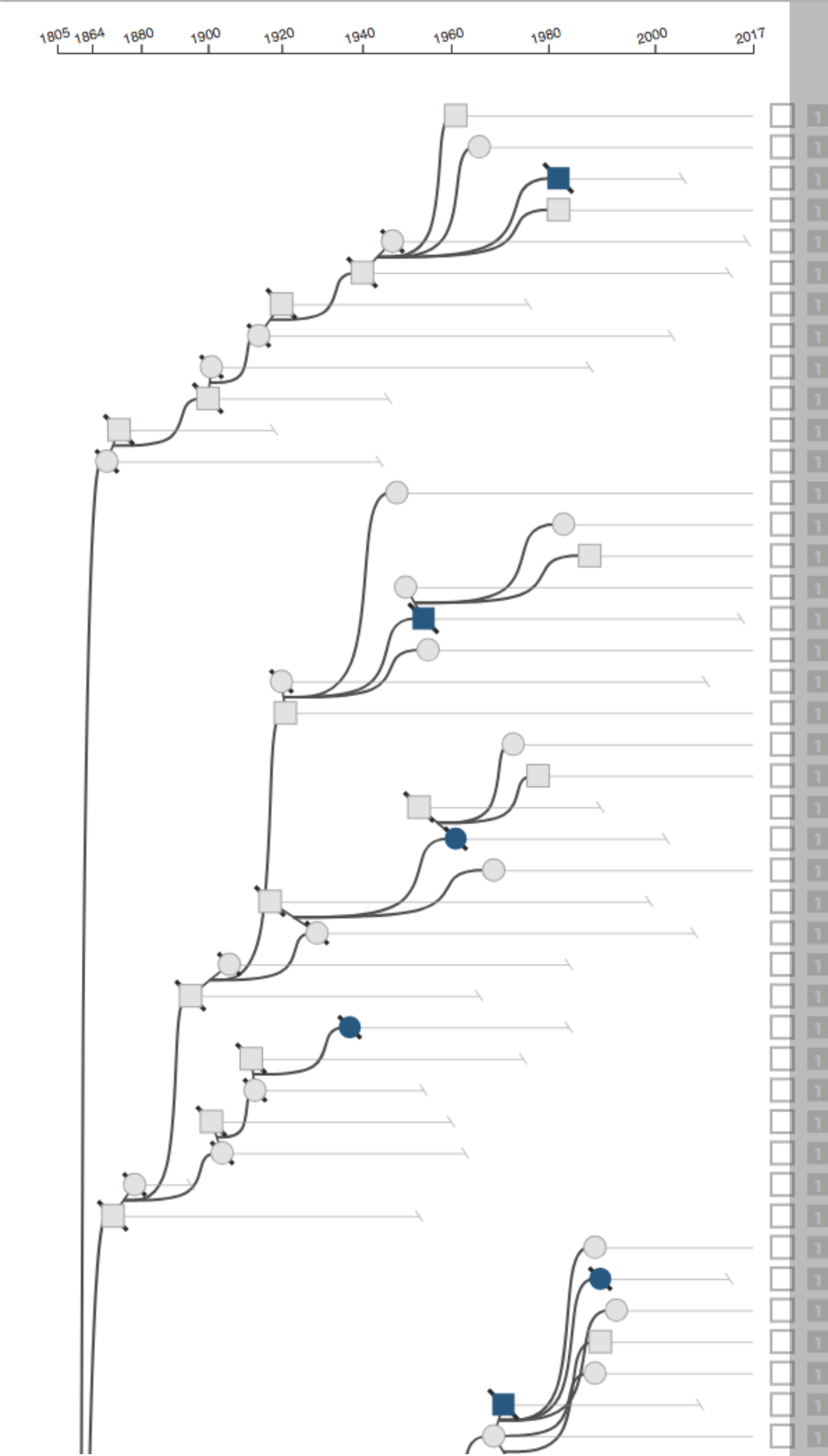
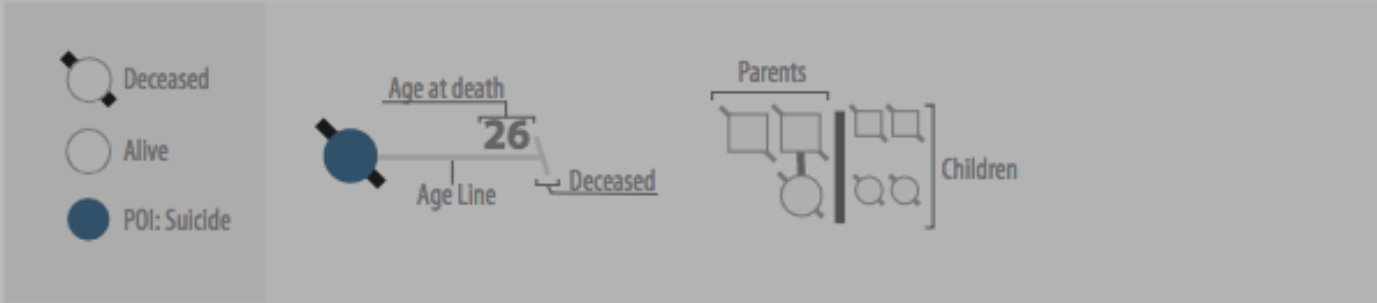


Lineage



Family Selector		Expand
ID	#People	#POI
 38	121	12 (9.9%)

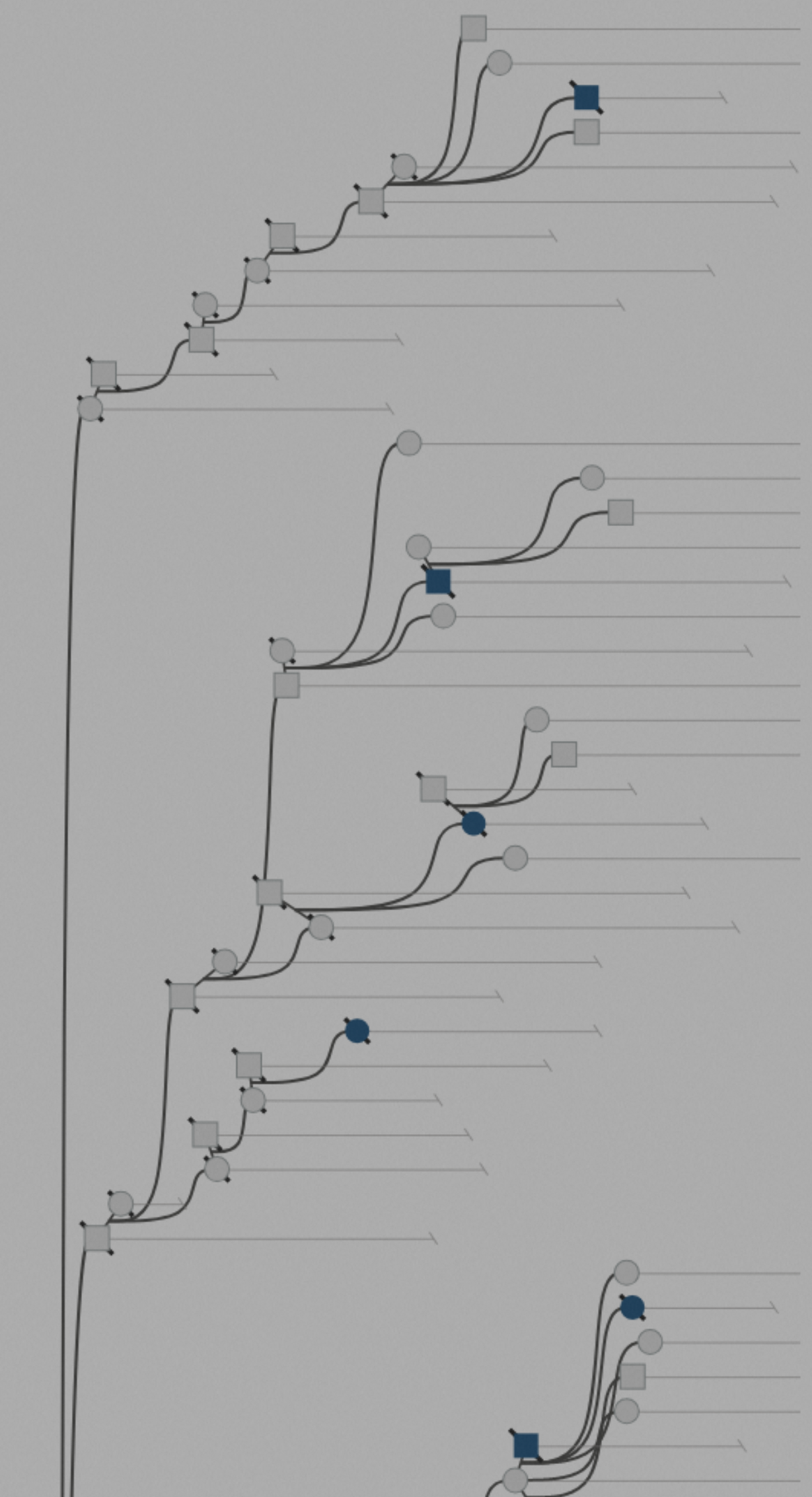
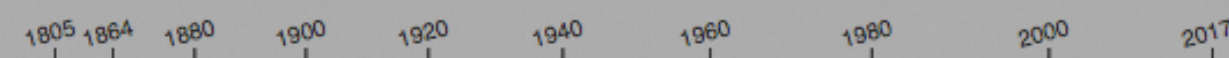
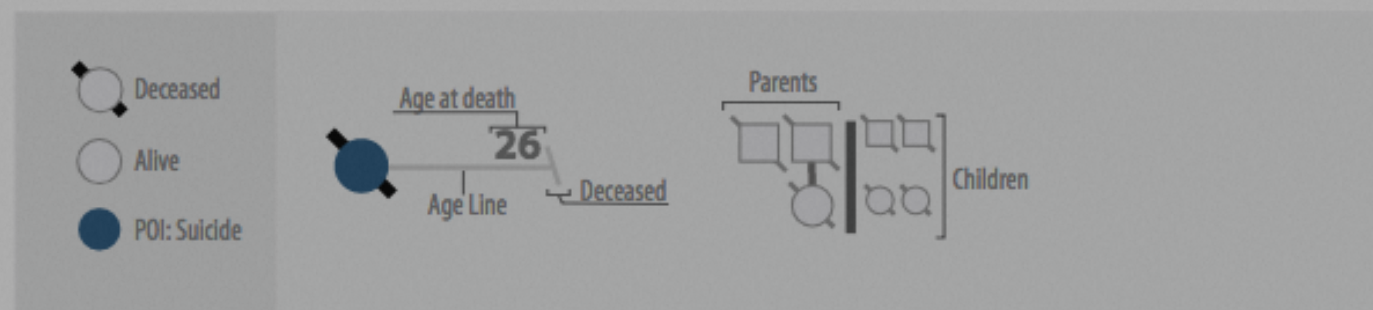
38	121	12 (9.9%)
149	113	10 (8.8%)
27251	404	39 (9.7%)
42623	81	10 (12.3%)
68939	244	23 (9.4%)
176860	426	44 (10.3%)
603481	181	19 (10.5%)
791533	114	10 (8.8%)
903988	58	5 (8.6%)



KindredI	Relative	sex (F)	deceased	suicide	Age	bipolar spectrum ill.	anxiety-non-trauma	alcohol	PD	psychosis	depression	cause_de
		50%	61%	10%		0.0%	0.0%	0.8%	2%	0.0%	2%	
1	38	#781										
1	38	#784										
1	38	#56604										gunshot wo...
1	38	#5444										
1	38	#778										
1	38	#777										
1	38	#11574										
1	38	#11575										
1	38	#23088										
1	38	#23087										
1	38	#37										
1	38	#35										
1	38	#66559										
1	38	#4033										
1	38	#41582										
1	38	#65051										
1	38	#66561										gunshot wo...
1	38	#66560										
1	38	#53797										
1	38	#53798										
1	38	#9348										
1	38	#1073										
1	38	#24070										
1	38	#61046										mixed drug...
1	38	#47326										
1	38	#22124										
1	38	#61047										
1	38	#66556										
1	38	#66557										
1	38	#54490										
1	38	#34847										
1	38	#39657										
1	38	#705										
1	38	#28375										
1	38	#34										
1	38	#32										
1	38	#59713										
1	38	#42257										gunshot wo...
1	38	#17565										
1	38	#40786										
1	38	#16807										
1	38	#42258										gunshot wo...
1	38	#40787										

