

network medicine: what do we learn from co-morbidity networks?

stefan thurner



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with

Peter Klimek, Silke Aichberger, Anna Chmiel,
Nina Haug, Caspar Matzhold, Sarah Etter, Ruggiero
Lo Sardo, Michaela Kaleta, Johannes Sorger

Alexandra Kautzky-Willer, Gottfried Endel, Miriam
Leitner, Irmgard Schiller-Frühwirth, Thomas
Niederkrotenthaler, Ellenor Mittendorfer-Rutz,
Michael Leutner

support by

FP7, H2020, WWTF, FFG, Hauptverband SV



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National medical claims data

every paid health service → one data line



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date — patient ID — healthcare practitioner ID — diagnosis — side diagnosis — prescription — price if generic drug/treatment/therapy — pharmacy ID — price of medication — date of purchase



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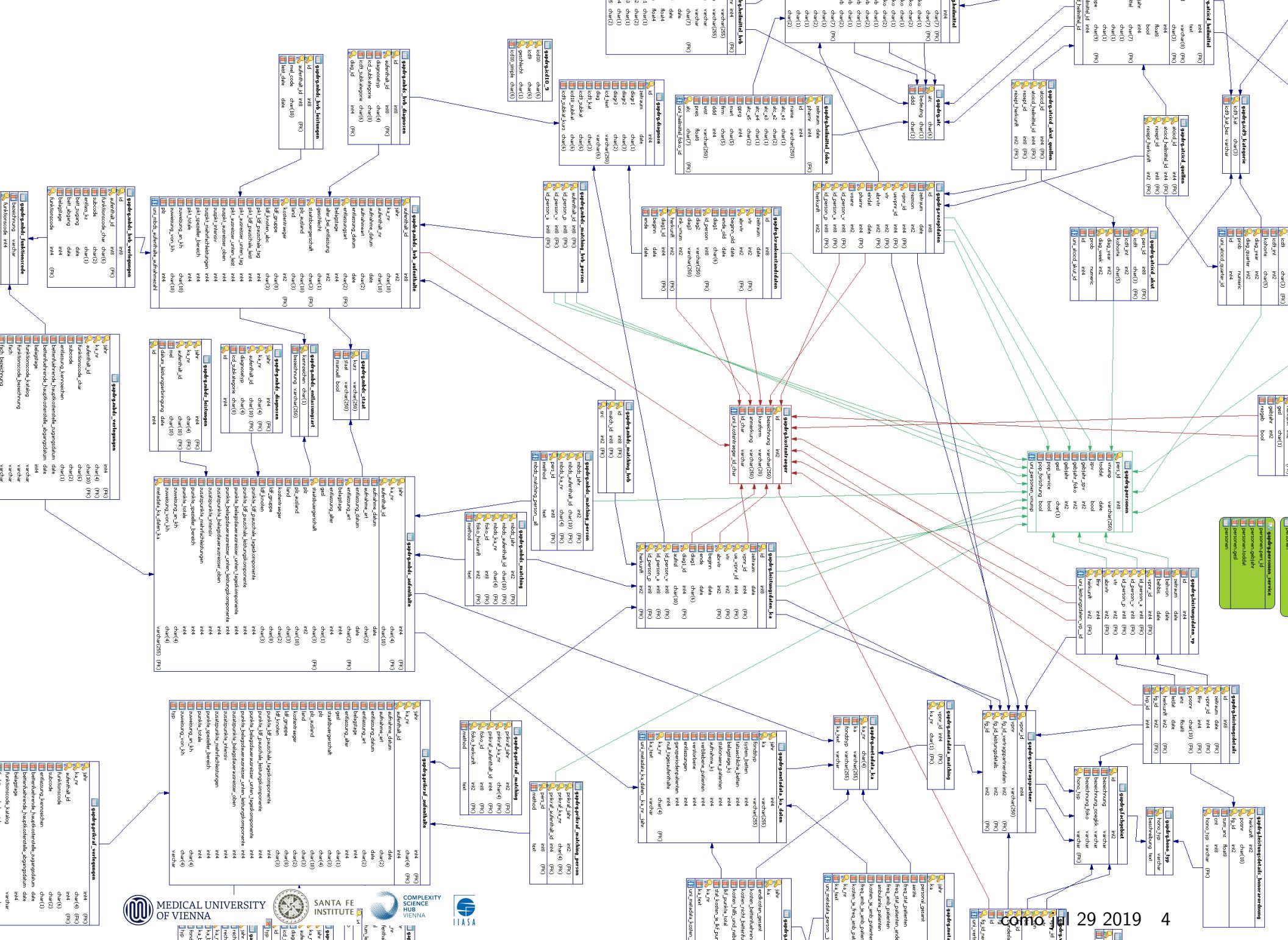
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100.000.000 data-lines / year



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The data

- 8,000,000 patients
- 100,000,000 patient contacts per year
- 2,000,000 hospitalizations per year
- 12,000 health care providers
- 6,102 diseases (ICD10 code)
- 1,171 substances (ATC code)
- 255 hospitals
- 1,238 pharmacies



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How sick are Austrians?



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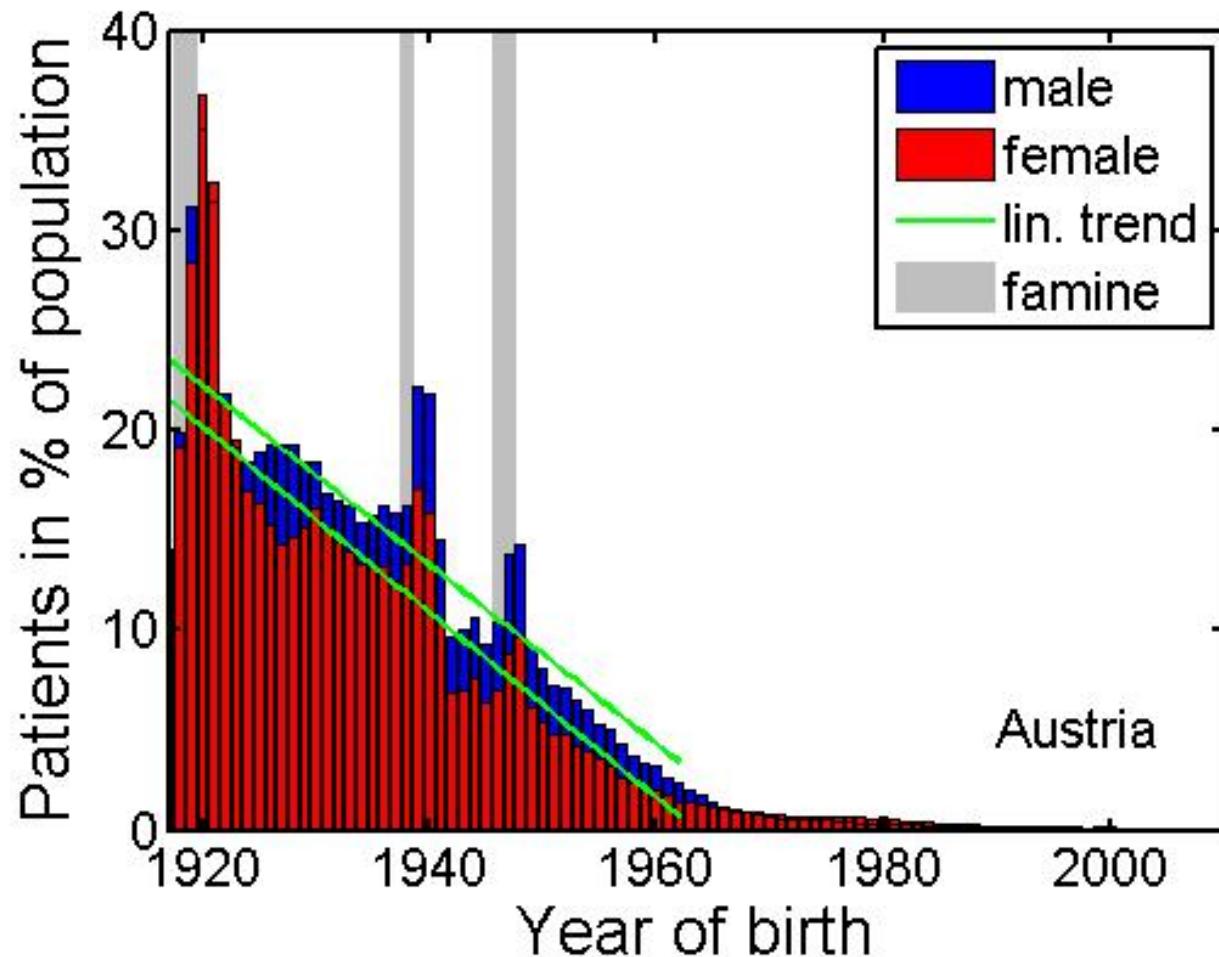


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Epigenetics of diabetes take all 300.000 diabetes patients



malnutrition during pregnancy
→ baby develops diabetes

S Turner et al. PNAS 110, 4703-4707 (2013)



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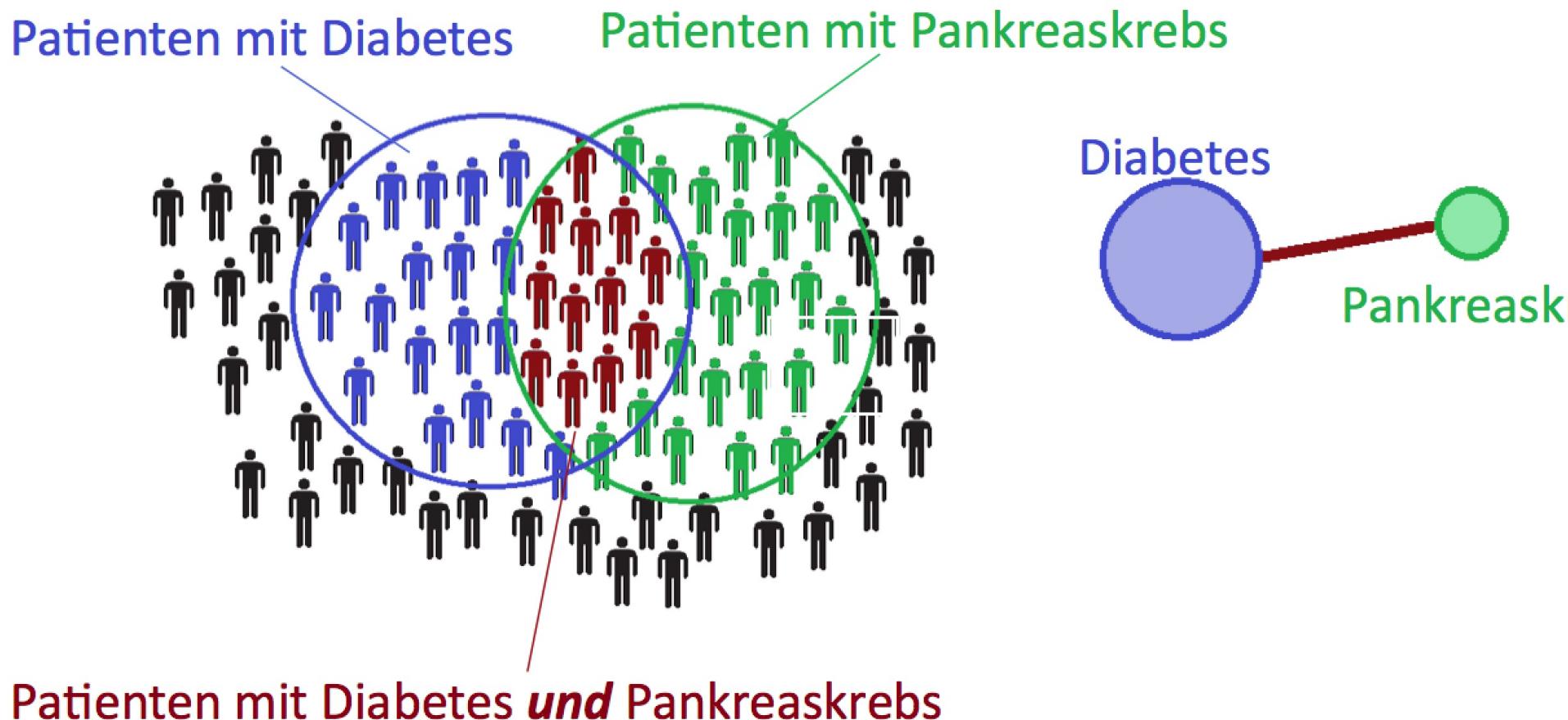


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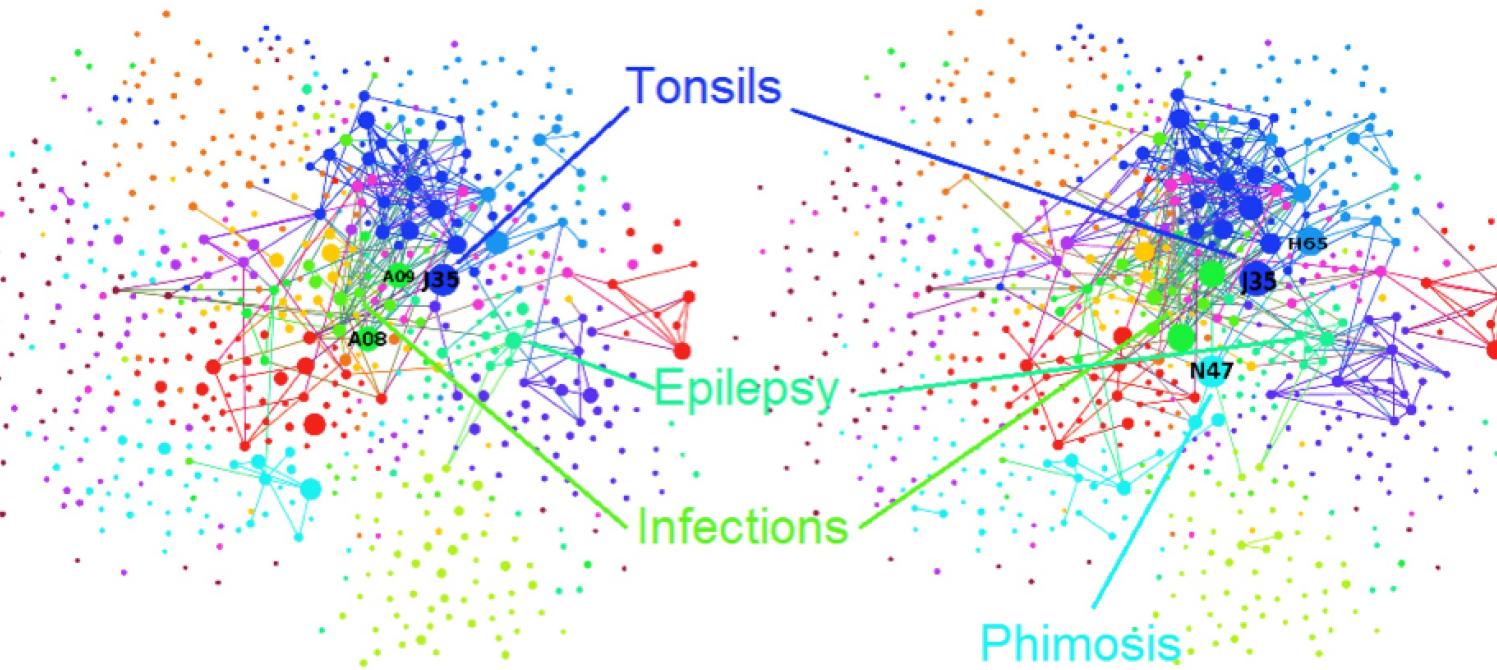


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How sick are Austrians?