Can't show
many people

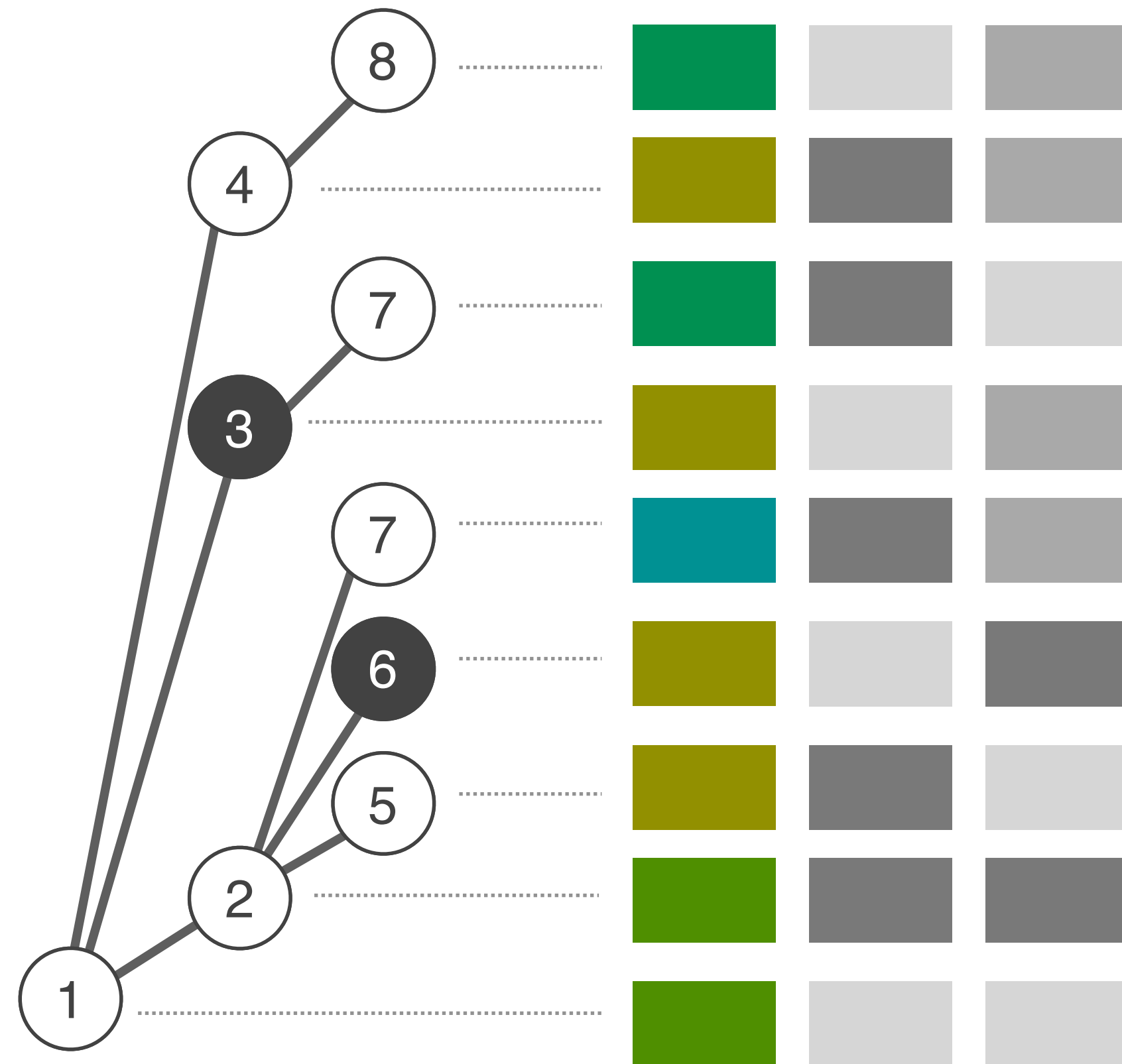
Family Selector		Expand
ID	#People	#POI
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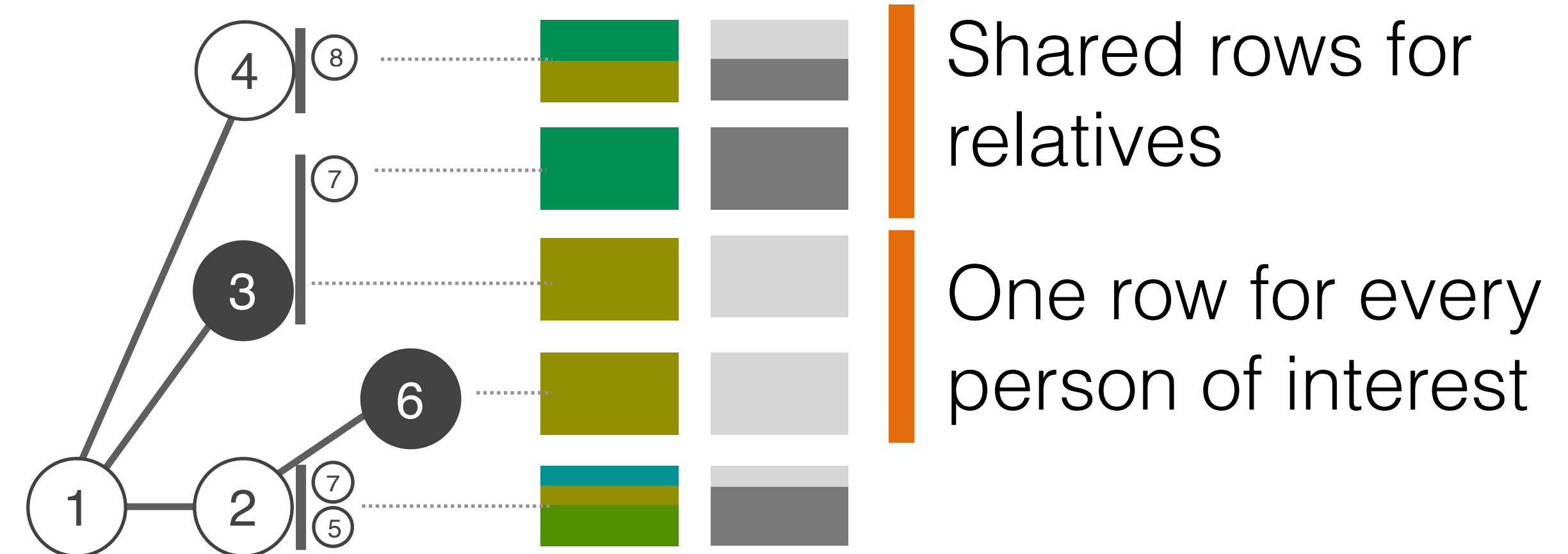
	KindredI	Relative	se	de	su	Age	bip	an	alc	Pt	ps	det	cause_de
			50%	61%	10%		0.0%	0.0%	0.8%	2%	0.0%	2%	
	1	38	#781					-	-	-	-	-	
	1	38	#784					-	-	-	-	-	
	1	38	#56604										gunshot wo...
	1	38	#5444					-	-	-	-	-	
	1	38	#778					-	-	-	-	-	
	1	38	#777					-	-	-	-	-	
	1	38	#11574					-	-	-	-	-	
	1	38	#11575					-	-	-	-	-	
	1	38	#23088					-	-	-	-	-	
	1	38	#23087					-	-	-	-	-	
	1	38	#37					-	-	-	-	-	
	1	38	#35					-	-	-	-	-	
	1	38	#66559					-	-	-	-	-	
	1	38	#4033					-	-	-	-	-	
	1	38	#41582					-	-	-	-	-	
	1	38	#65051					-	-	-	-	-	
	1	38	#66561										gunshot wo...
	1	38	#66560					-	-	-	-	-	
	1	38	#53797					-	-	-	-	-	
	1	38	#53798					-	-	-	-	-	
	1	38	#9348					-	-	-	-	-	
	1	38	#1073					-	-	-	-	-	
	1	38	#24070					-	-	-	-	-	
	1	38	#61046										mixed drug...
	1	38	#47326					-	-	-	-	-	
	1	38	#22124					-	-	-	-	-	
	1	38	#61047					-	-	-	-	-	
	1	38	#66556					-	-	-	-	-	
	1	38	#66557					-	-	-	-	-	
	1	38	#54490										
	1	38	#34847					-	-	-	-	-	
	1	38	#39657					-	-	-	-	-	
	1	38	#705					-	-	-	-	-	
	1	38	#28375					-	-	-	-	-	
	1	38	#34					-	-	-	-	-	
	1	38	#32					-	-	-	-	-	
	1	38	#59713					-	-	-	-	-	
	1	38	#42257										gunshot wo...
	1	38	#17565					-	-	-	-	-	
	1	38	#40786					-	-	-	-	-	
	1	38	#16807					-	-	-	-	-	
	1	38	#42258										gunshot wo...
	1	38	#40787					-	-	-	-	-	