Comorbidity network Austrians



females

- A and B - Certain infectious
- C - Neoplasms
- D - Benign neoplasms and blood diseases
- E - Endocrine, nutritional and metabolic diseases
- F - Mental and behavioural disorders
- G - Diseases of the nervous system
- H - Diseases of the eye and ear

males

- I - Diseases of the circulatory system
- J - Diseases of the respiratory system
- K - Diseases of the digestive system
- L - Diseases of the skin and subcutaneous tissue
- M - Diseases of the musculoskeletal system
- N - Diseases of the genitourinary system

0-8 Jahre

9-16 Jahre

17-24 Jahre

25-32 Jahre

33-40 Jahre

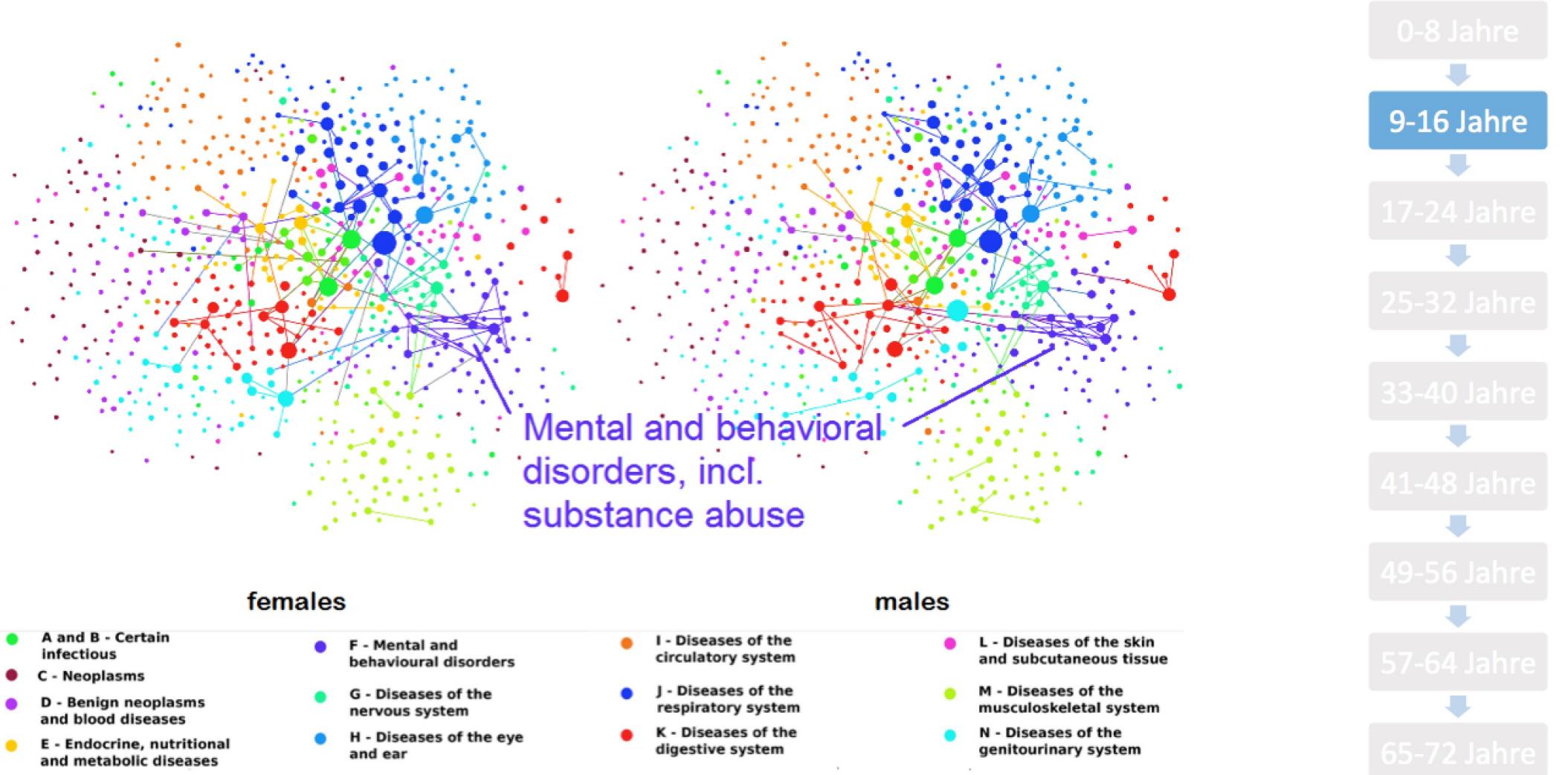
41-48 Jahre

49-56 Jahre

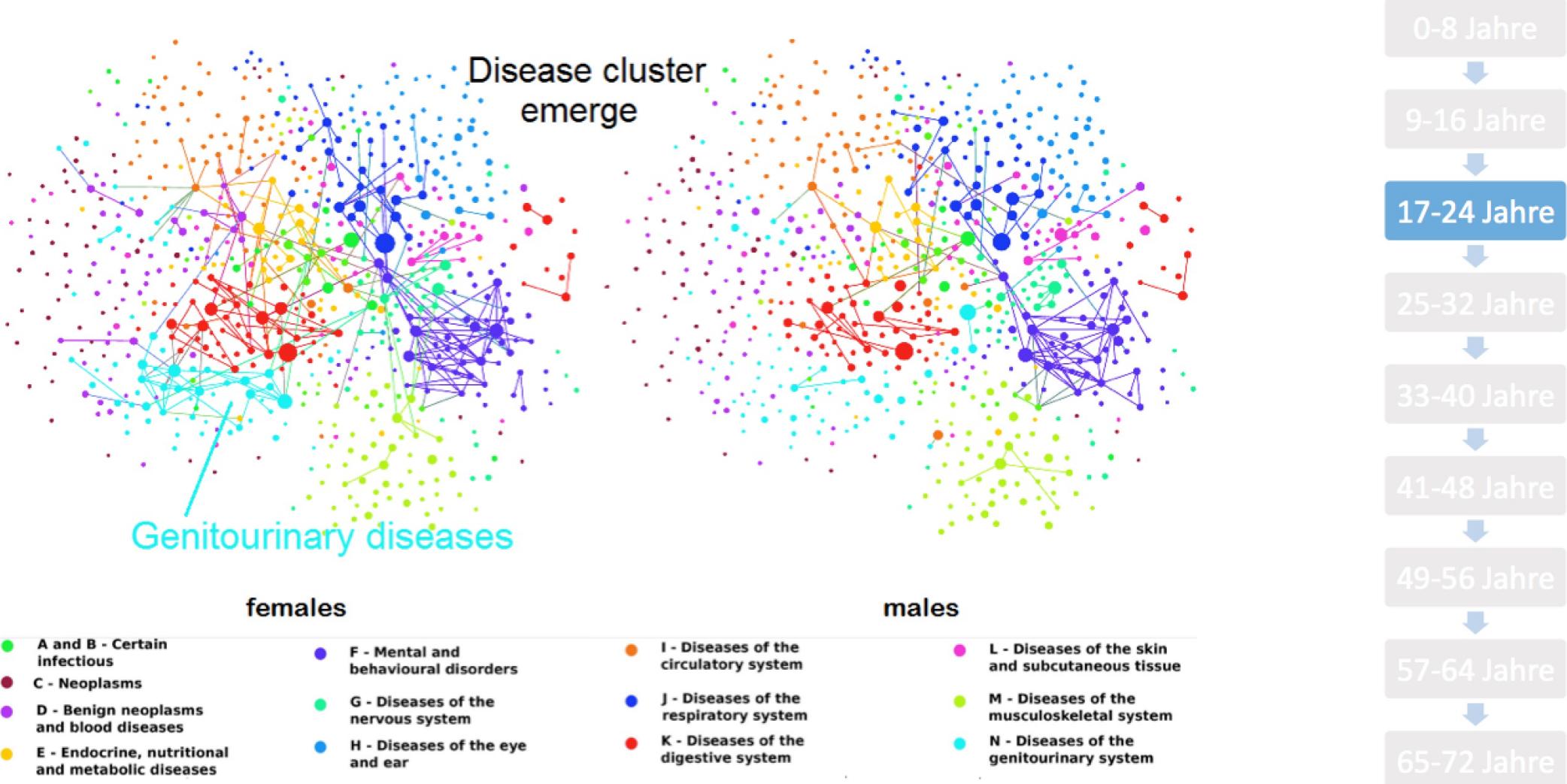
57-64 Jahre

65-72 Jahre

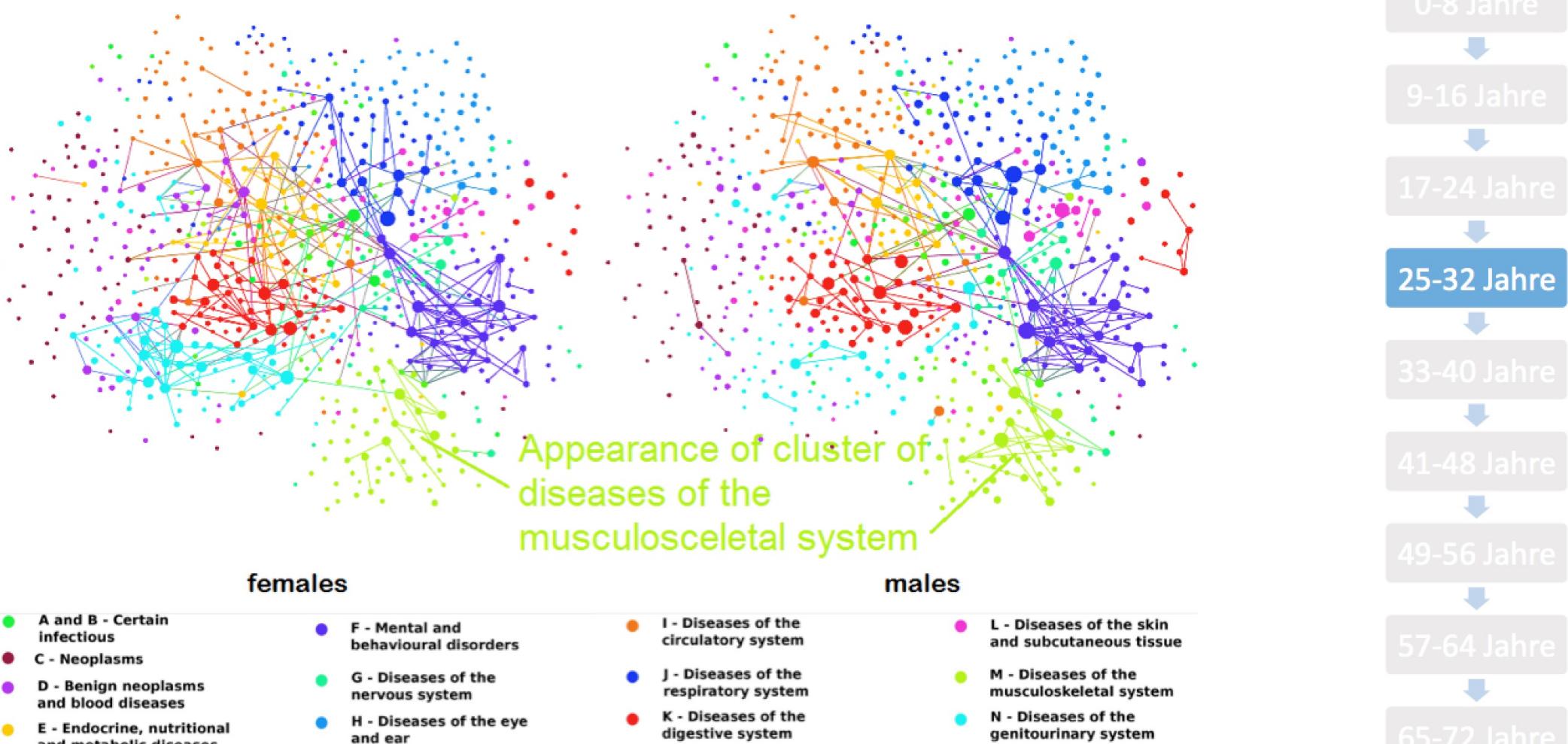
Comorbidity network Austrians



Comorbidity network Austrians



Comorbidity network Austrians



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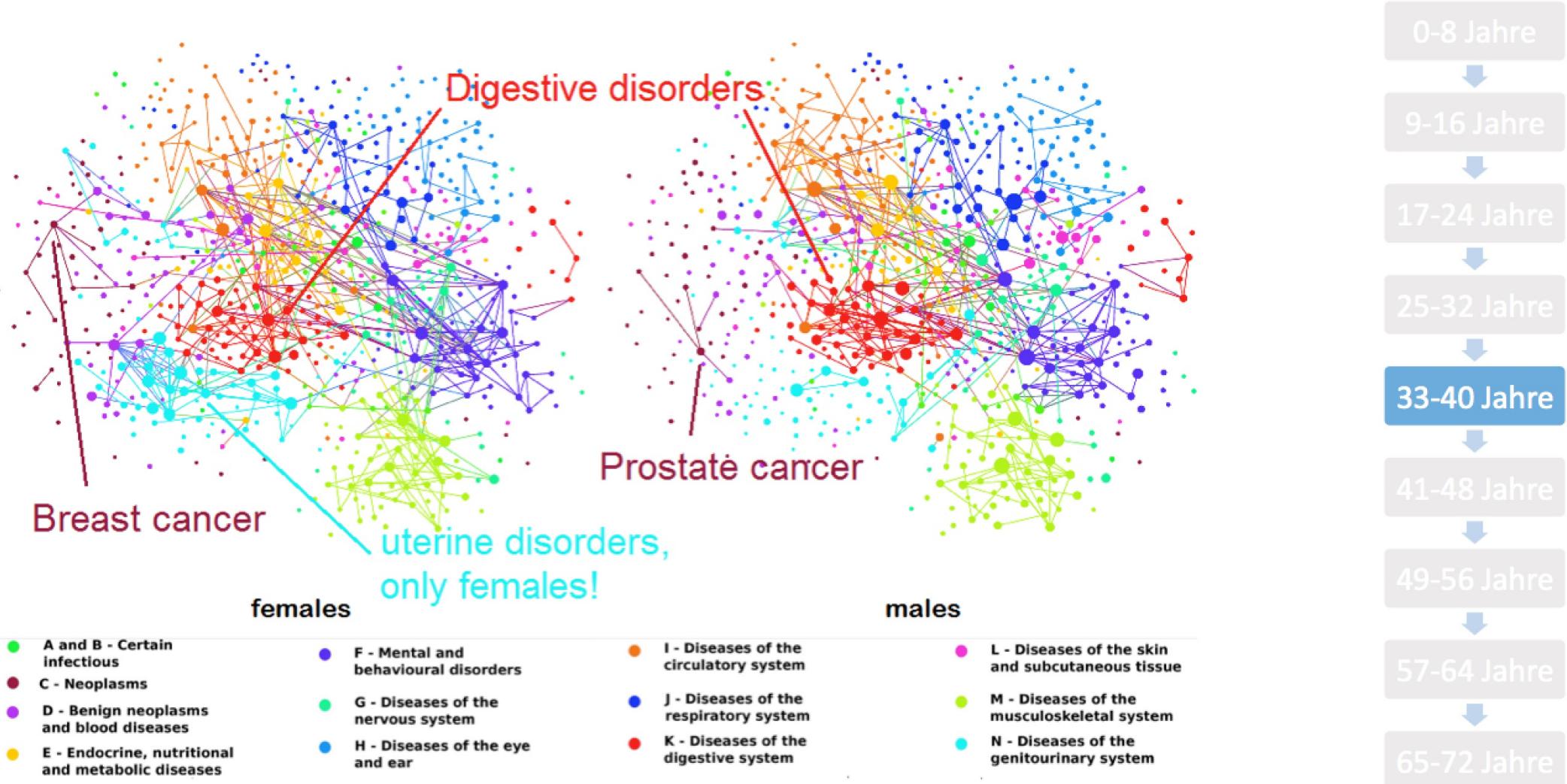
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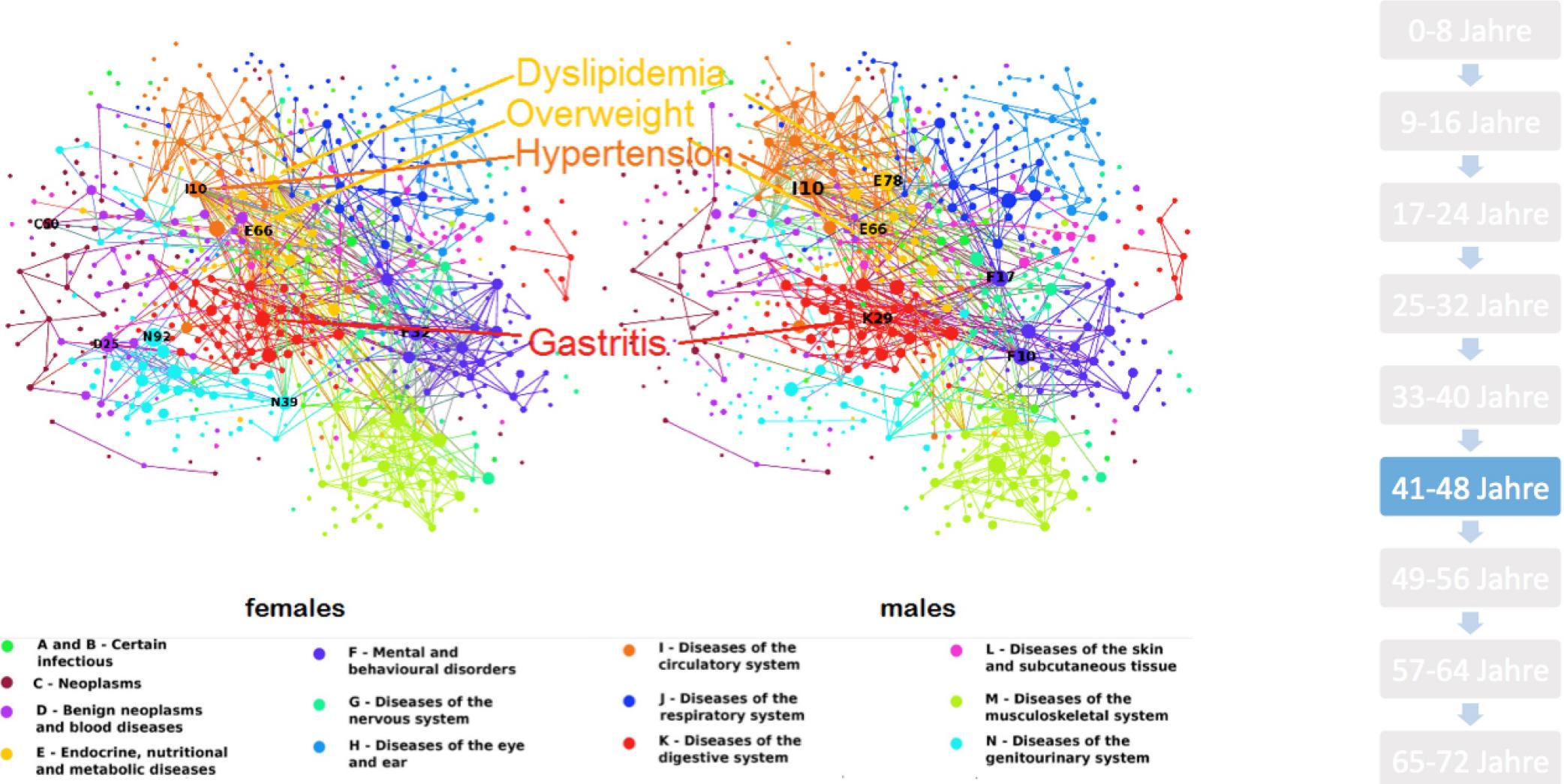
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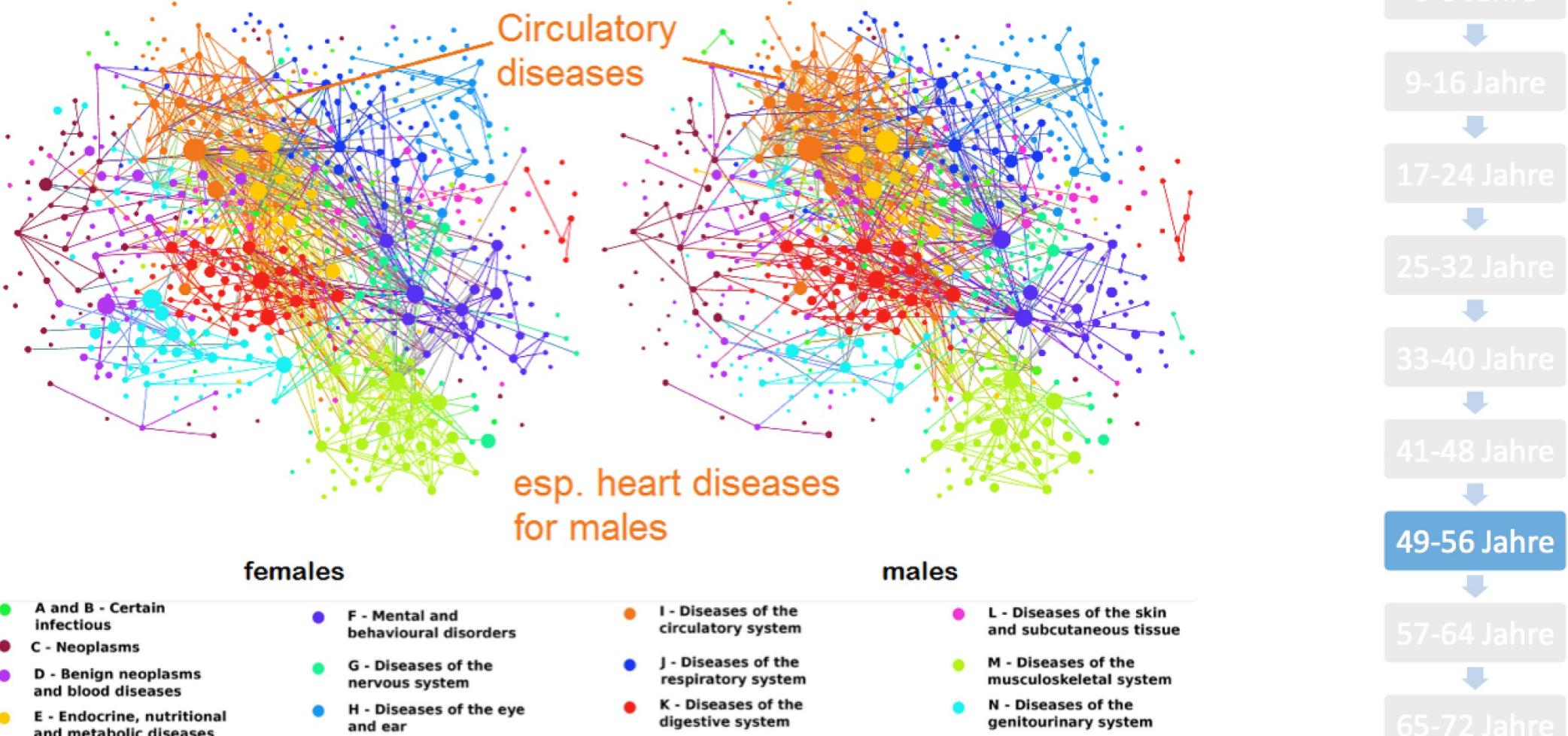
Comorbidity network Austrians



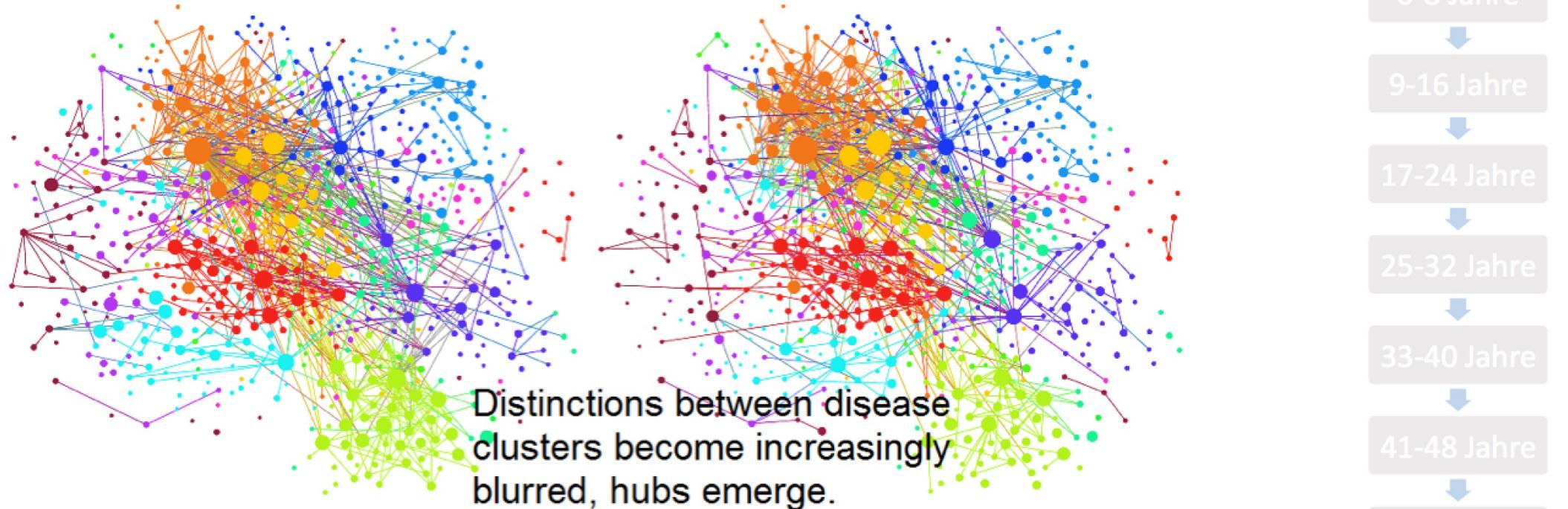
Comorbidity network Austrians



Comorbidity network Austrians



Comorbidity network Austrians



females

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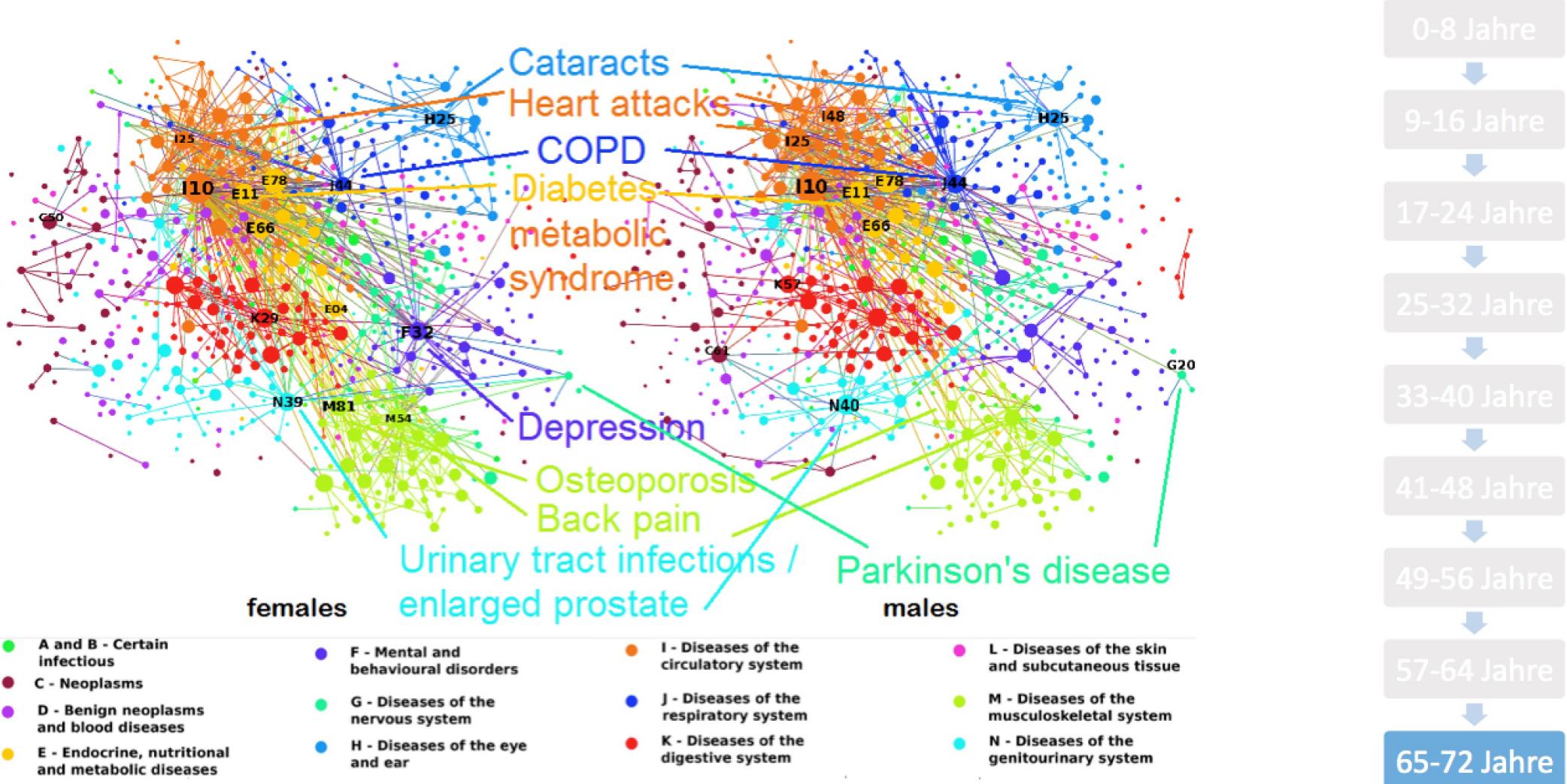
41-48 Jahre

49-56 Jahre

57-64 Jahre

65-72 Jahre

Comorbidity network Austrians



Discovery !

individual health trajectories → follow these networks

A Chmiel, P Klimek, S Thurner, New Journal of Physics 16, 115013 (2014)



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predict likely disease trajectories



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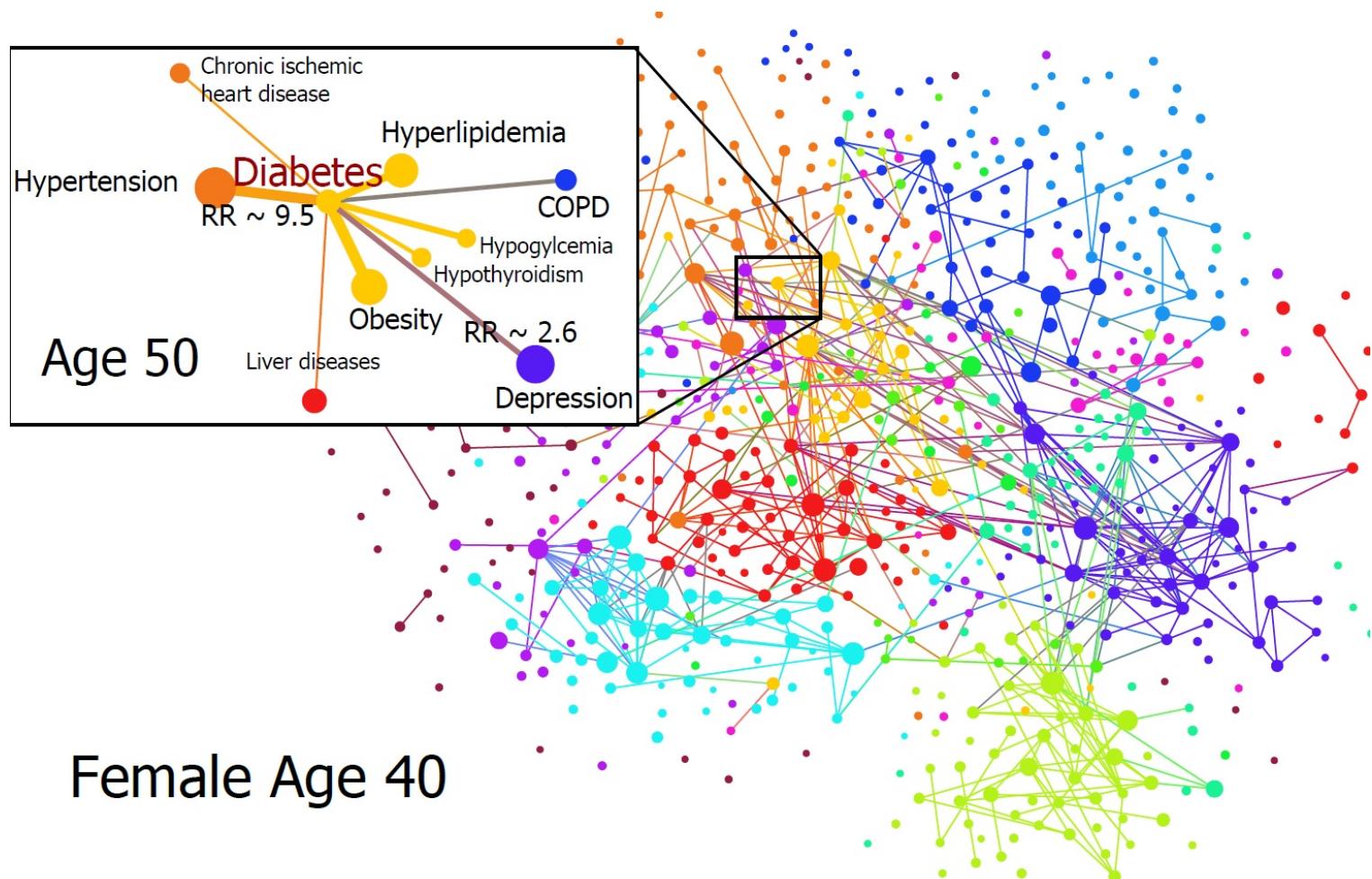
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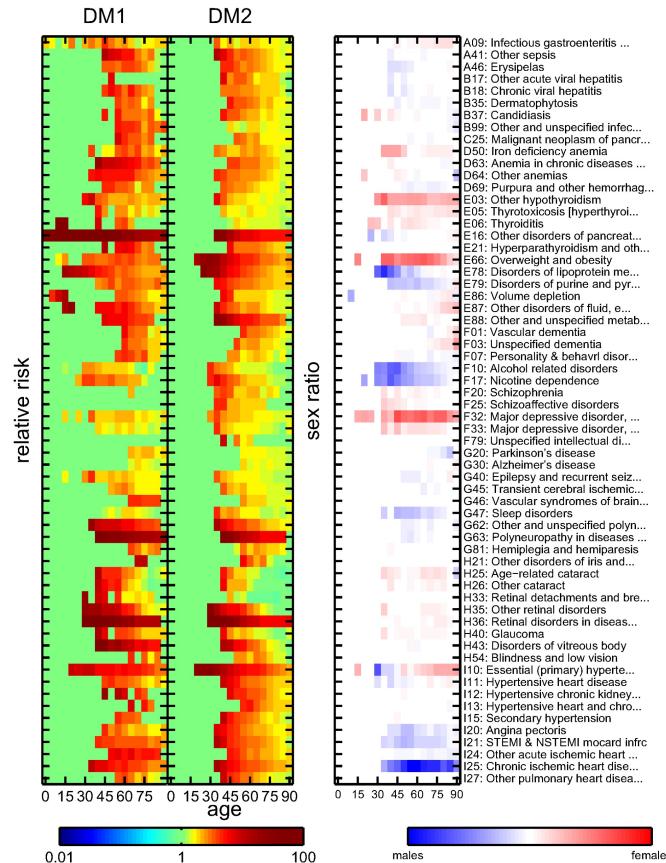
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como jul 29 2019 21

Individualized predictions



Given, you suffer diabetes: with what probability do you get other diseases?