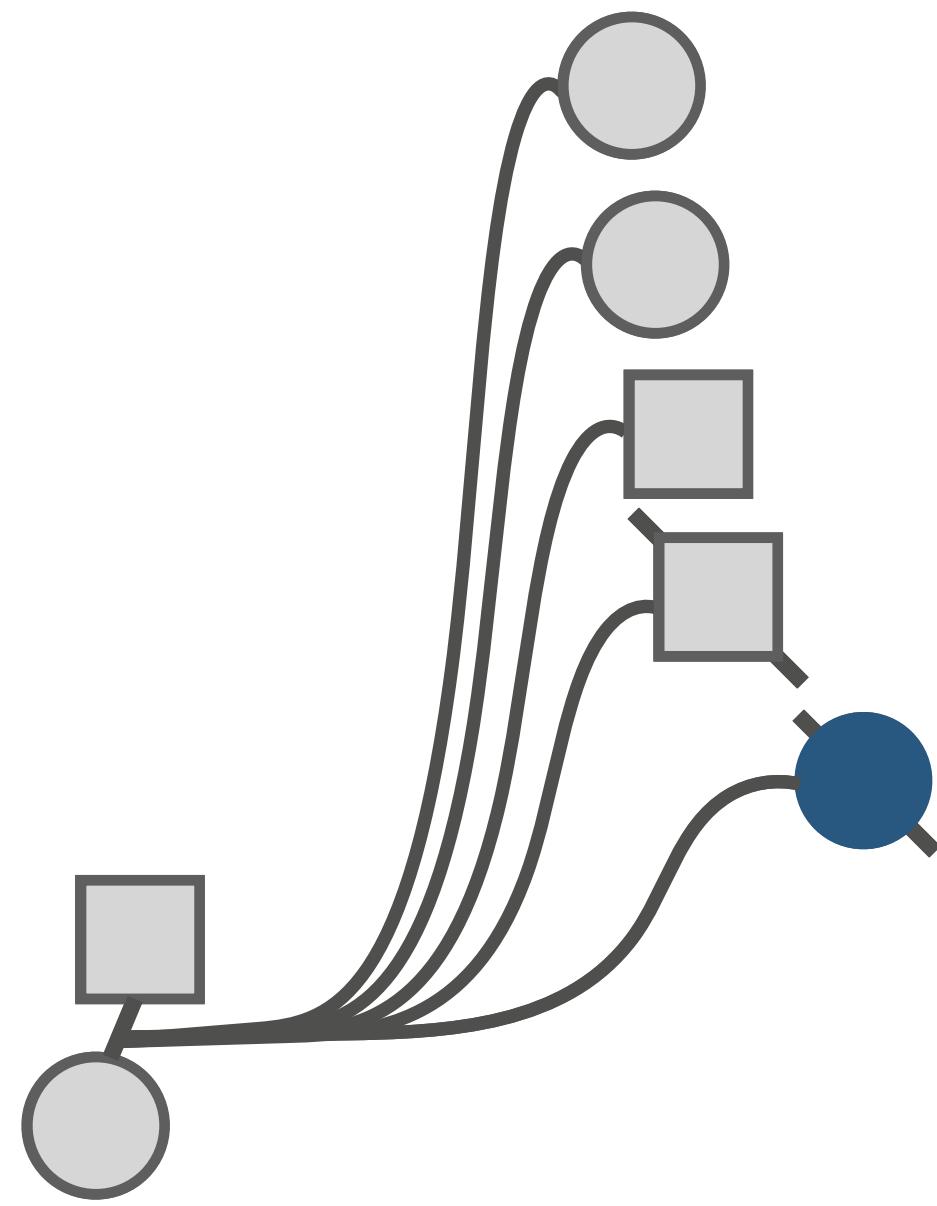
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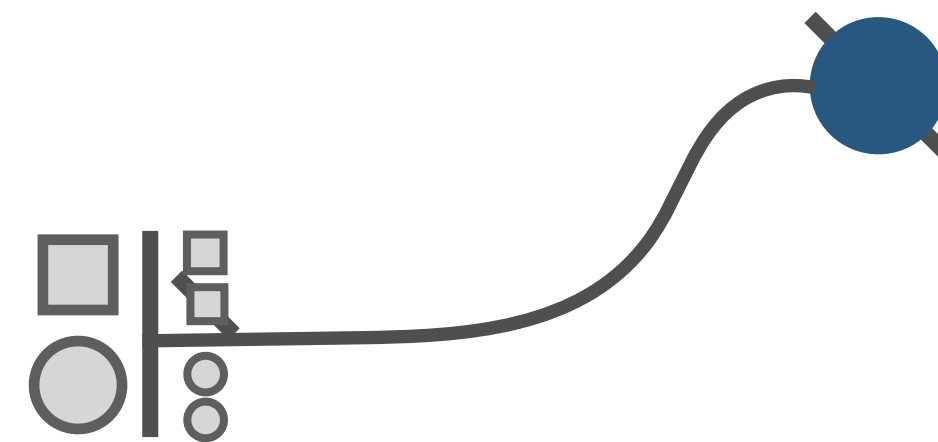
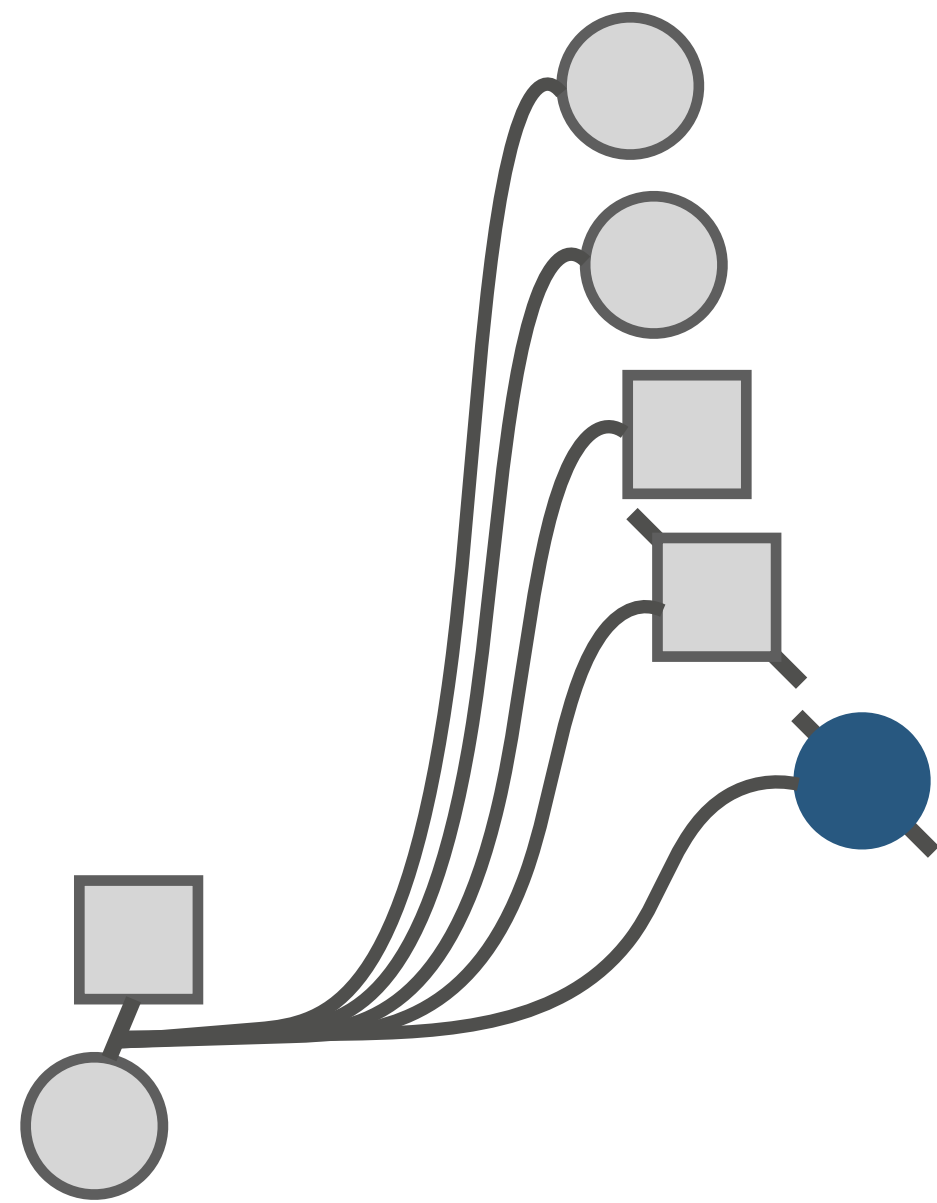
Aggregation

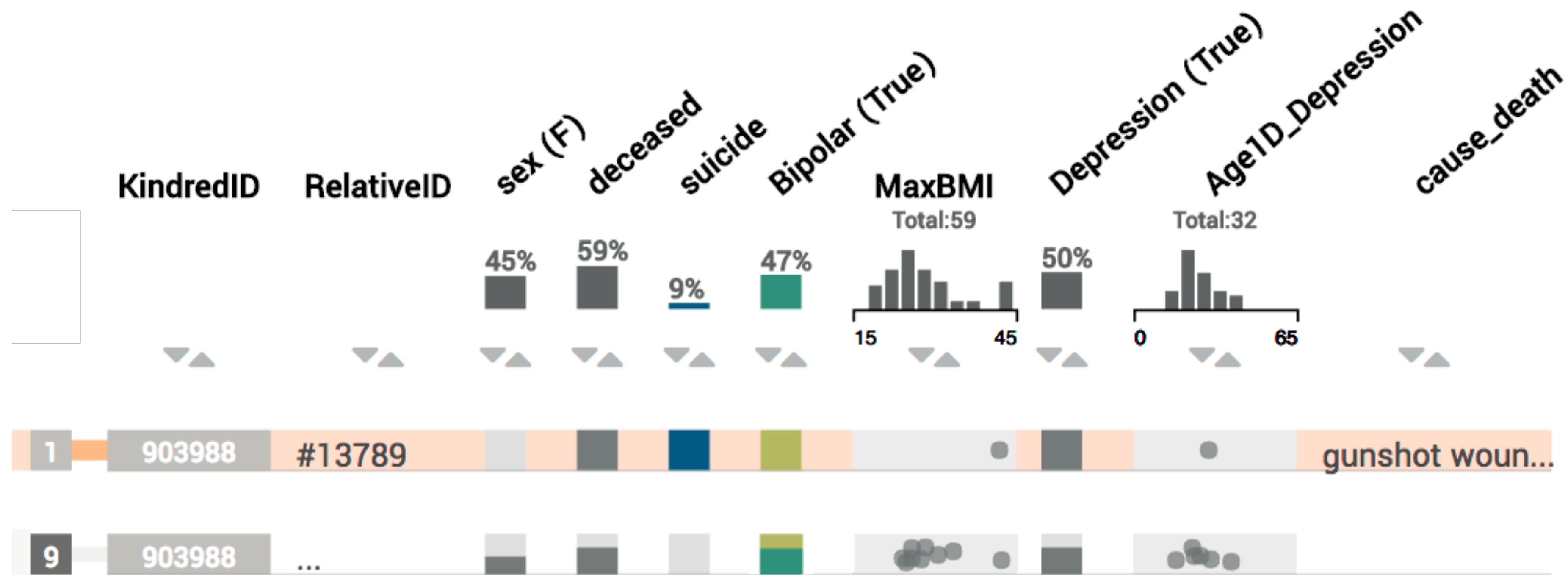
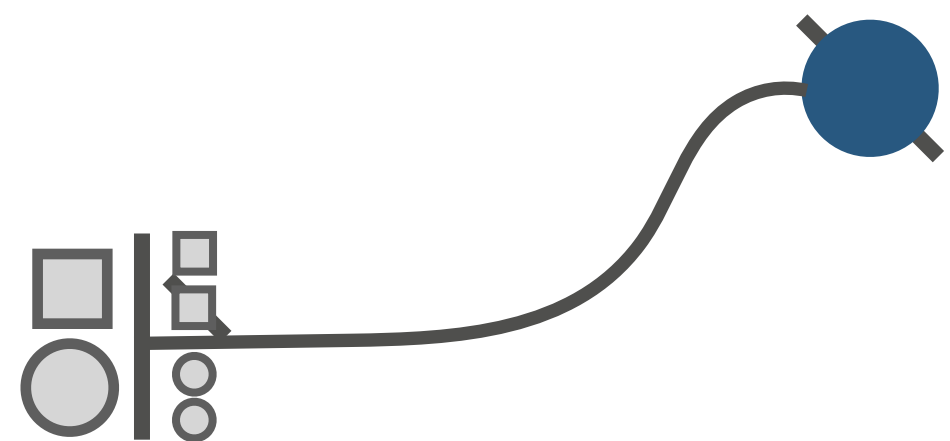


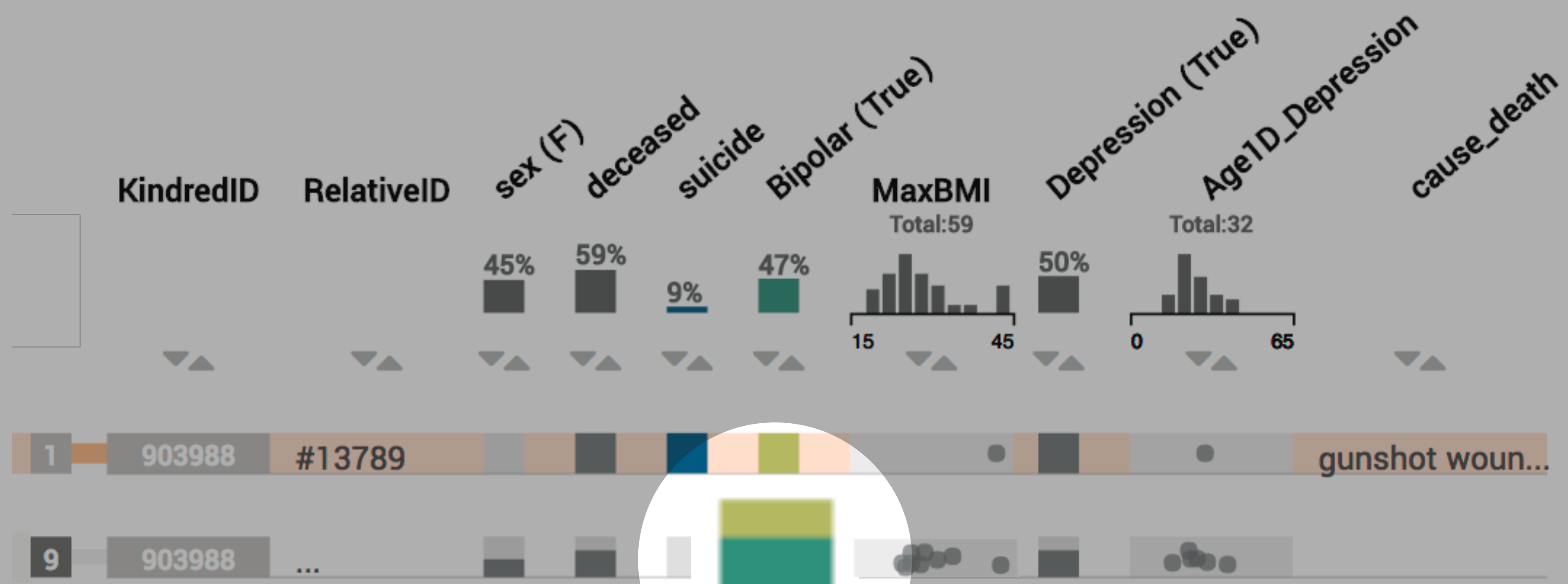
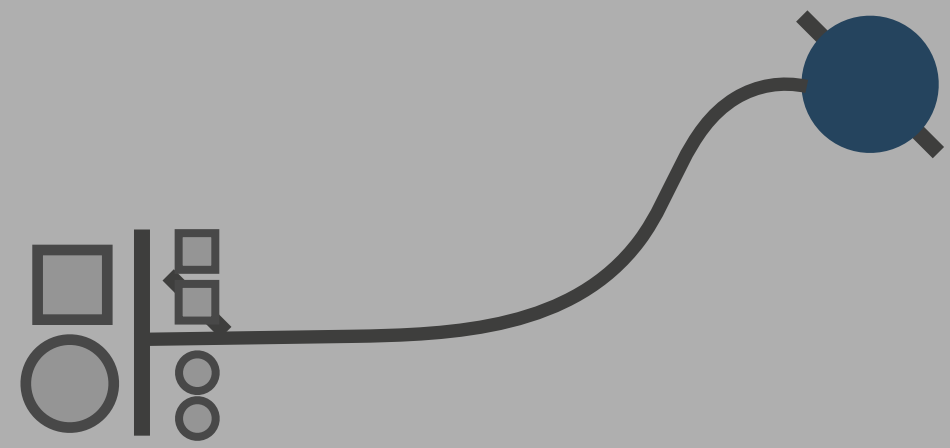
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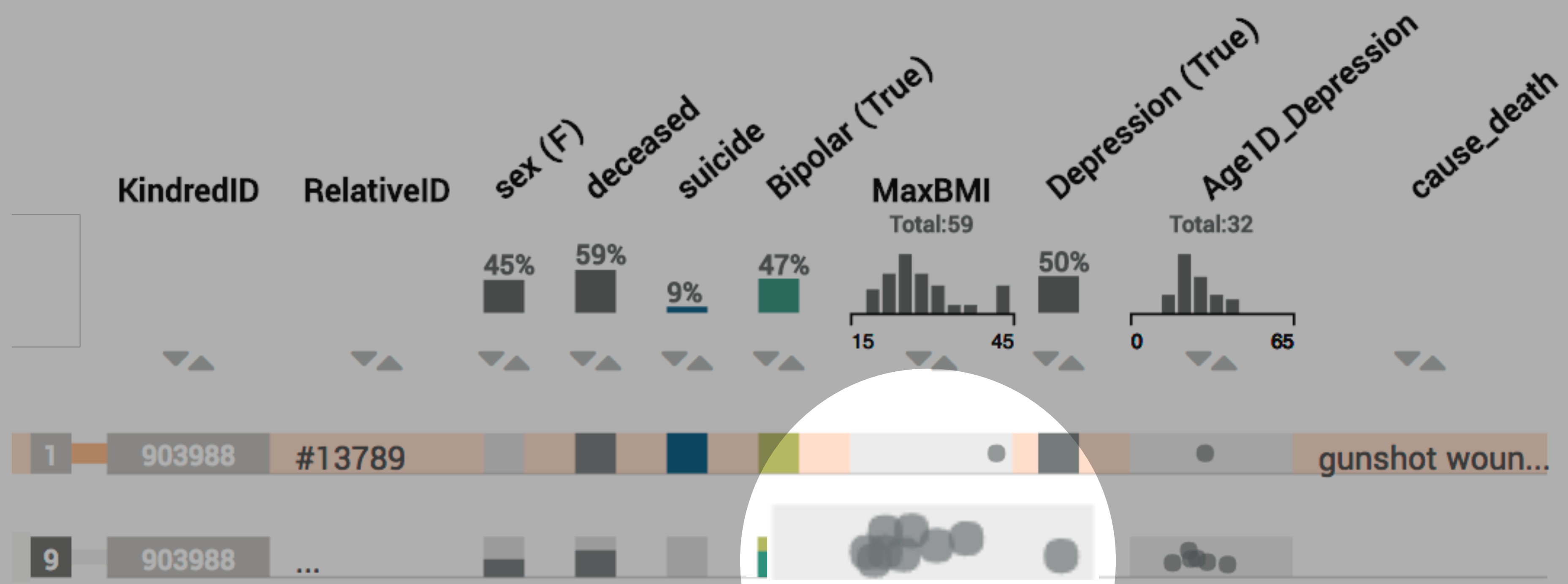
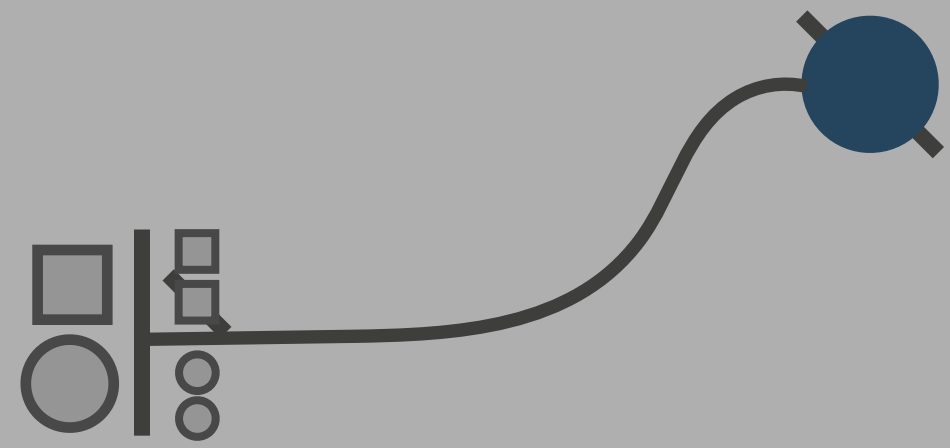