P Klimek, A Kautzky, A Chmiel, S Thurner, PLoS Comput Biol 11, e1004125 (2015)



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- equivalent to 40,000 epidemiological studies
- which co-morbidities are causal?
- which are significant $p < 0.00001$?
- decide controversial debates: DM → Parkinson's
- gender medicine
- **all** cases



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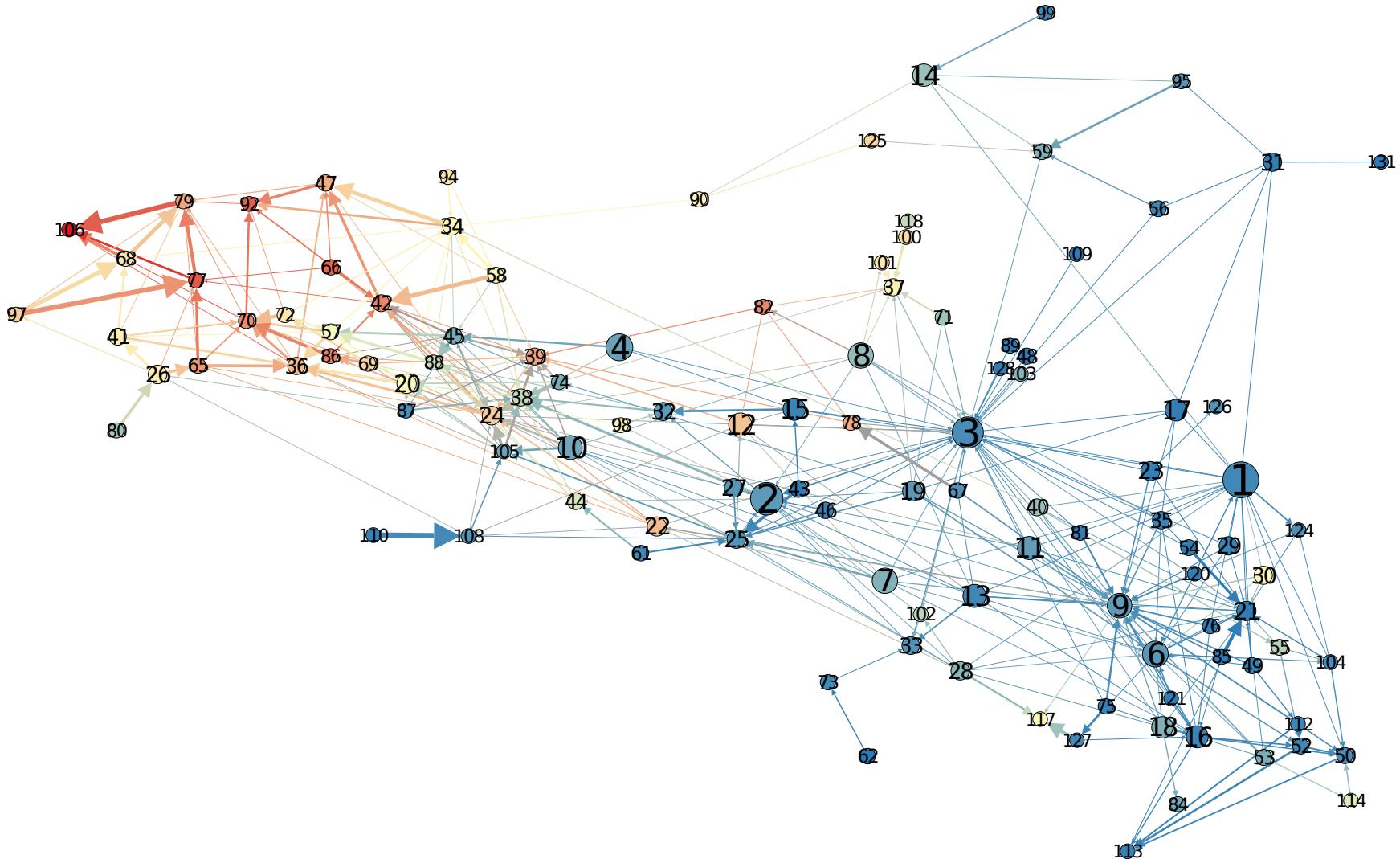


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Predicting disease trajectories



How effective is prevention?



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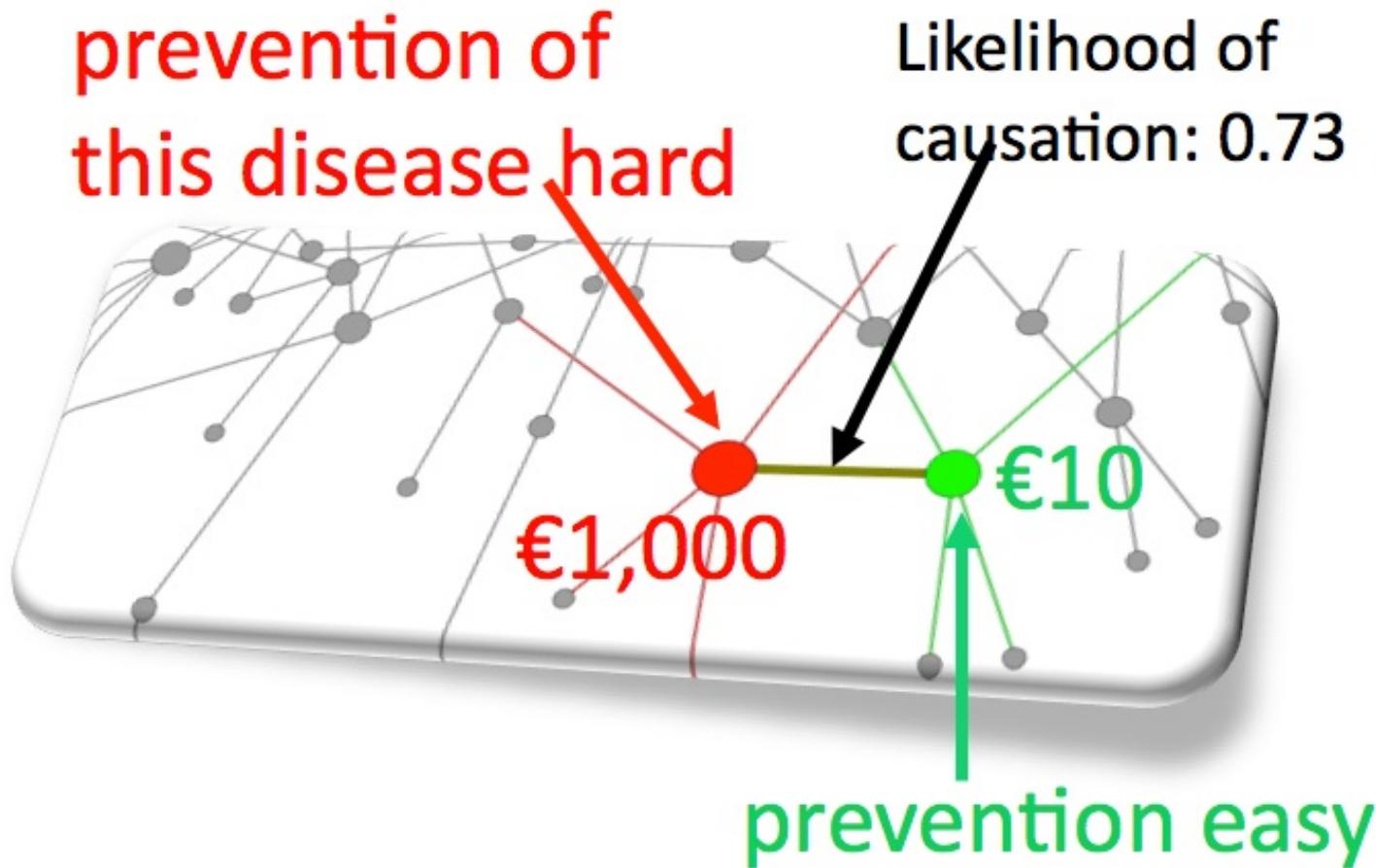


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Co-morbidity networks and prevention



Co-morbidity → check causality → fight causes



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new classification of diseases?



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Co-morbidity of diabetes

group 1: diabetes + A, B, C

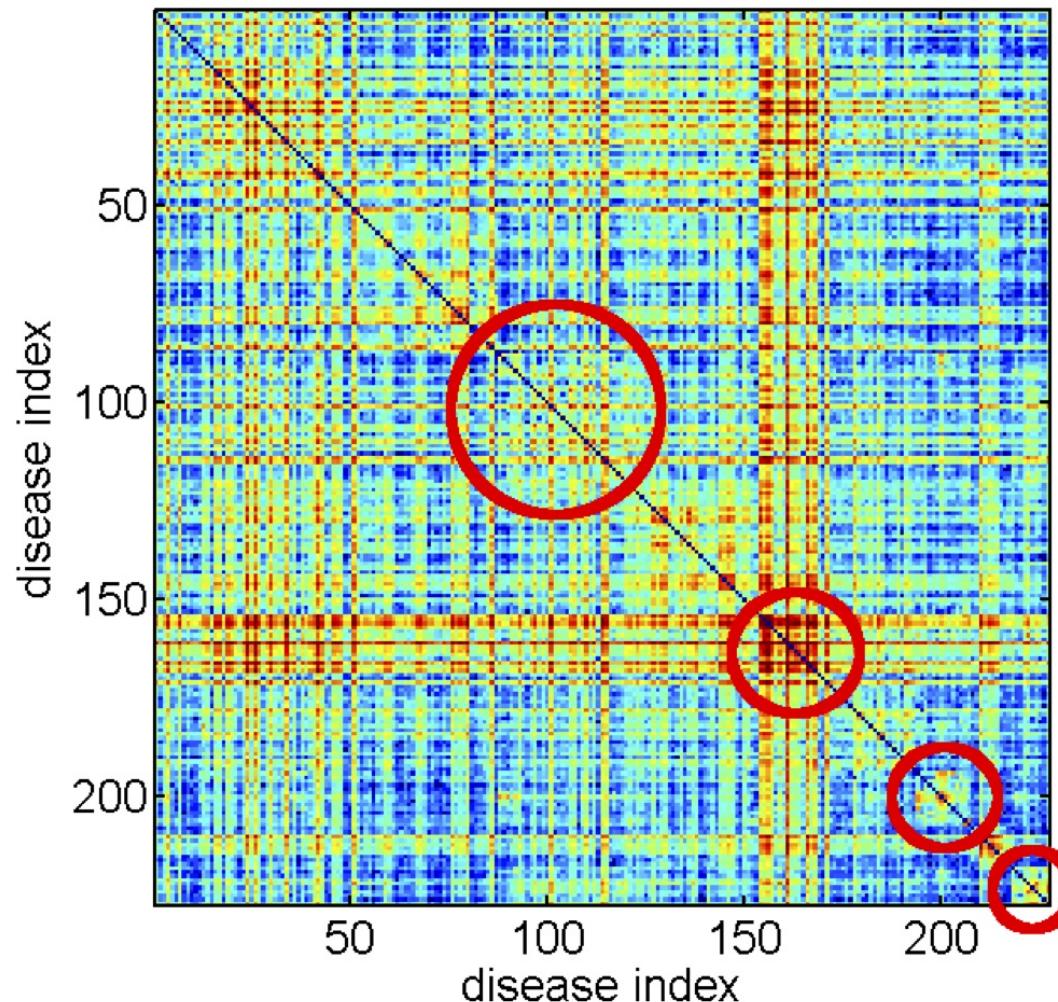
group 2: diabetes + E, F

group 3: diabetes + Y, X, Z

...

→ **alternative classification of diabetes**

Co-morbidity types of diabetes



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which therapy works? which doesn't?



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- group 1: therapy A
 - group 2: therapy B
 - compute all co-morbidities after therapy A
 - berechne all co-morbidities after therapy B
- **compare:** follow up costs, hospitalization times, ...



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How genetic is a disease?



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Causes of diseases

- genetic factors
- metabolic factors
- environment / toxico-genetic
- epigenetic factors

→ compare with phenotype-network



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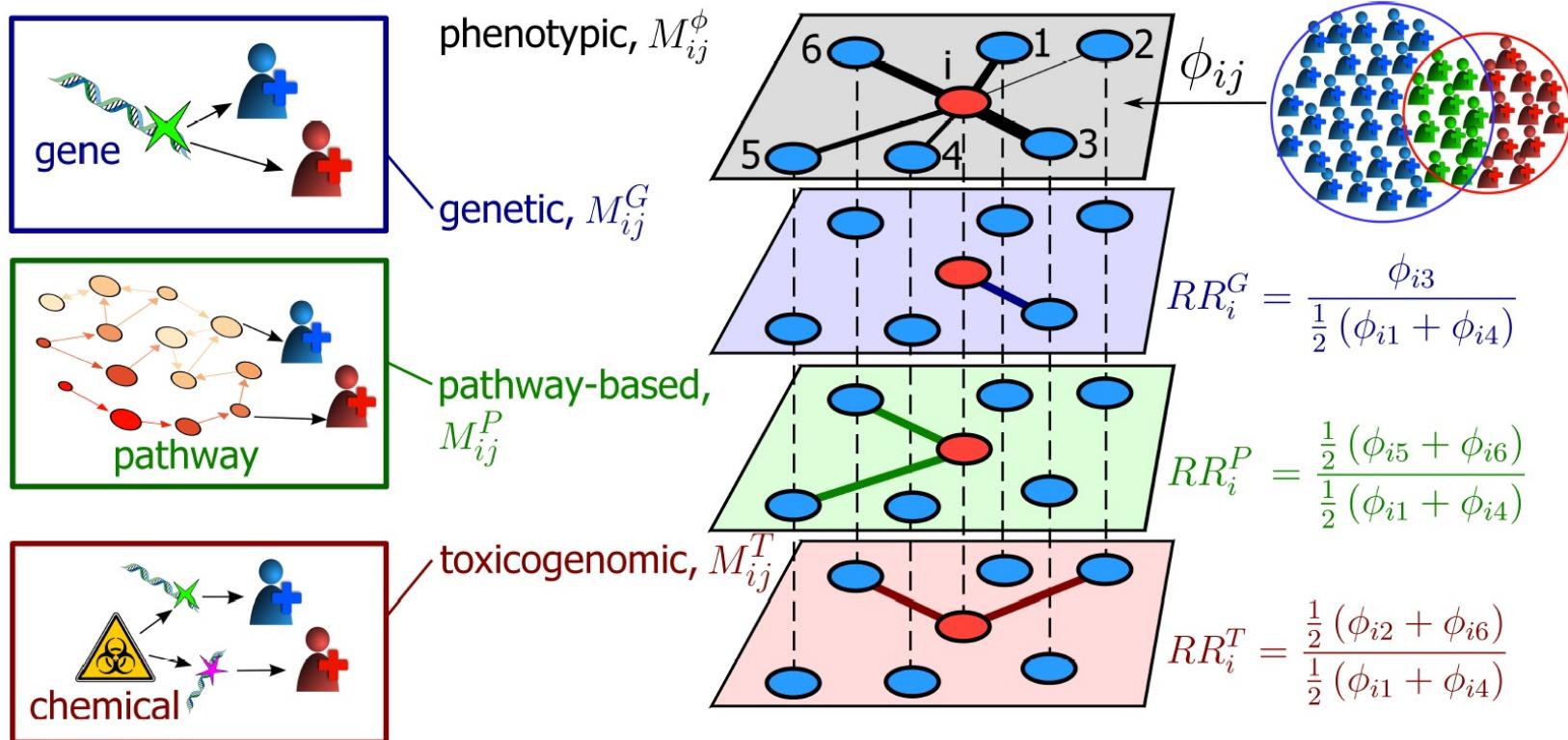
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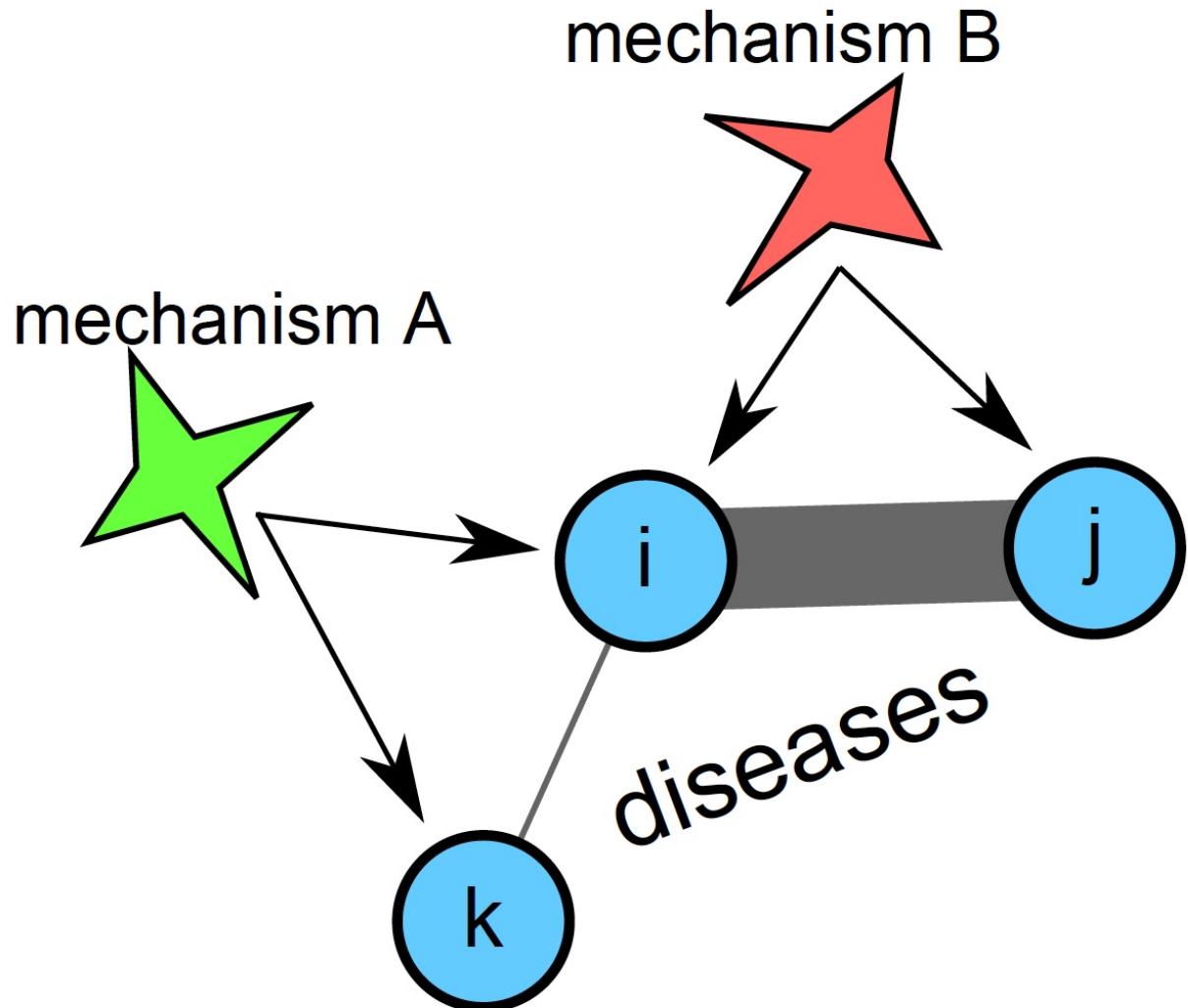


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Compare co-morbidity with genotype-network





if co-morbidity and genotype-network are similar

→ disease is genetic



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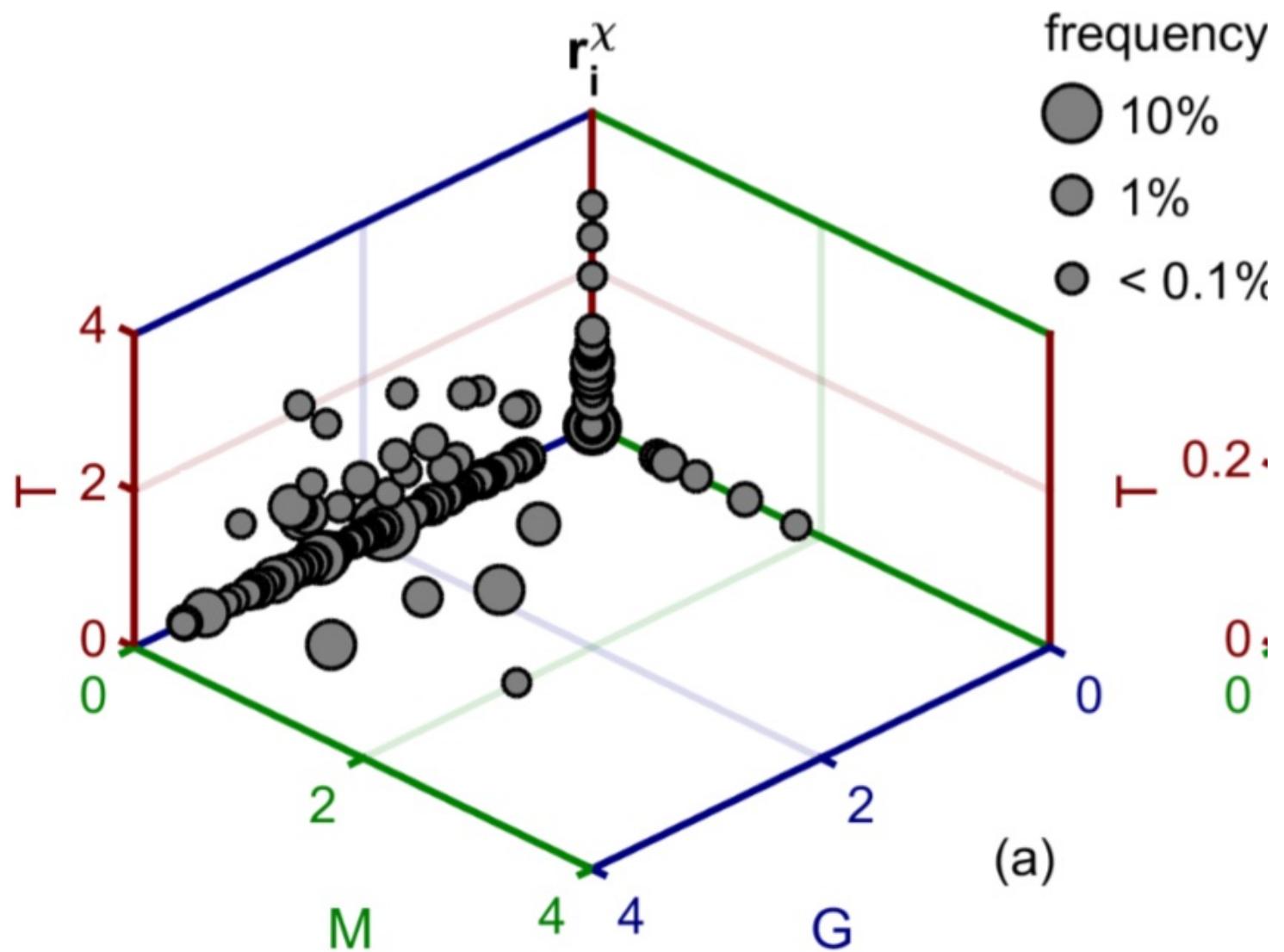
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Type 1 diabetes mellitus		
Transient cerebral ischemic attacks and related syndromes	E10	0,50
Benign neoplasm of colon, rectum, anus and anal canal	G45	0,50
Eating disorders	D12	0,33
Polycythemia vera	F50	0,33
Other diseases of intestine	D45	0,25
Other cerebrovascular diseases	K63	0,25
Other and unsp diseases of blood and blood-forming organs	I67	0,21
Other congenital malformations of heart	D75	0,21
Malignant neoplasm of heart, mediastinum and pleura	Q24	0,20
Mesothelioma	C38	0,16
Specific personality disorders	C45	0,16
Overweight and obesity	F60	0,16
Other cardiac arrhythmias	E66	0,13
Cerebral infarction	I49	0,13
Type 2 diabetes mellitus	E11	0,13
Secondary parkinsonism	I63	0,13
Other and unspecified myopathies	E21	0,11
Congenital malformations of cardiac chambers and connections	G72	0,11
Other congenital malformations of eye	Q20	0,10
Congenital malformations of aortic and mitral valves	Q15	0,09
Parkinsons disease	Q23	0,09
Primary disorders of muscles	Q20	0,08
Essential (primary) hypertension	G71	0,07
Anoph	I10	0,07
	Q11	0,06





wanted side effects



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what do Austrians take?



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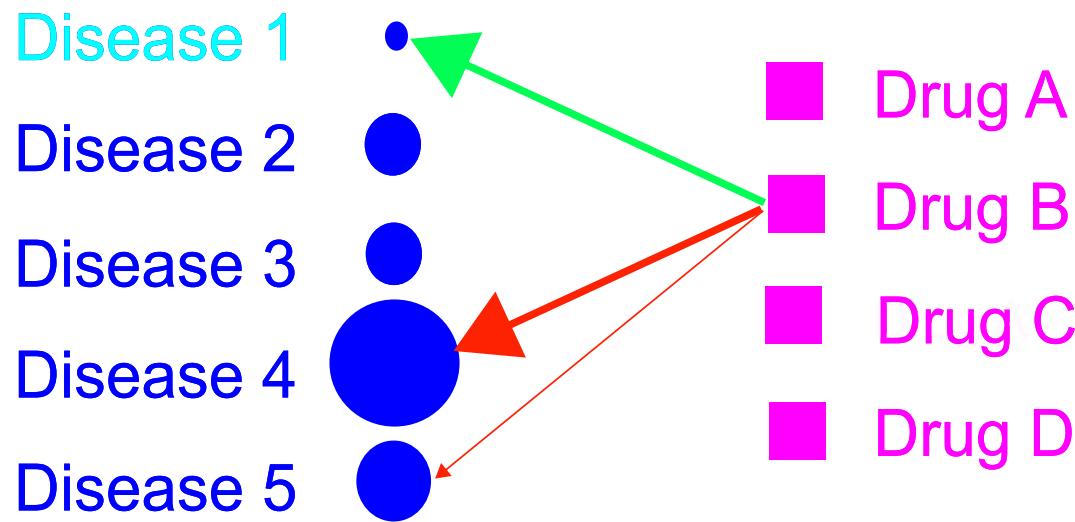


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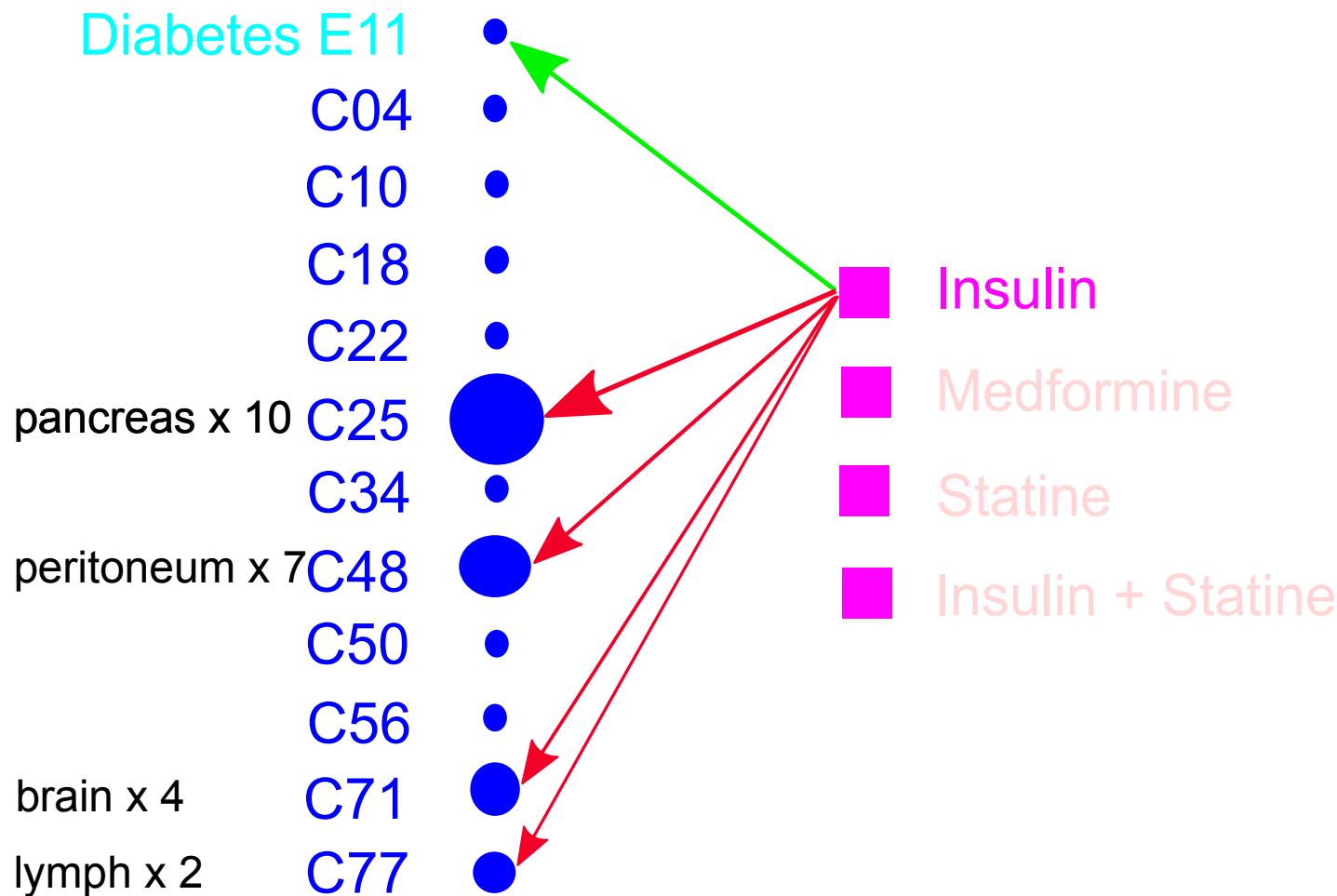


I suffer disease 1 and get medication B

B can cause a problem 4 — side effect



Side effects: insulin



A. Kautzky-Willer, S. Thurner, and P. Klimek J Internal Medicine 281, 206-216 (2017)



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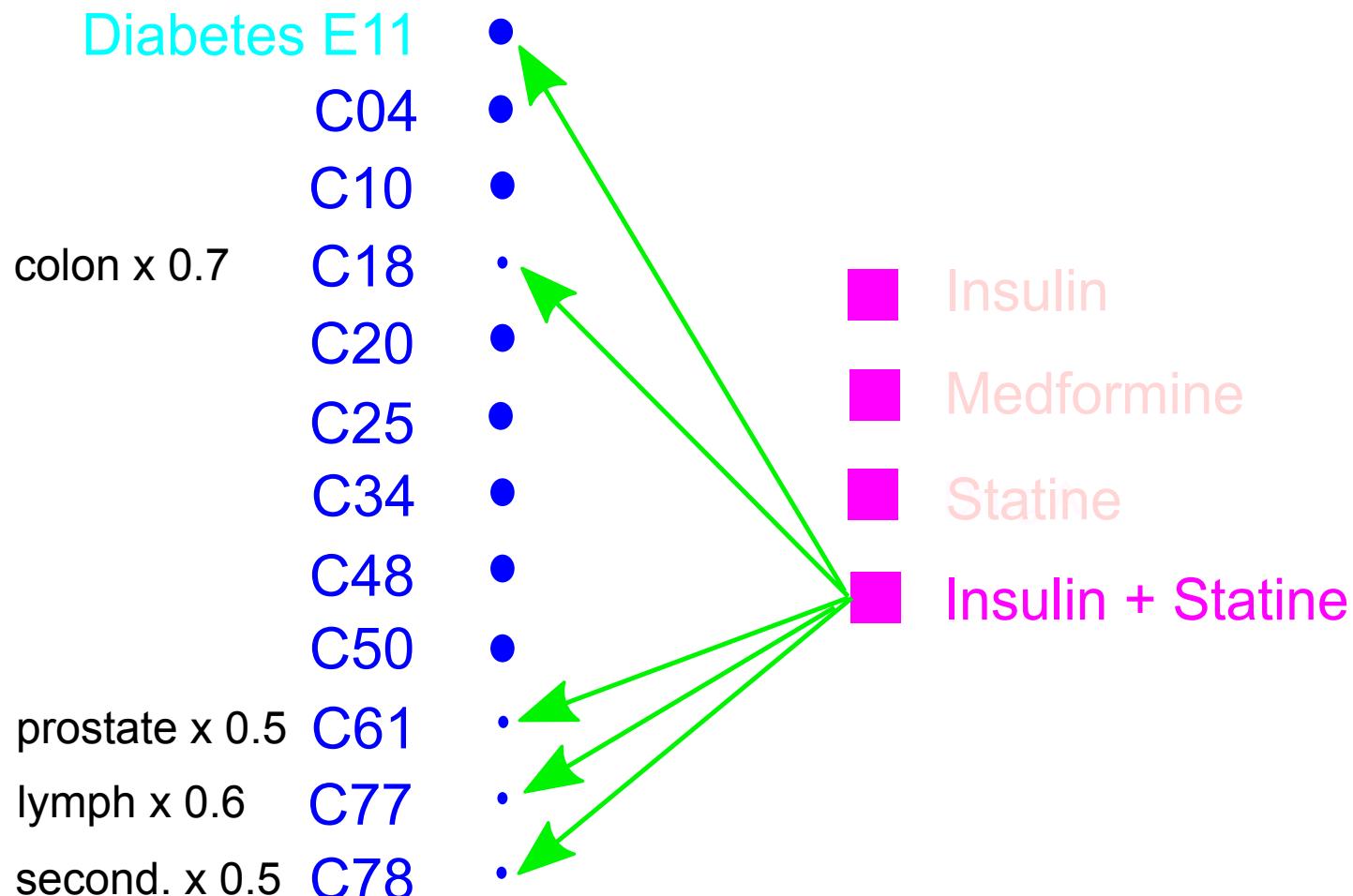
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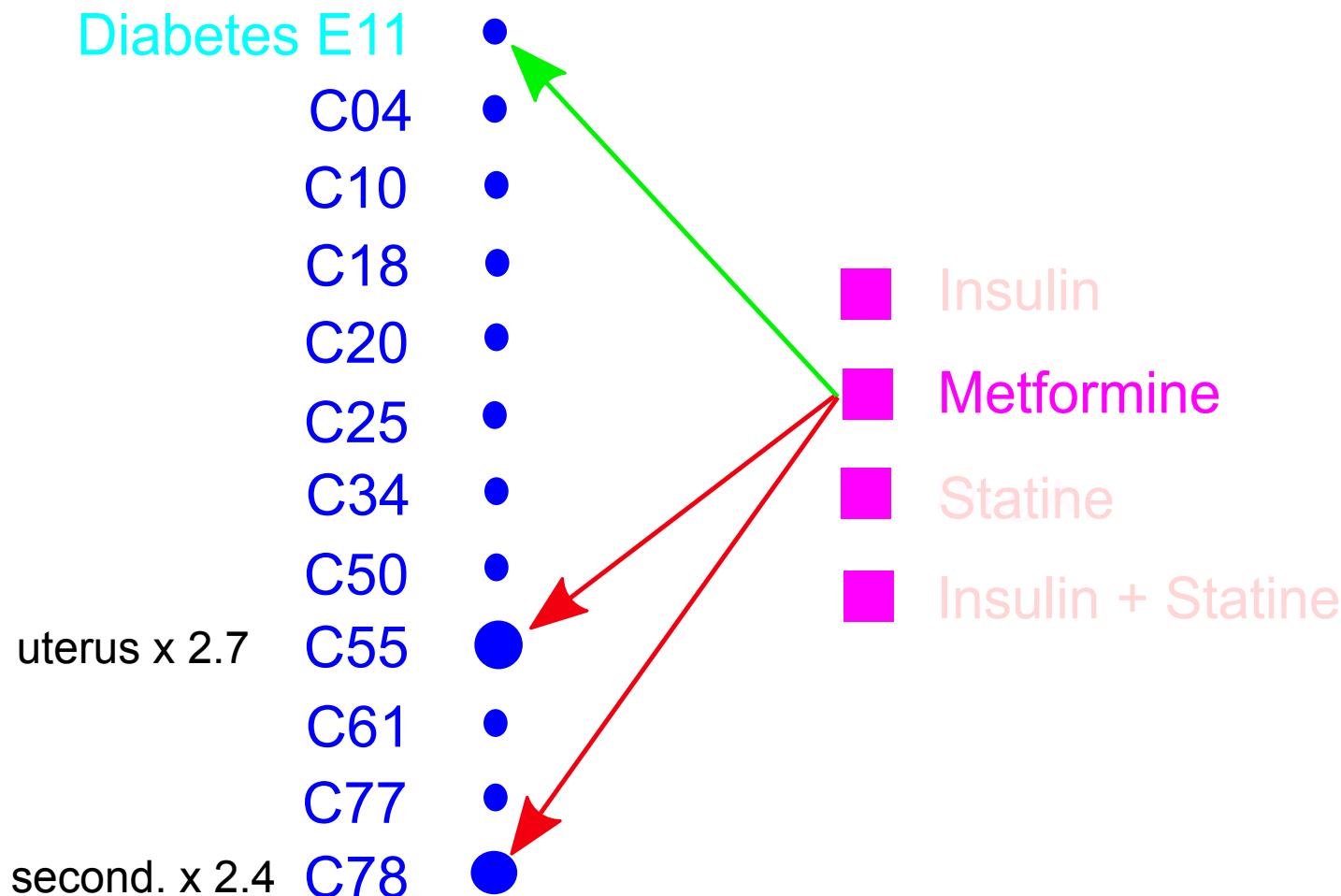