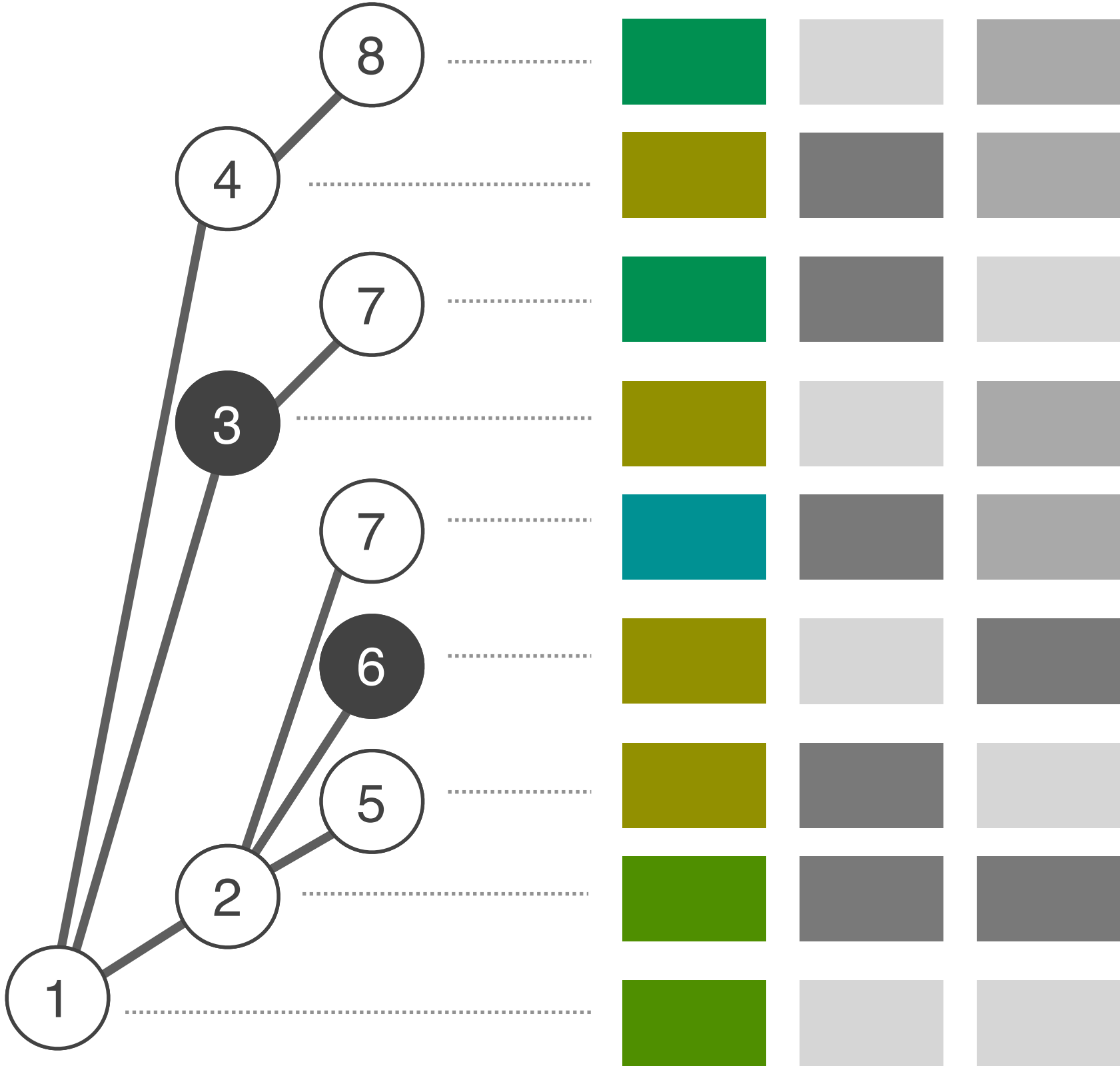




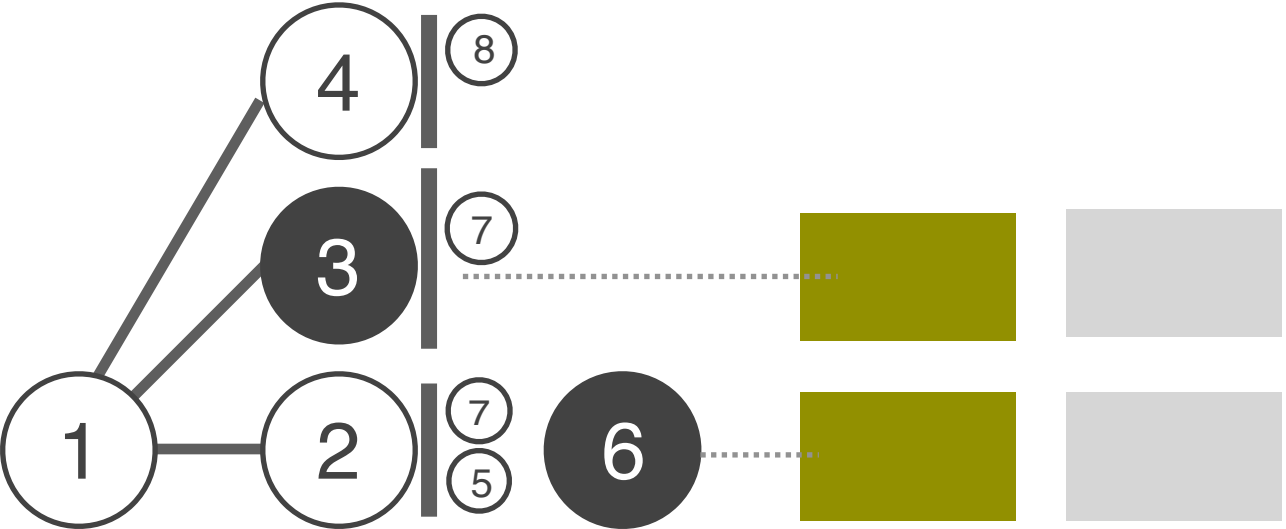
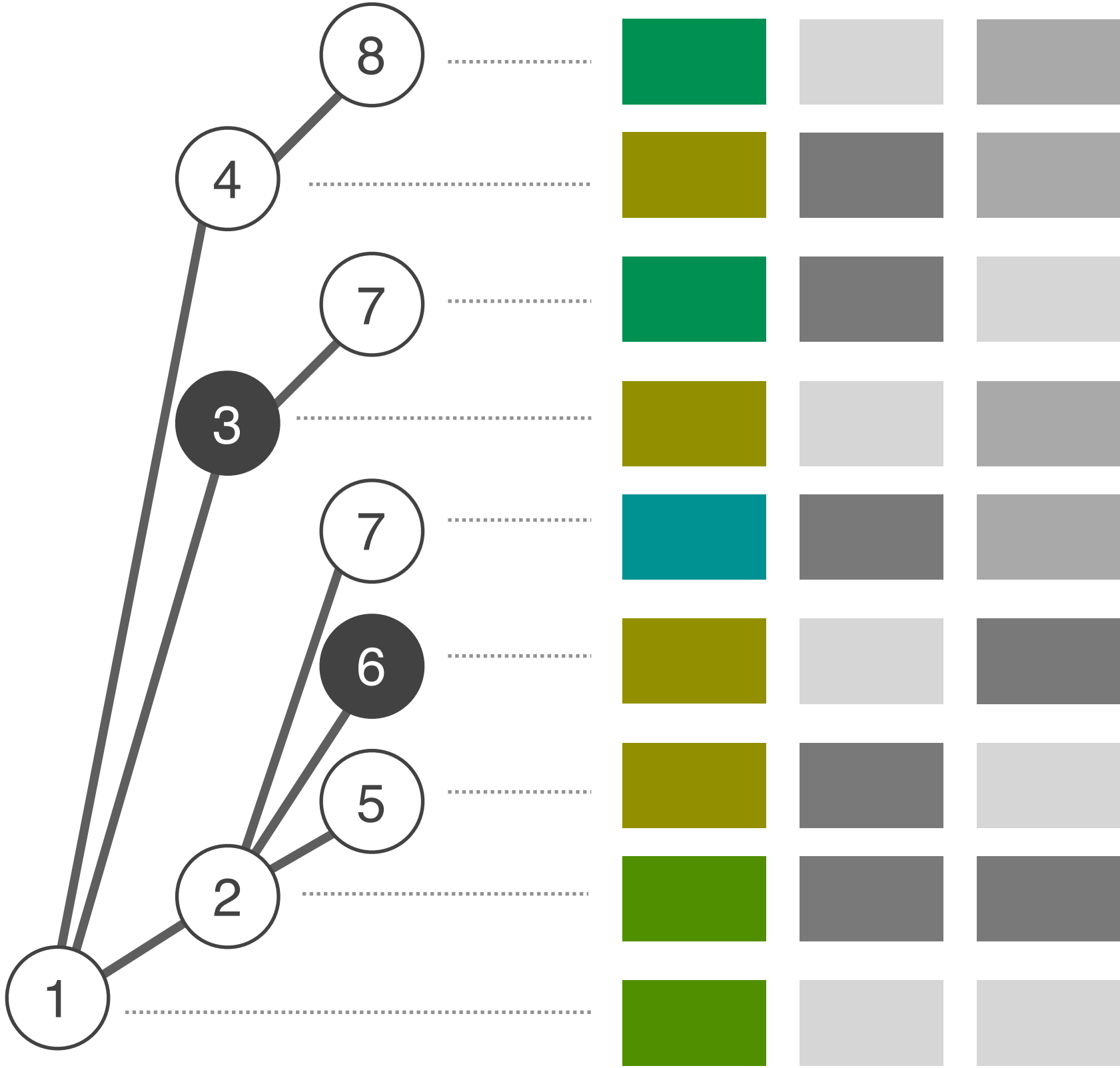