Side effects: insulin+statins



A. Kautzky-Willer, S. Thurner, and P. Klimek J Internal Medicine 281, 206-216 (2017)

Side effects: metformin



A. Kautzky-Willer, S. Thurner, and P. Klimek J Internal Medicine 281, 206-216 (2017)

Health care system



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where do Austrians get treatment?



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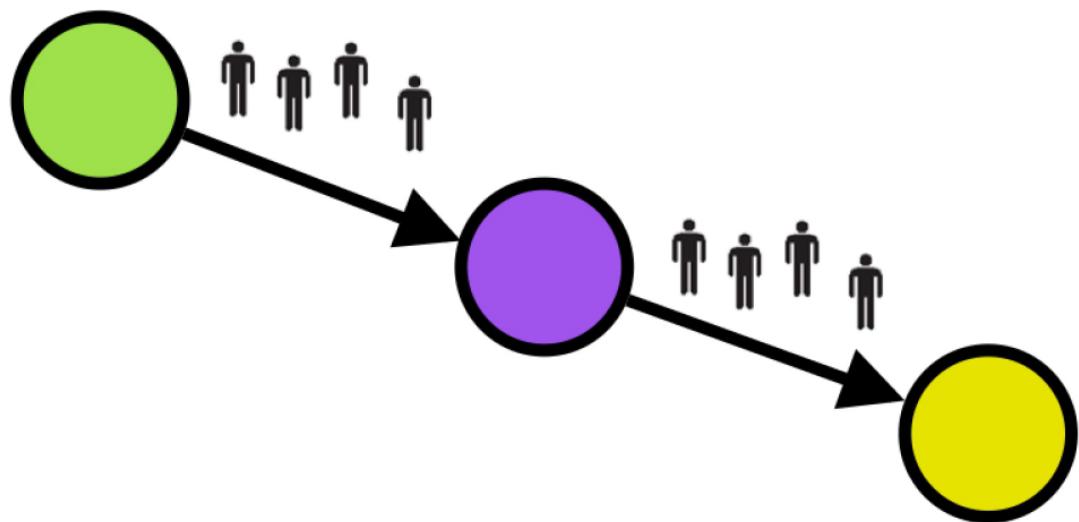
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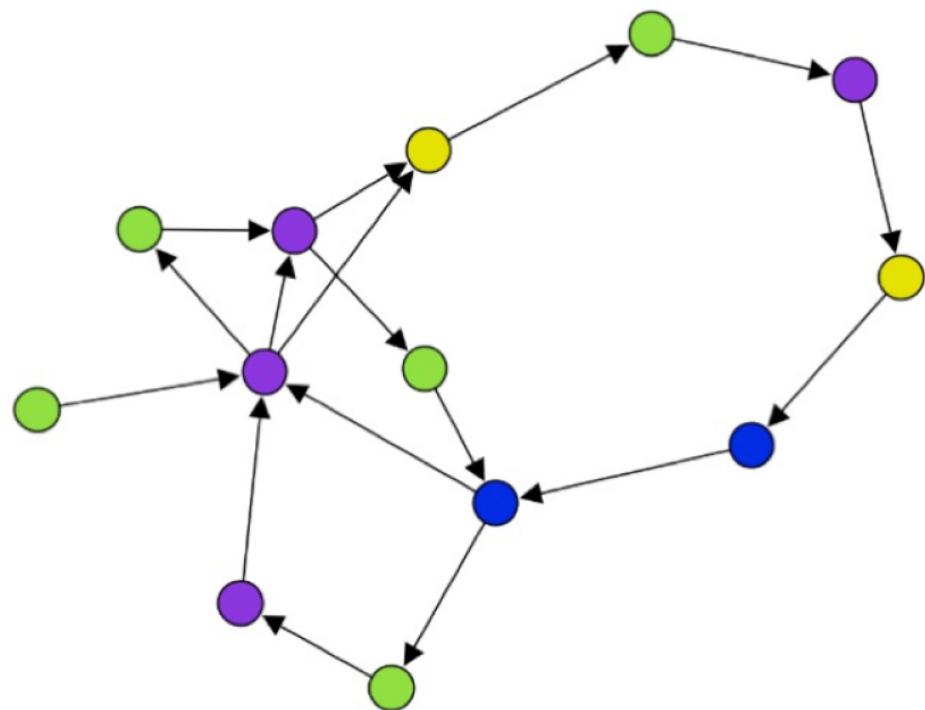
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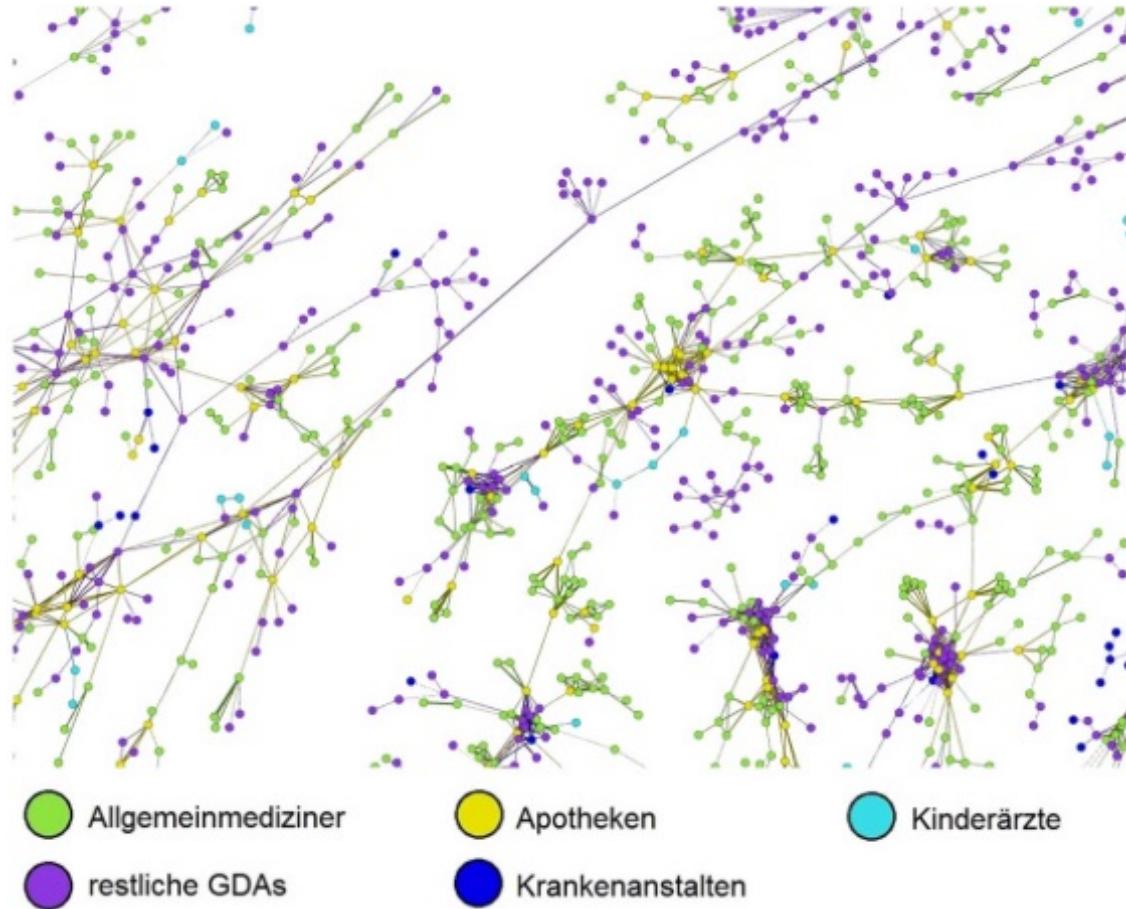


- GP (doctor)
- specialist
- pharmacy



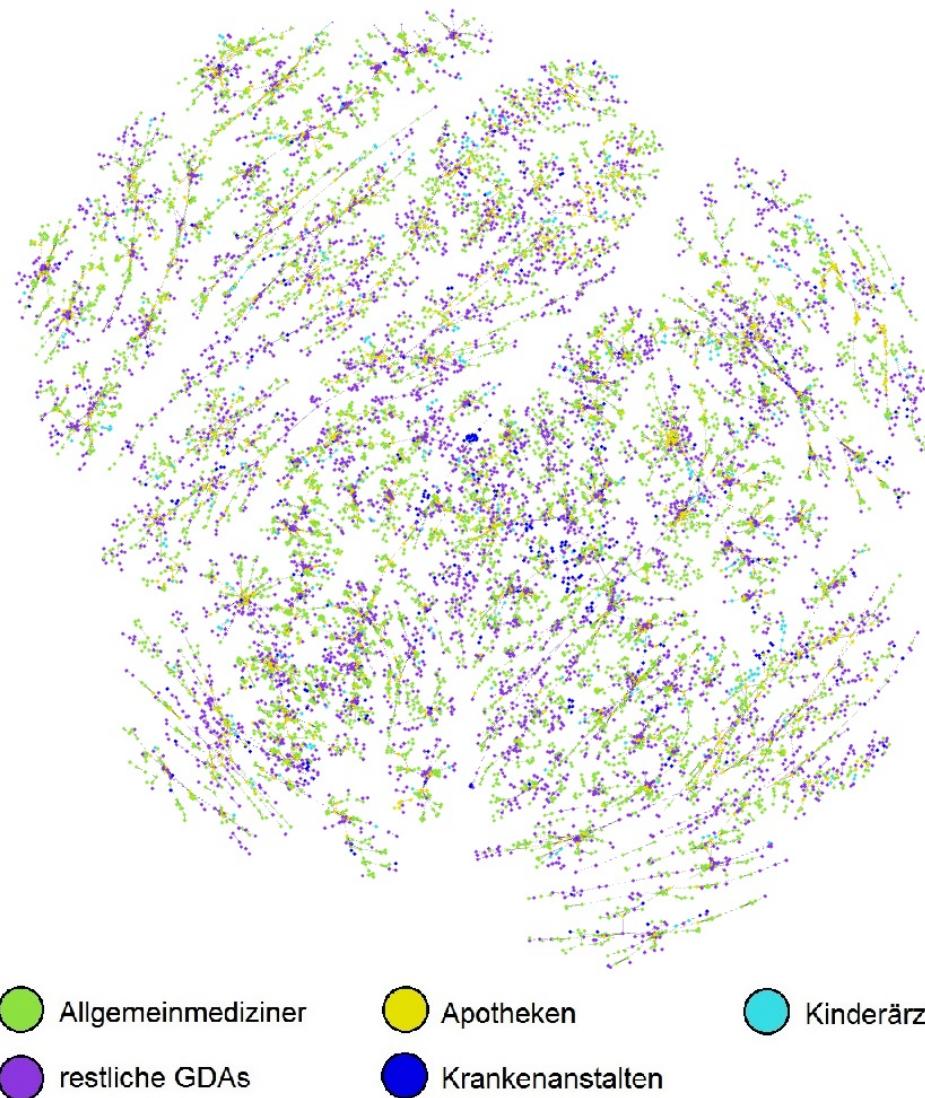
- GP
- specialist
- pharmacy
- hospital

Patient flows, Austria 2006



Dorda W, et al. Analyse von Behandlungsnetzwerken (HVB, 2013)

Patient flows



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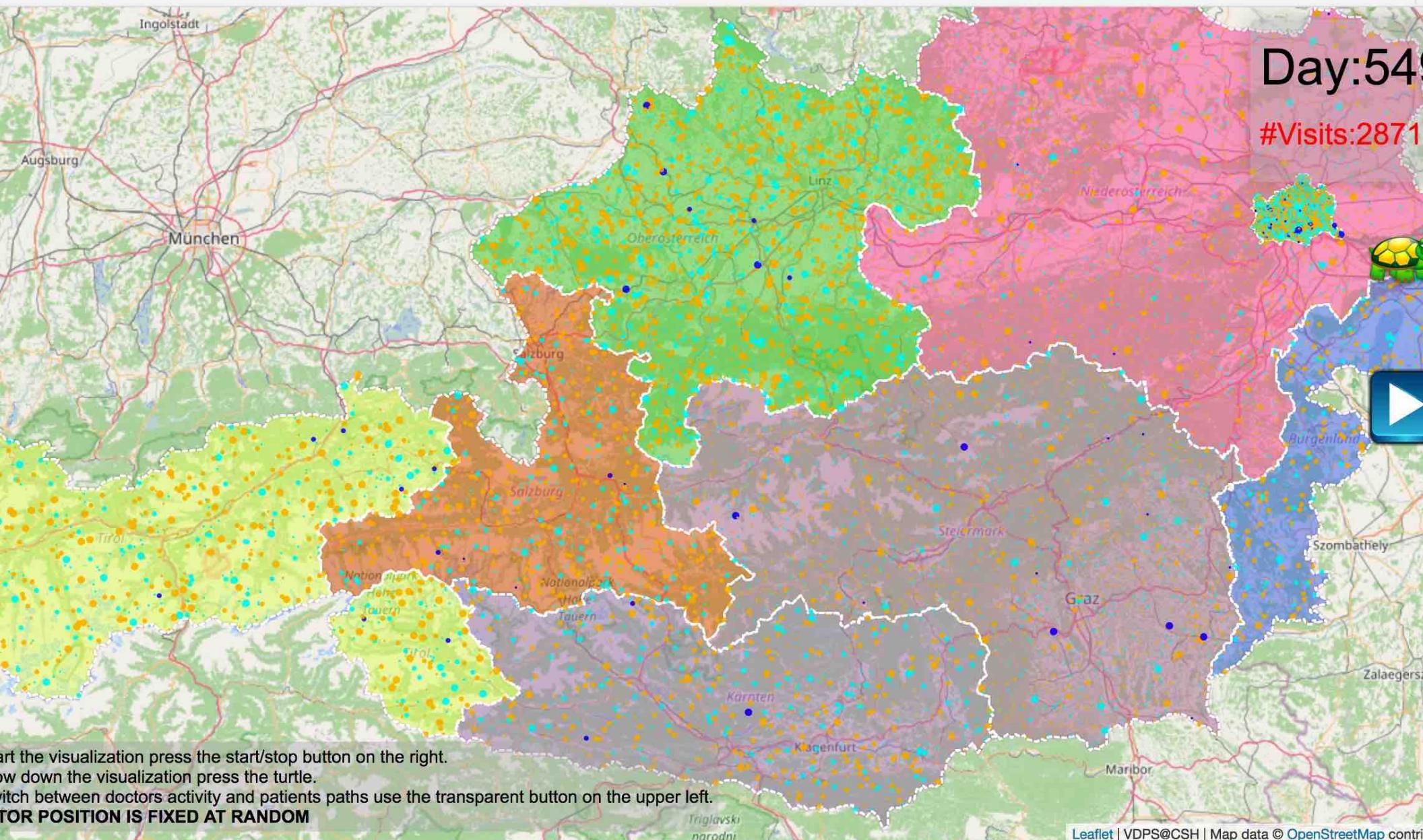


Search



Day:549

#Visits:2871



start the visualization press the start/stop button on the right.

Slow down the visualization press the turtle.

Switch between doctors activity and patients paths use the transparent button on the upper left.

DOCTOR POSITION IS FIXED AT RANDOM

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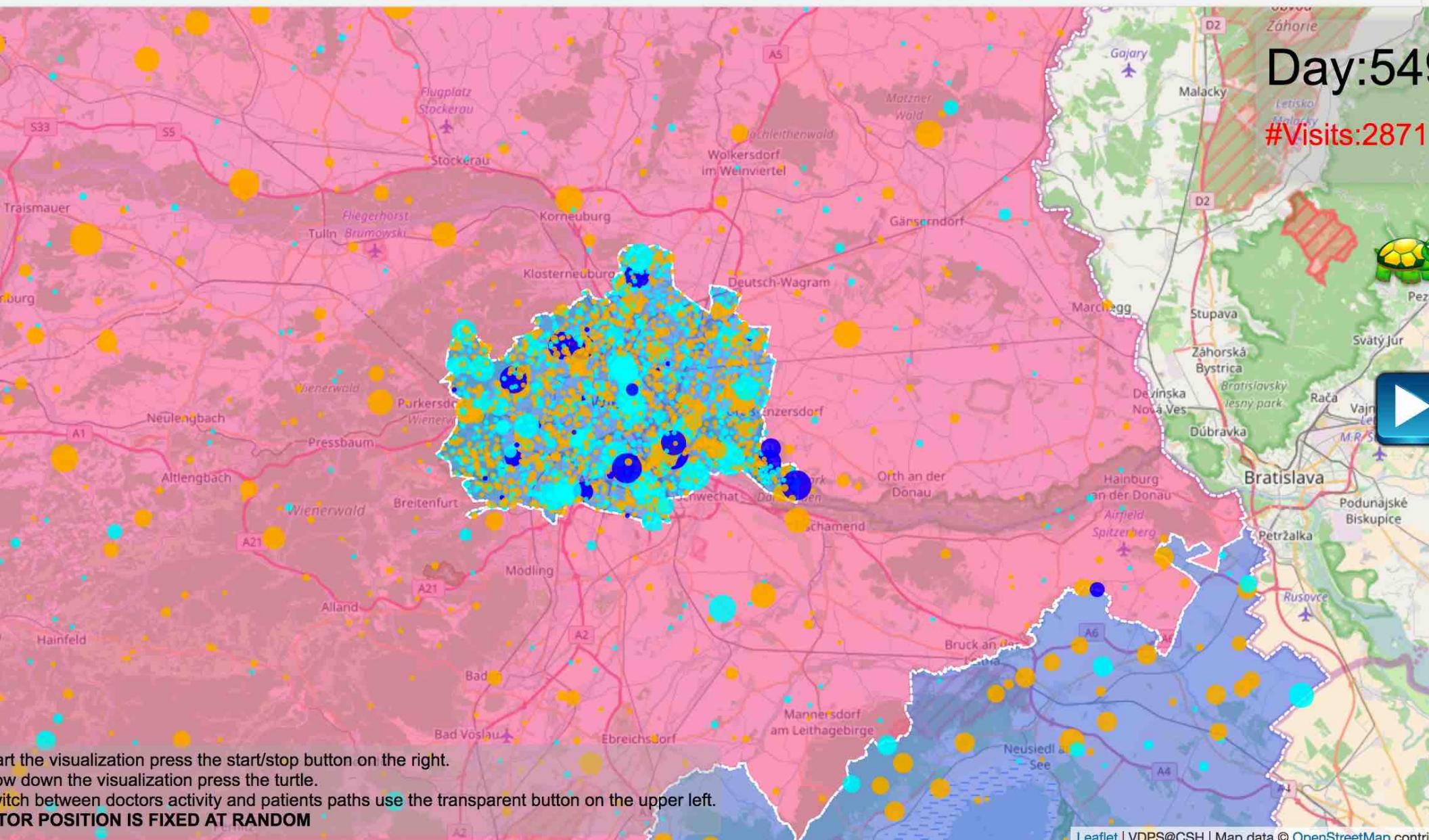


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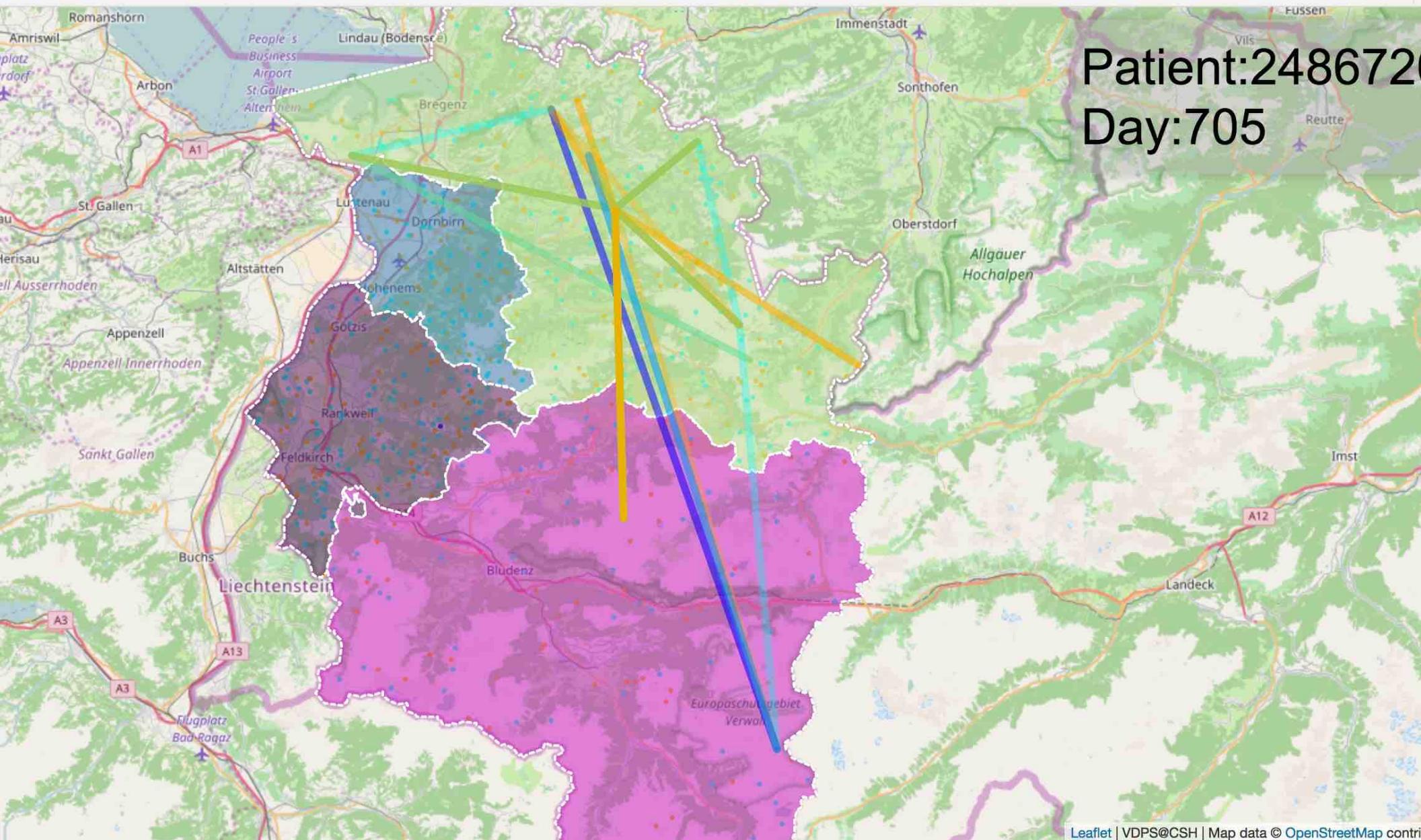
DOCTOR POSITION IS FIXED AT RANDOM

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how resilient is a health care system?



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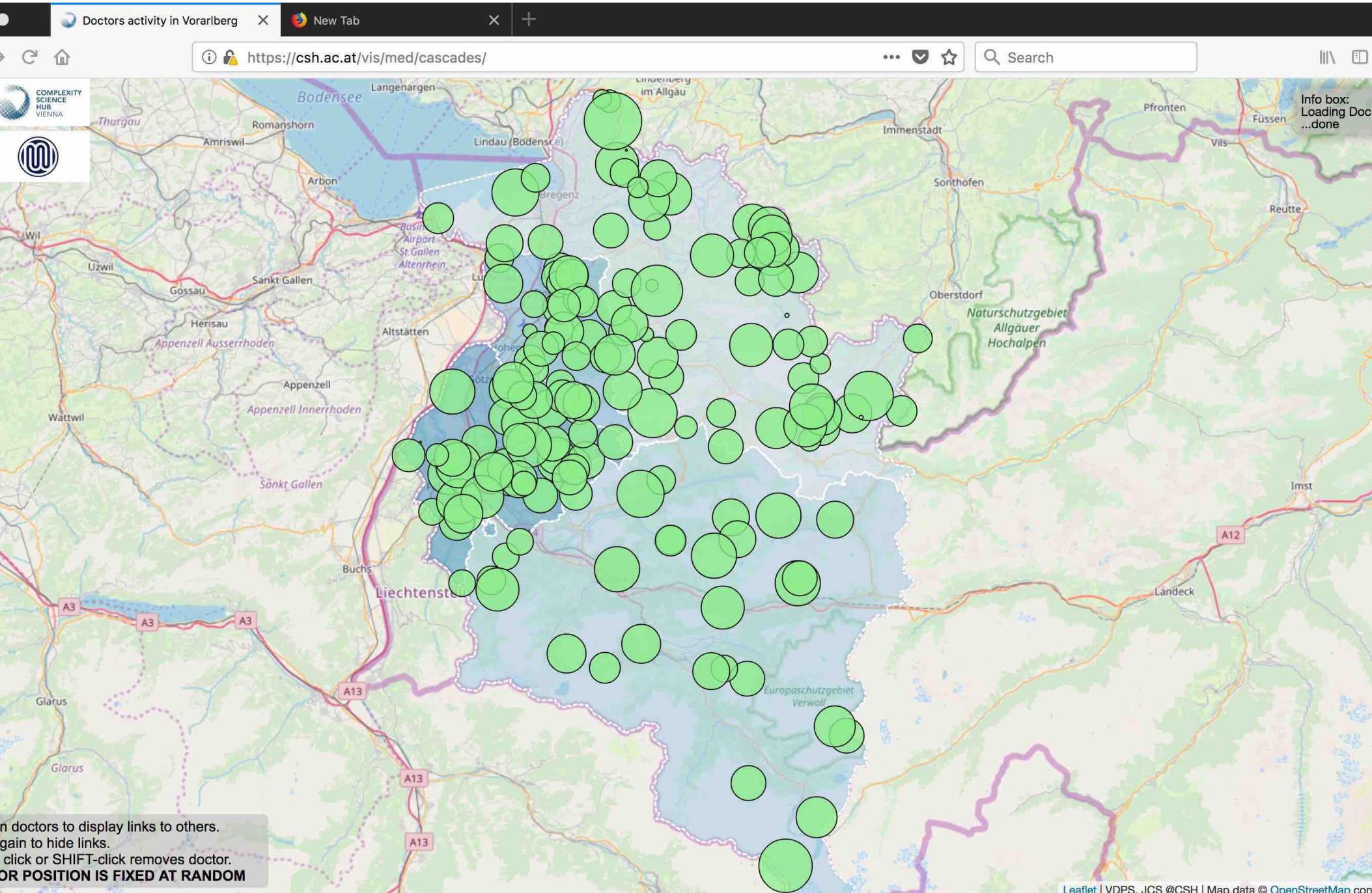
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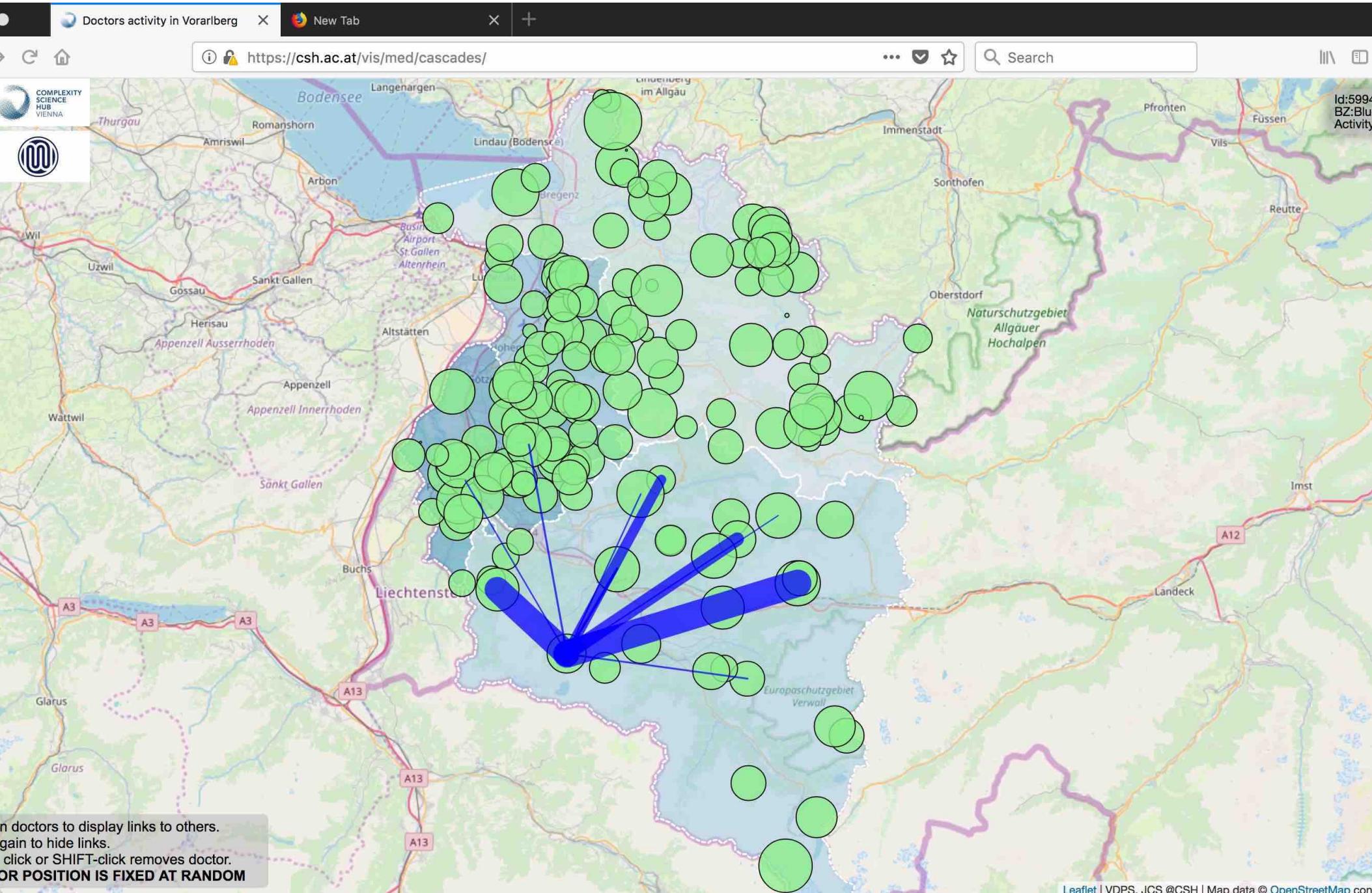