Hiding

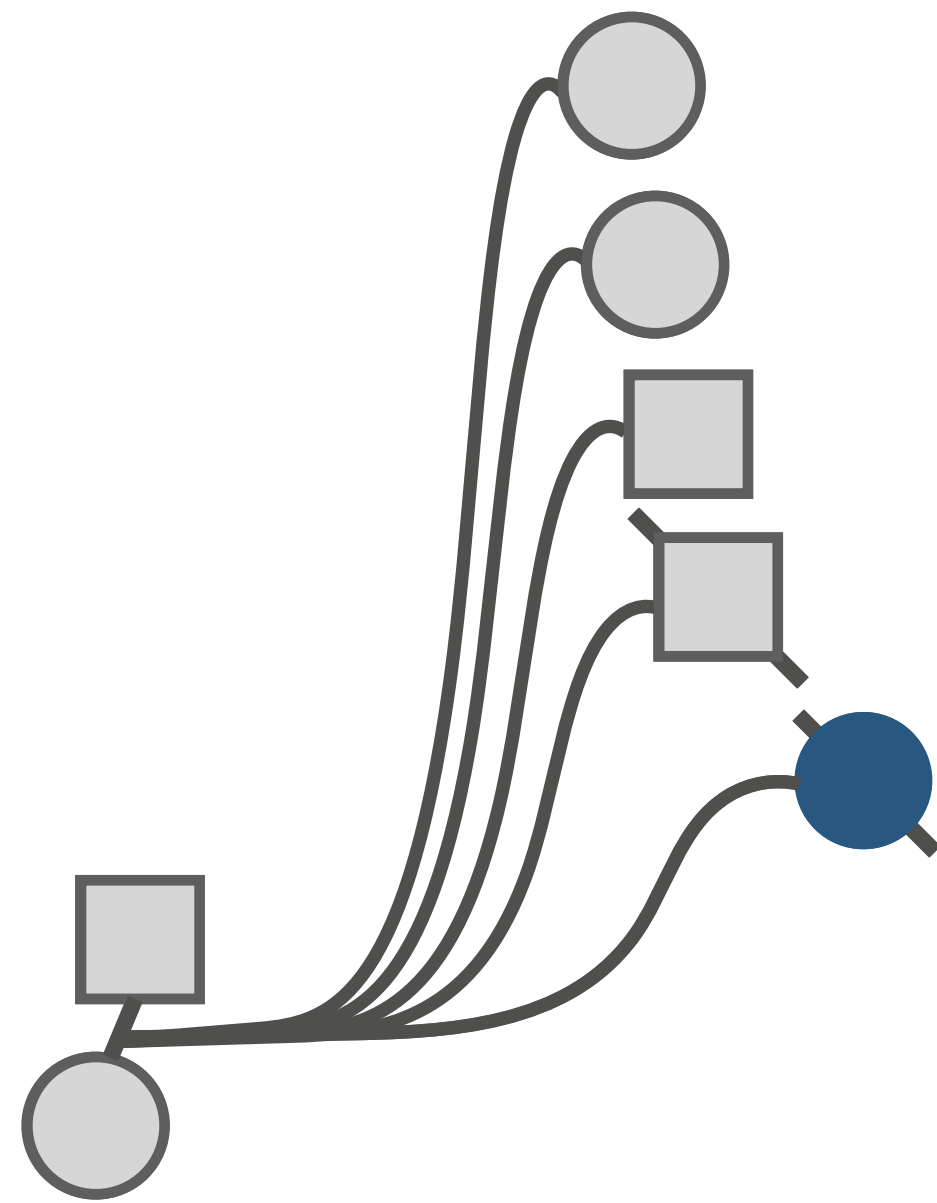


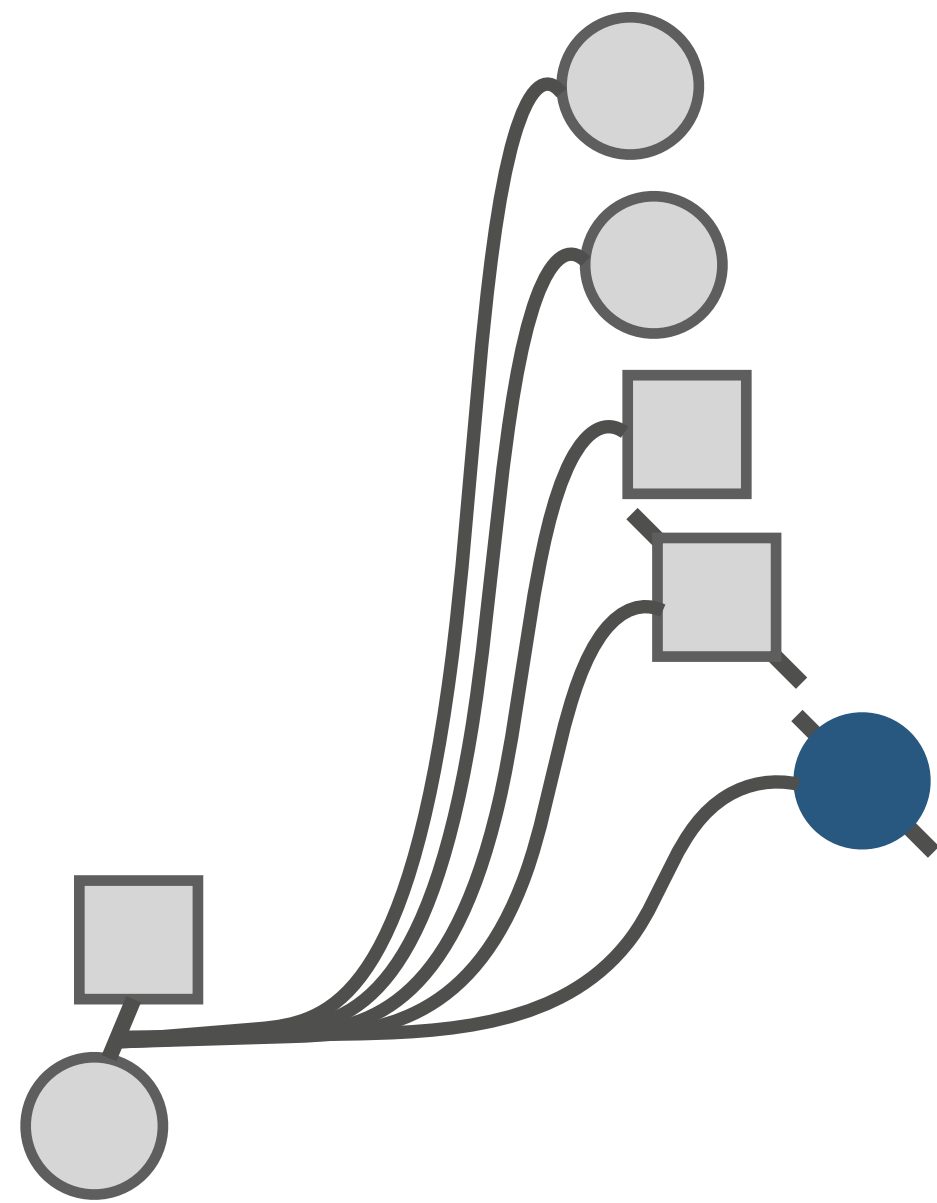
Hiding

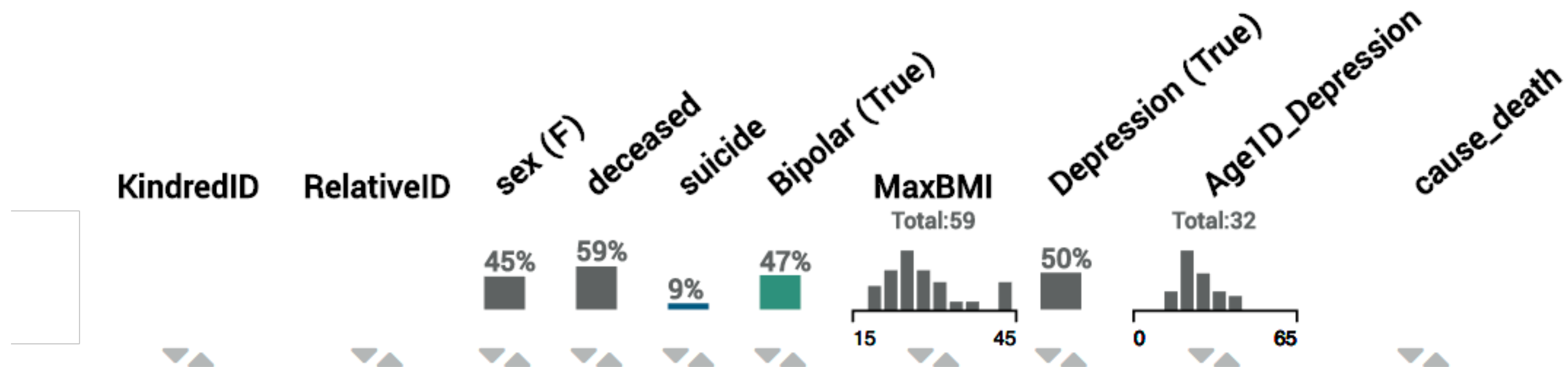


Empty Row

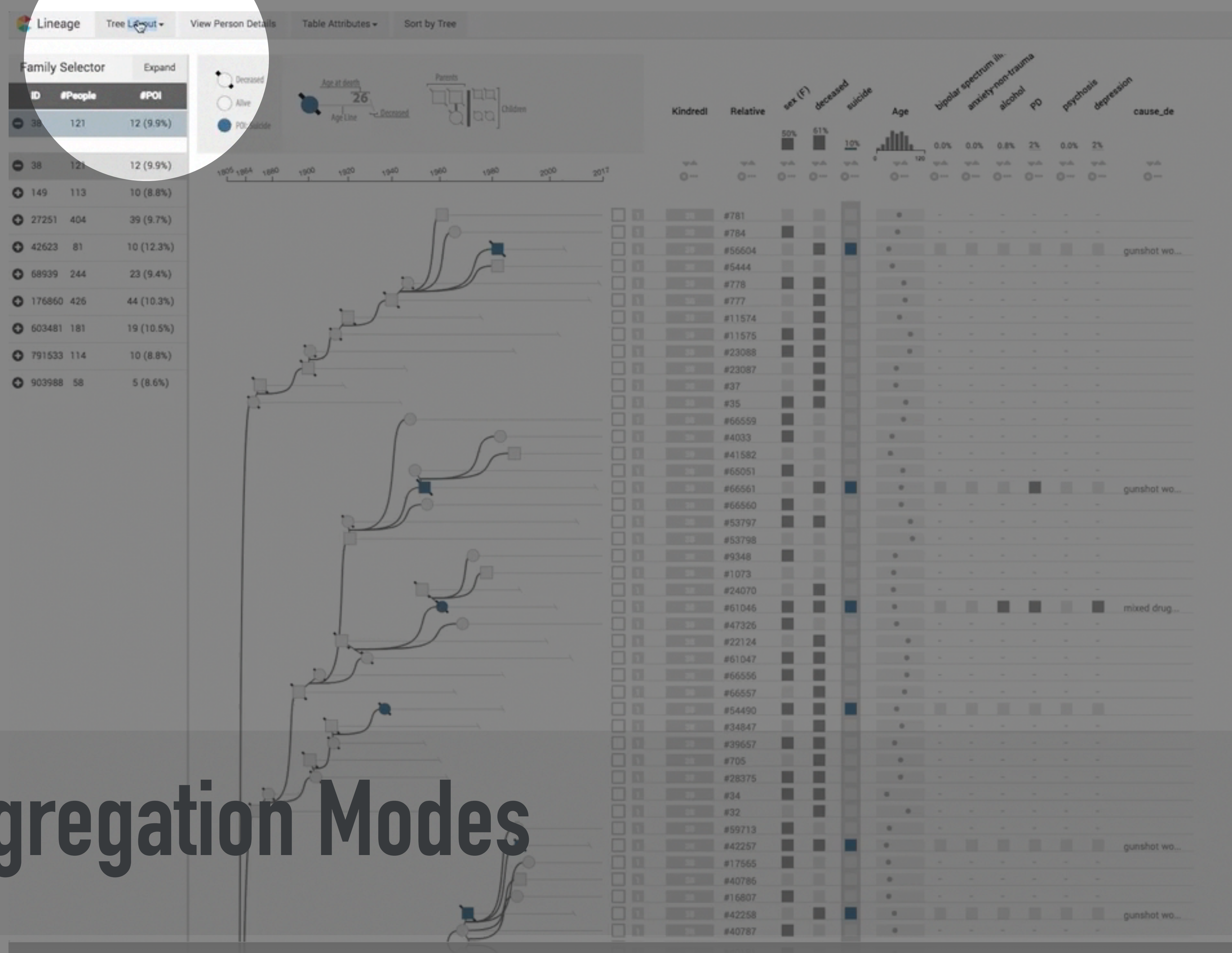
Only data for affected people

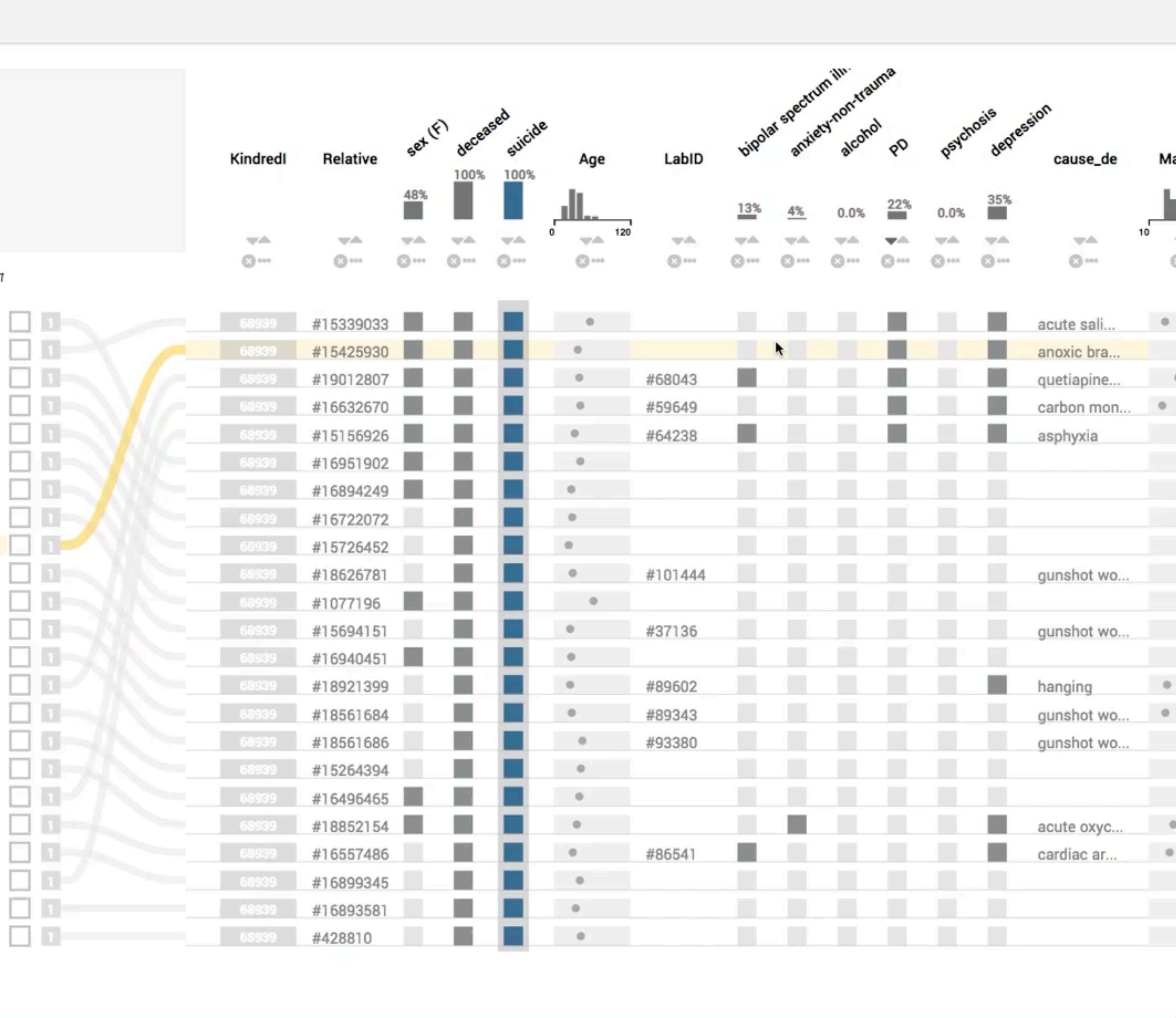






Aggregation Modes

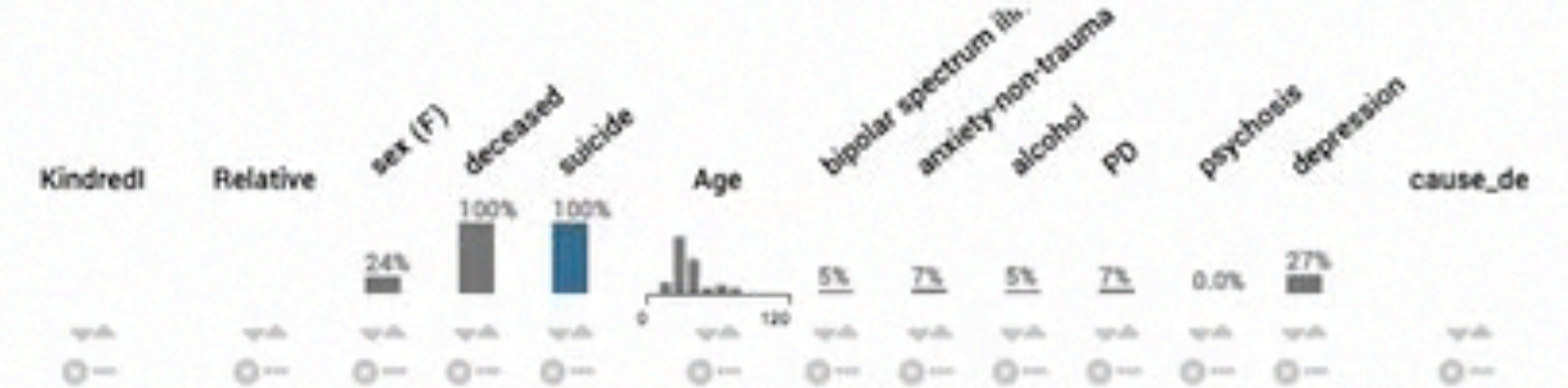
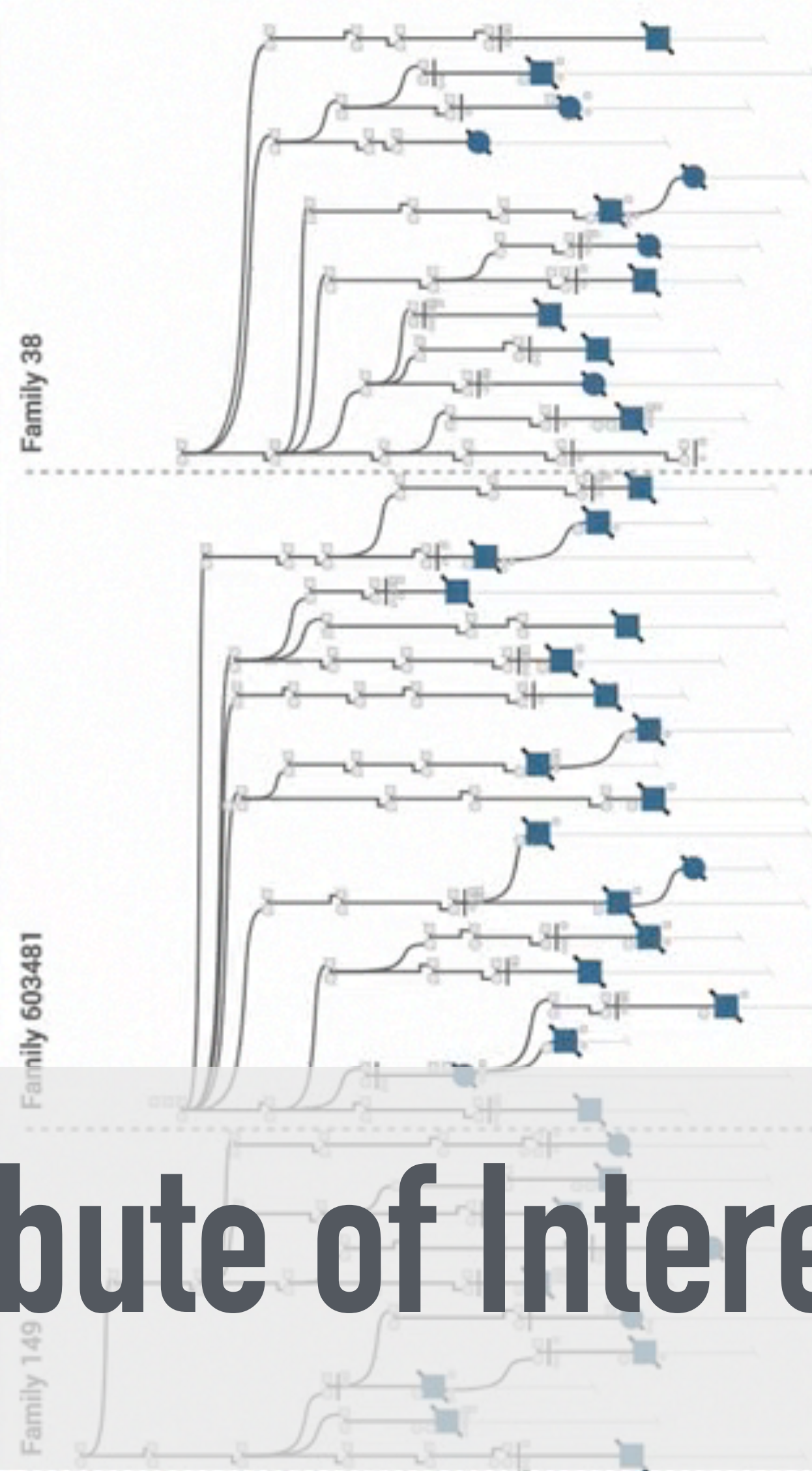
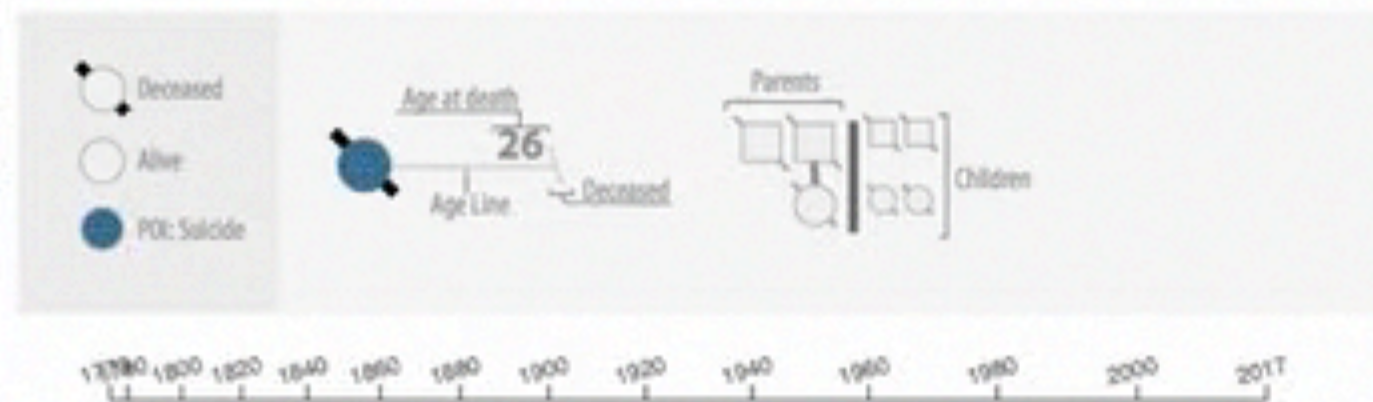




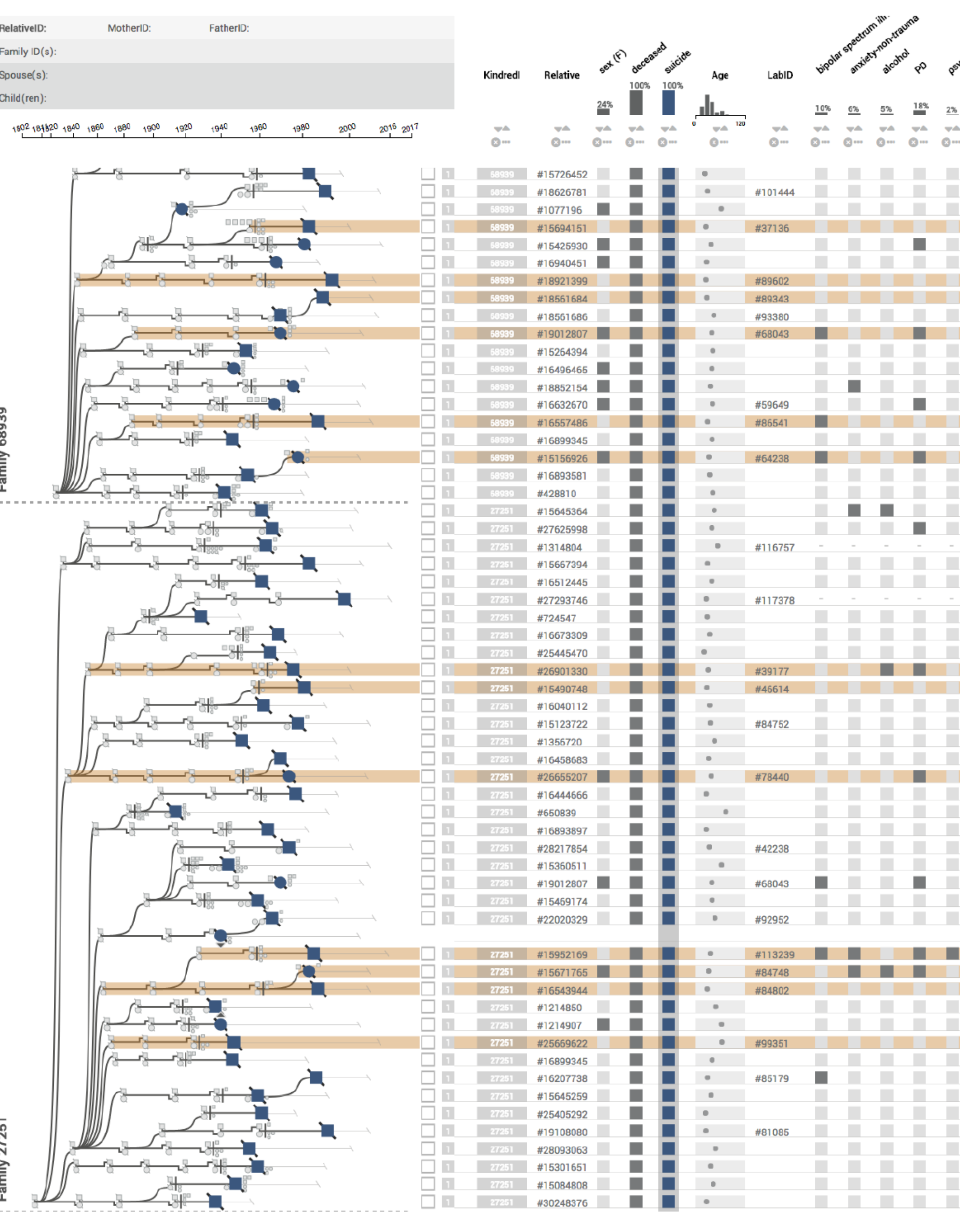
LINEAGE
IN ACTION

Family Selector		Expand
ID	#People	#POI
38	121	12 (9.9%)
149	113	10 (8.8%)
603481	181	19 (10.5%)

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791533	114	10 (8.8%)
903988	58	5 (8.6%)

[illegible]

New Attribute of Interest



CASE STUDIES

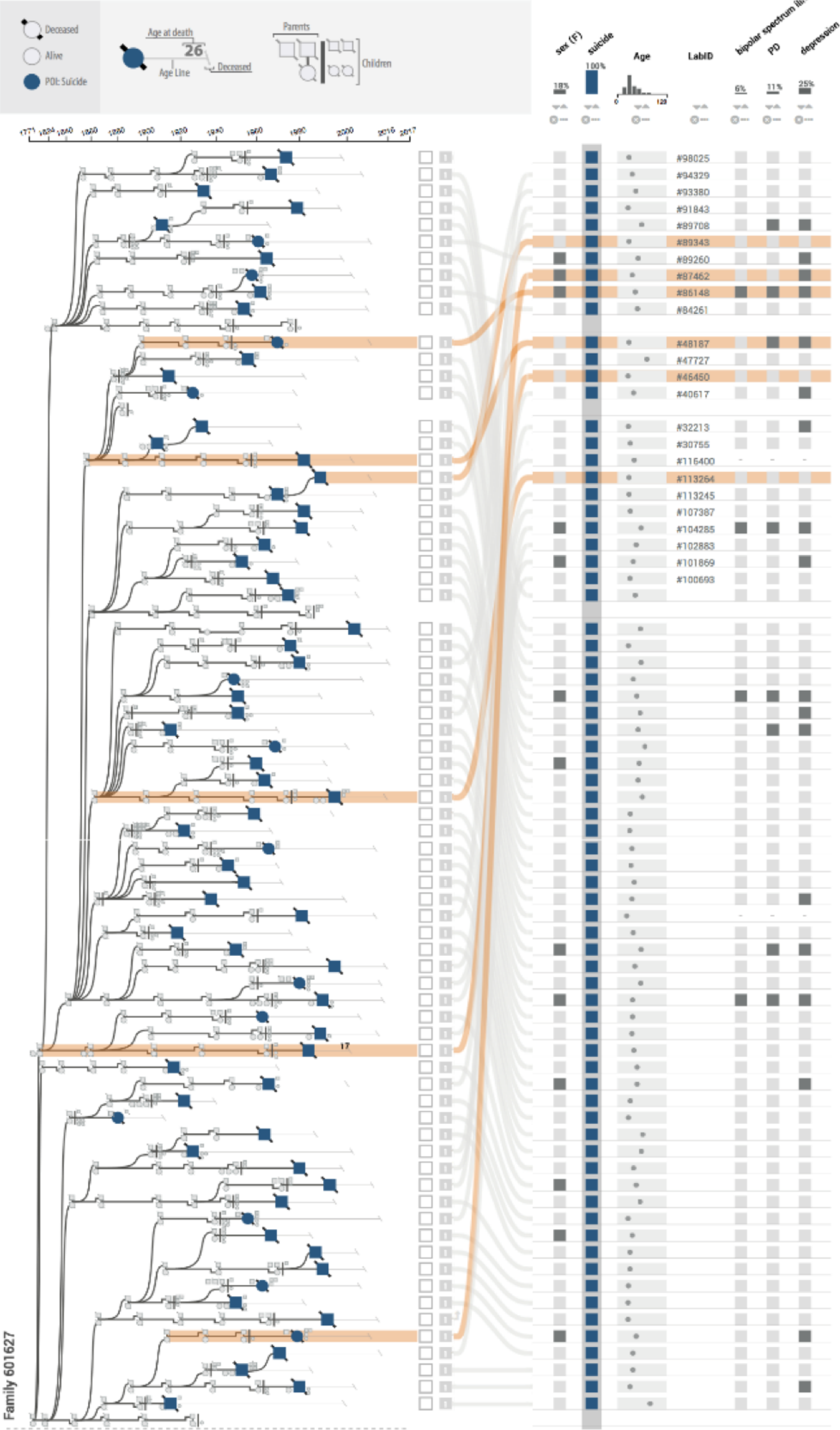
REAL INSIGHTS

FROM REAL DATA

Family Selector

Expand

ID	#People	#POI
601627	831	72 (8.7%)
581915	321	29 (9%)
582686	86	9 (10.5%)
582912	86	7 (8.1%)
582973	257	22 (8.6%)
583052	174	15 (8.6%)
583191	241	19 (7.9%)
583224	100	11 (11%)
584735	863	34 (3.9%)
584908	135	12 (8.9%)
586062	89	7 (7.9%)
586433	344	28 (8.1%)
587072	375	16 (4.3%)
588364	158	14 (8.9%)
589648	209	19 (9.1%)
590241	220	21 (9.5%)
590536	178	15 (8.4%)
592157	410	35 (8.5%)
592775	115	12 (10.4%)
592810	129	11 (8.5%)
593567	331	31 (9.4%)
594970	190	16 (8.4%)



#POI
72 (8.7%)
29 (9%)
9 (10.5%)
7 (8.1%)
22 (8.6%)
15 (8.6%)
19 (7.9%)
11 (11%)
34 (3.9%)
12 (8.9%)
7 (7.9%)
28 (8.1%)
16 (4.3%)
14 (8.9%)
19 (9.1%)
21 (9.5%)
15 (8.4%)
35 (8.5%)
12 (10.4%)

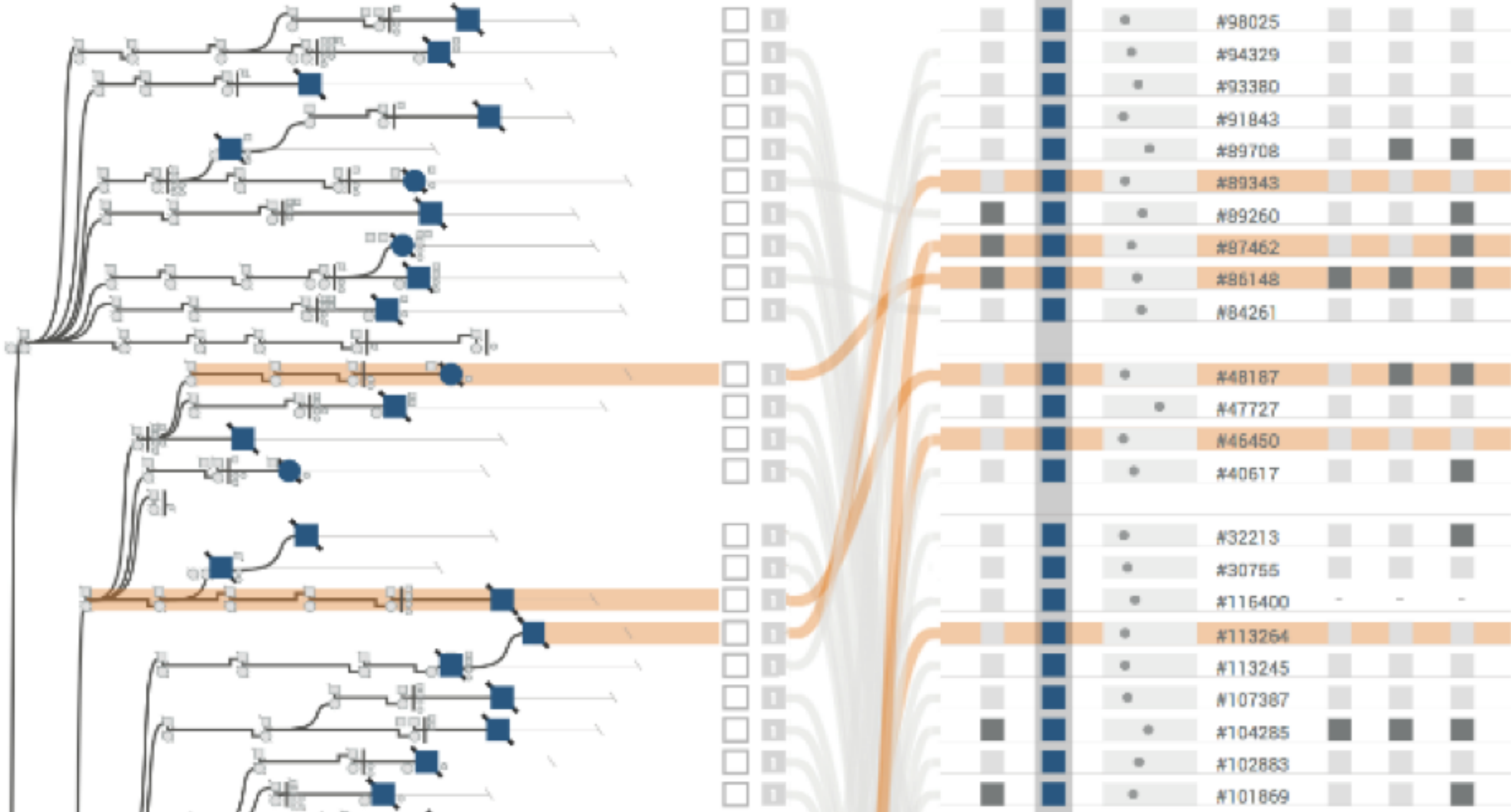
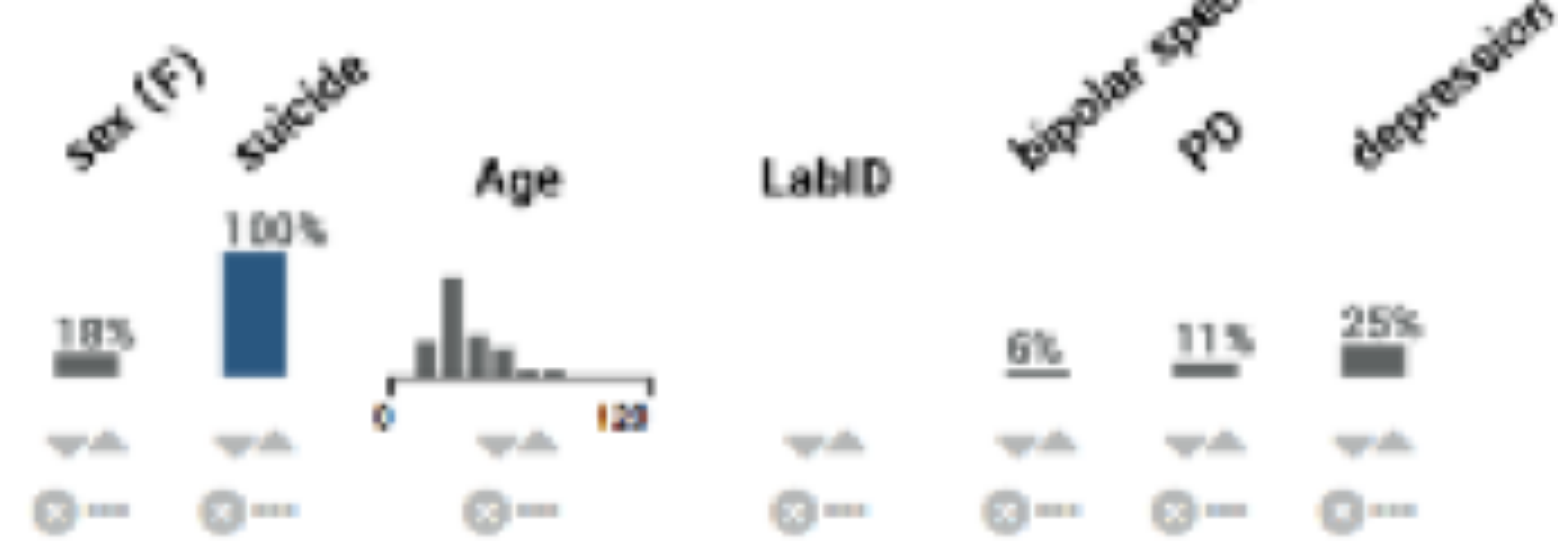
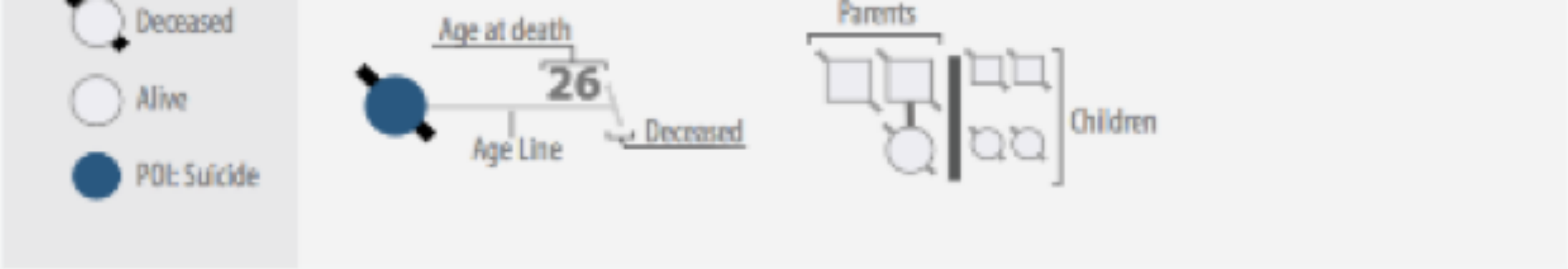
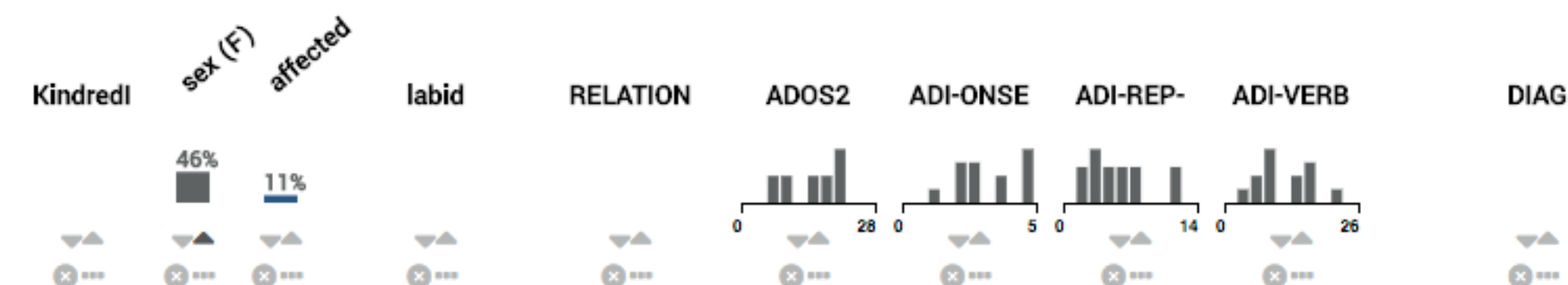
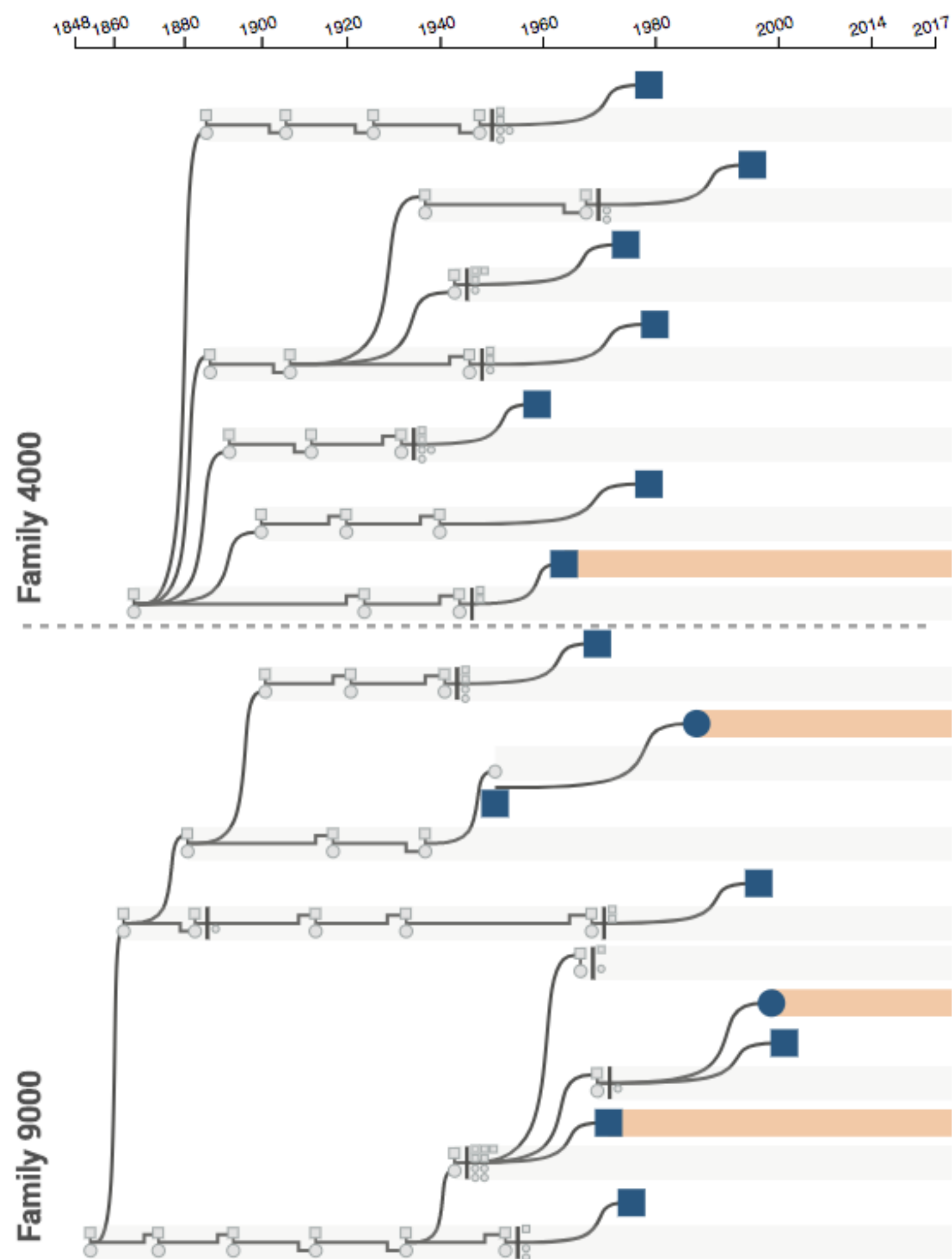
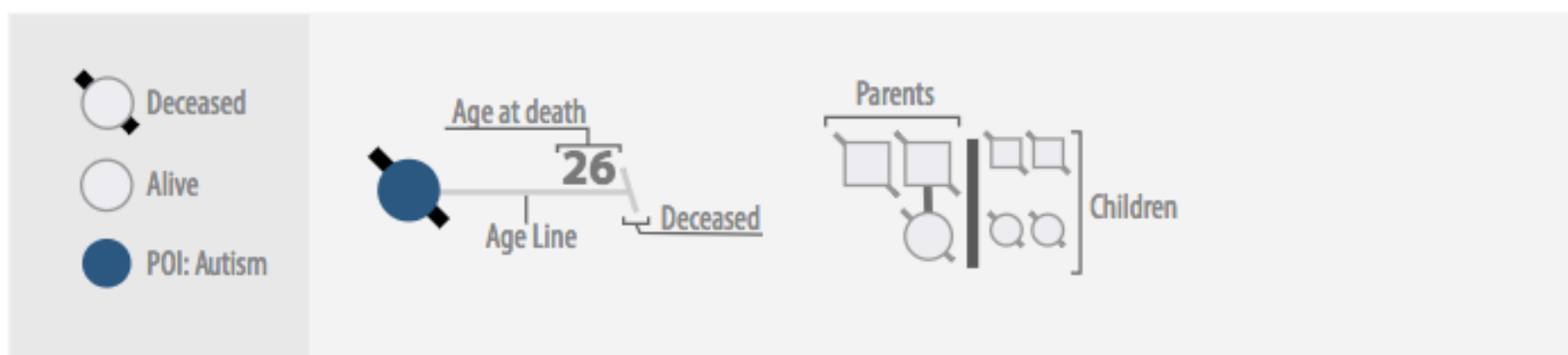




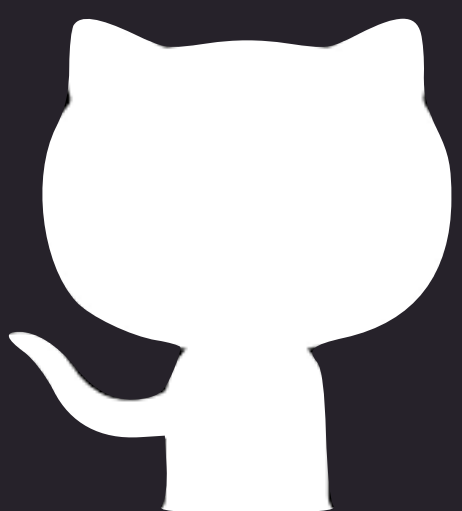
Figure S5: Personality Disorder (PD) Families 10724, 540781 and 565350 identified by browsing families with increased numbers of personality disorders, sorted to show all the PD cases together. These cases are also disproportionately female (10/17).

Family Selector		Expand
ID	#People	#POI
4000	68	8 (11.8%)
9000	71	8 (11.3%)

[illegible]

CURRENT & FUTURE WORK

- ▶ Using Lineage for several other datasets (cancer, longevity...)
- ▶ Improve multi-family exploration
- ▶ Find phenotype patterns across families
- ▶ Add genetic data



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www.vdl.sci.utah.edu

lineage.caleydoapp.org

JUNIPER: A TREE+TABLE APPROACH TO MULTIVARIATE GRAPH VISUALIZATION

WED, @ 11AM, GRAPHS AND TREES



visualization
design lab



HARVARD
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