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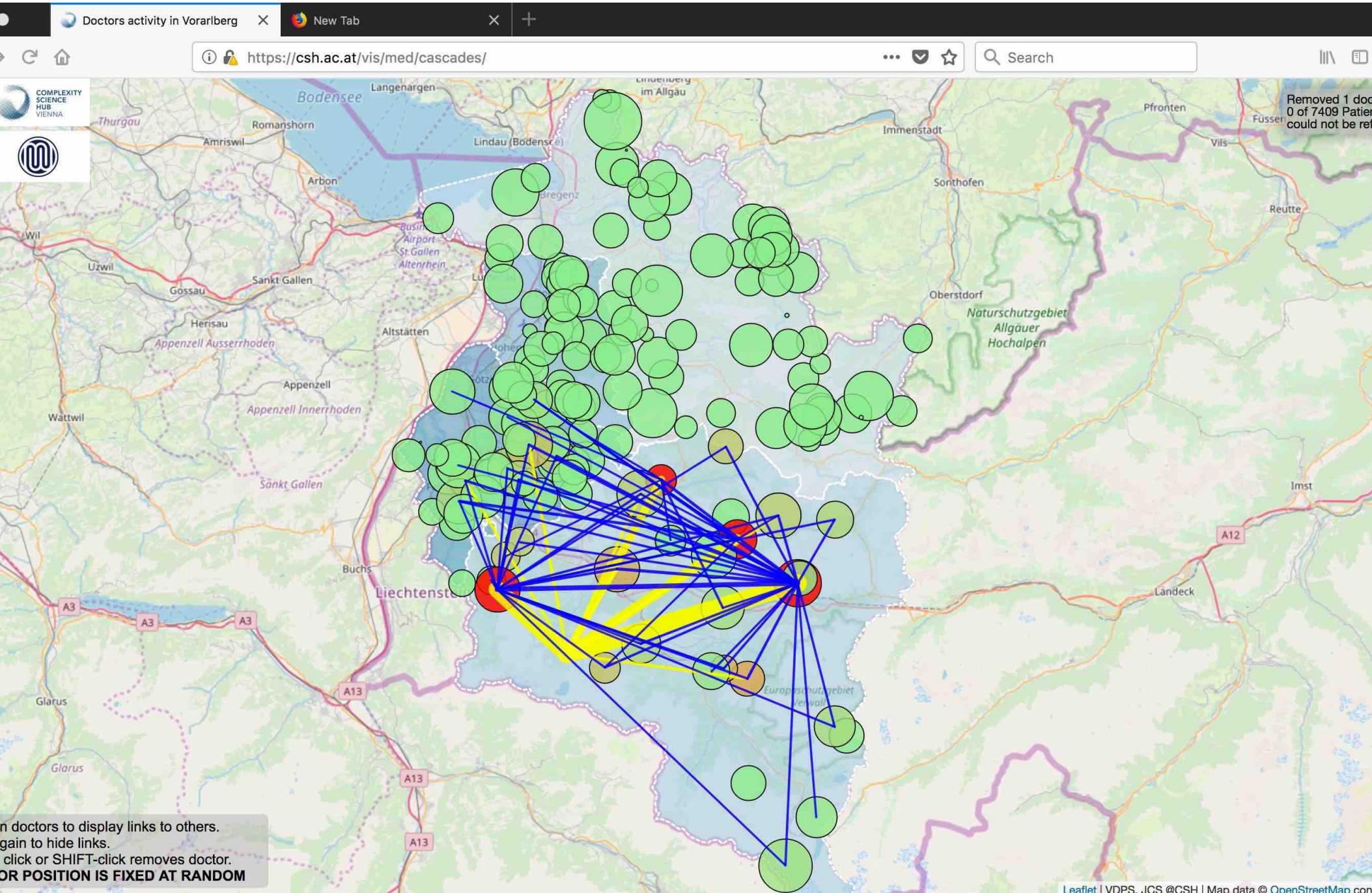


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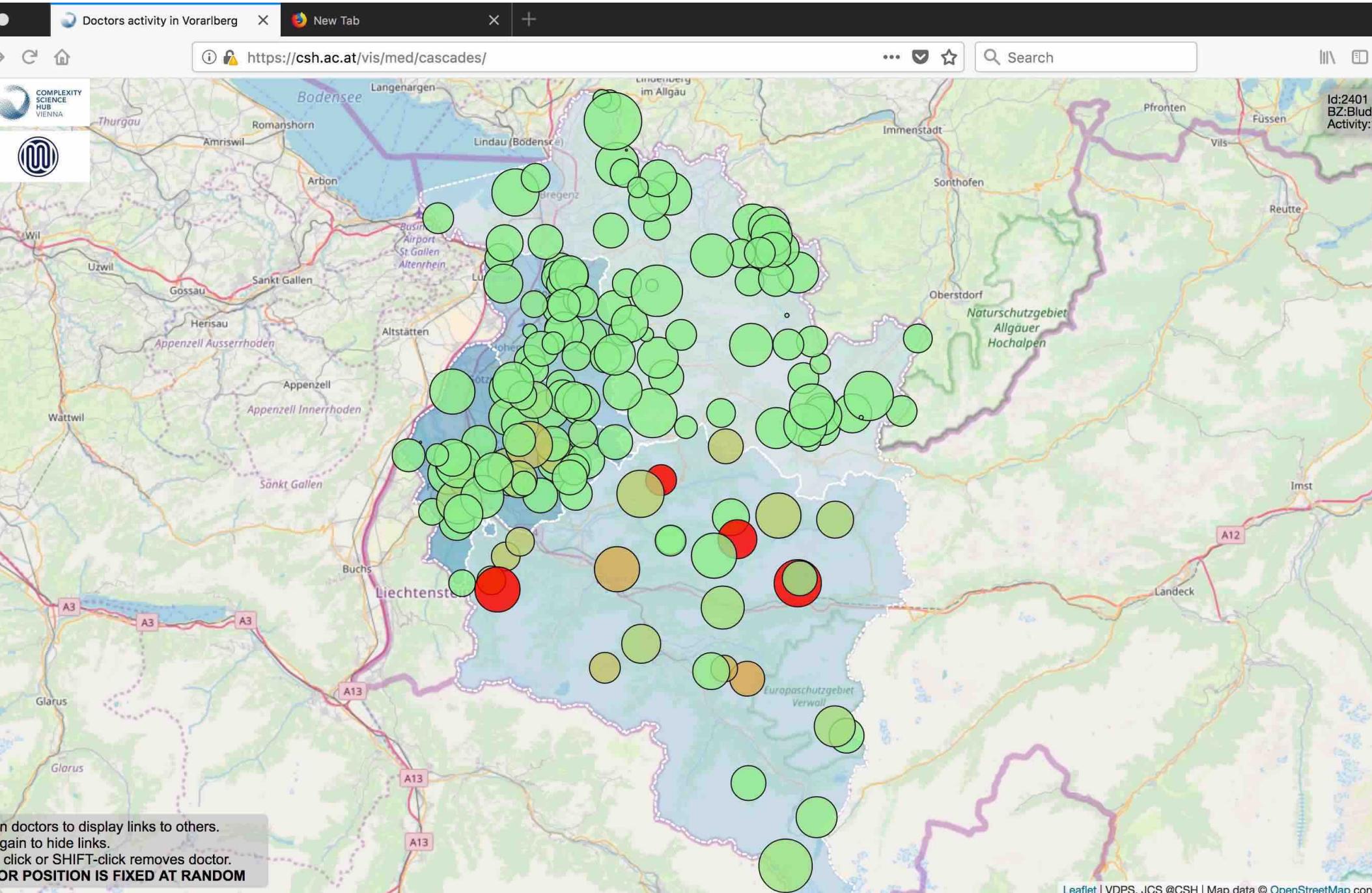


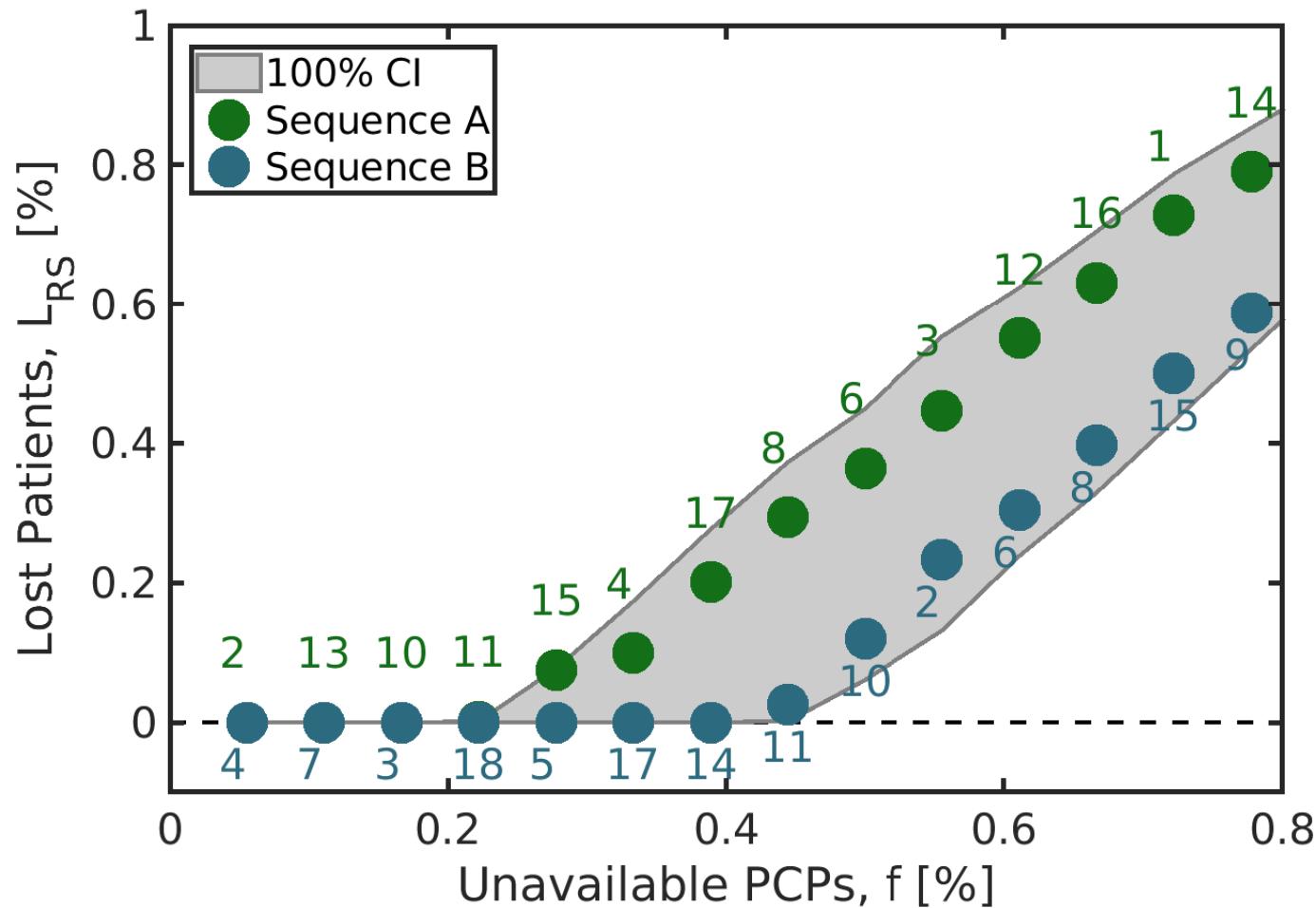
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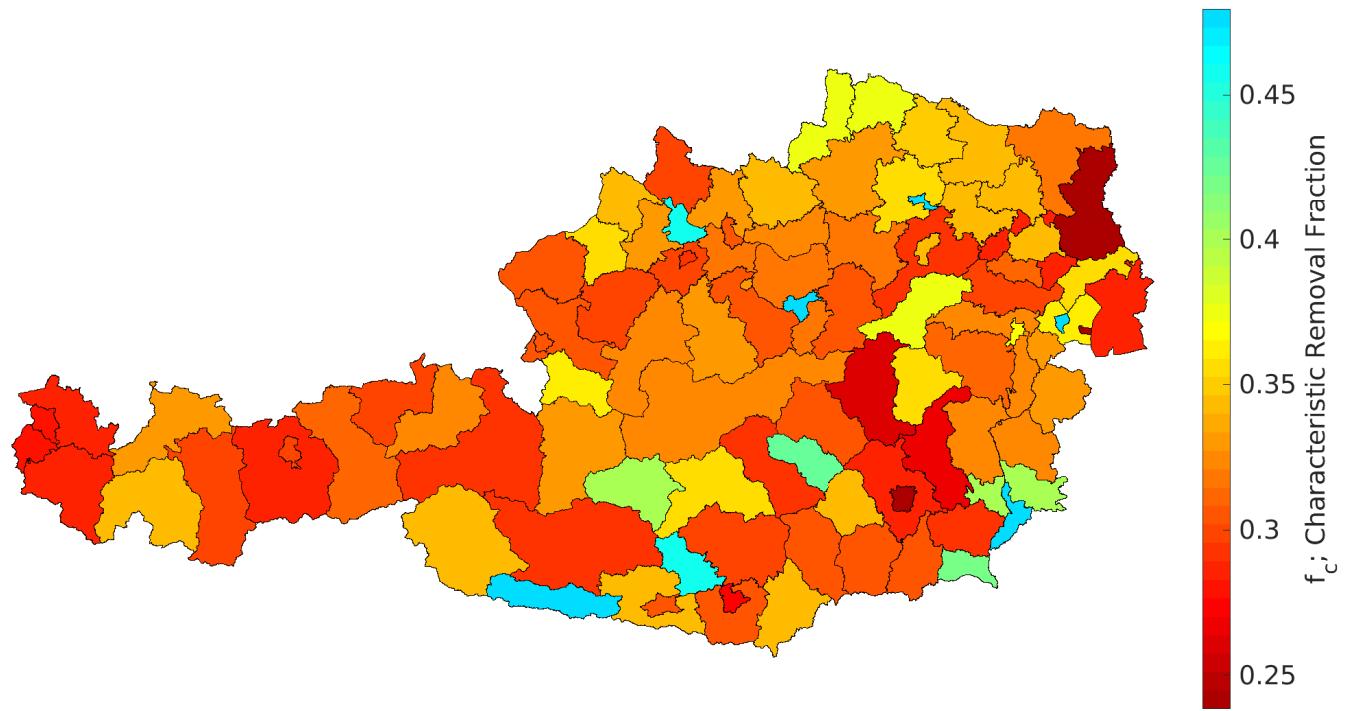


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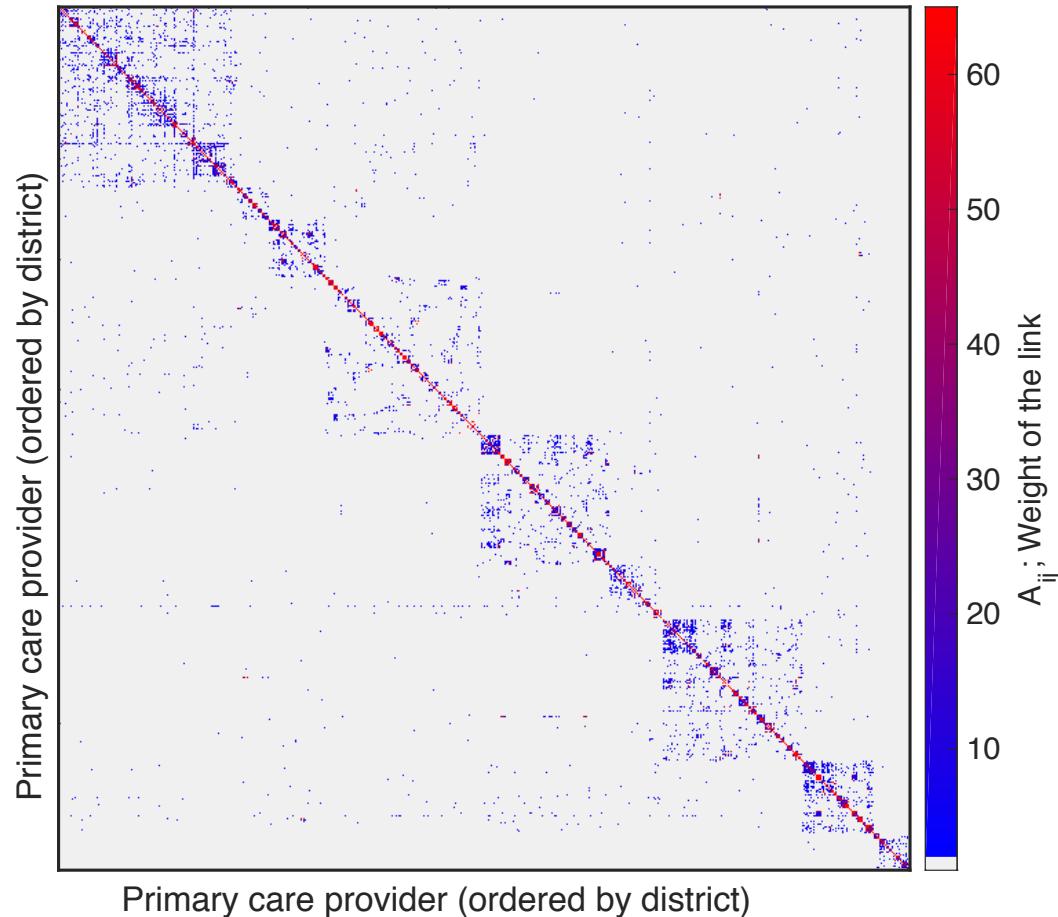
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Patient sharing network



What is the contribution?

- 1 what works when for whom under what conditions?
- 2 how efficient and resilient is the health care system?



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How will medicine change?

- machines and databases will do great diagnostics
- patients will take samples and assist the diagnosis process with their data and actions
- machines will assess: what works when for whom?
- machines will offer portfolios of treatment options

medicine must interpret those and guide patients to make optimal decisions for their life



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how much will we get from big data – really?



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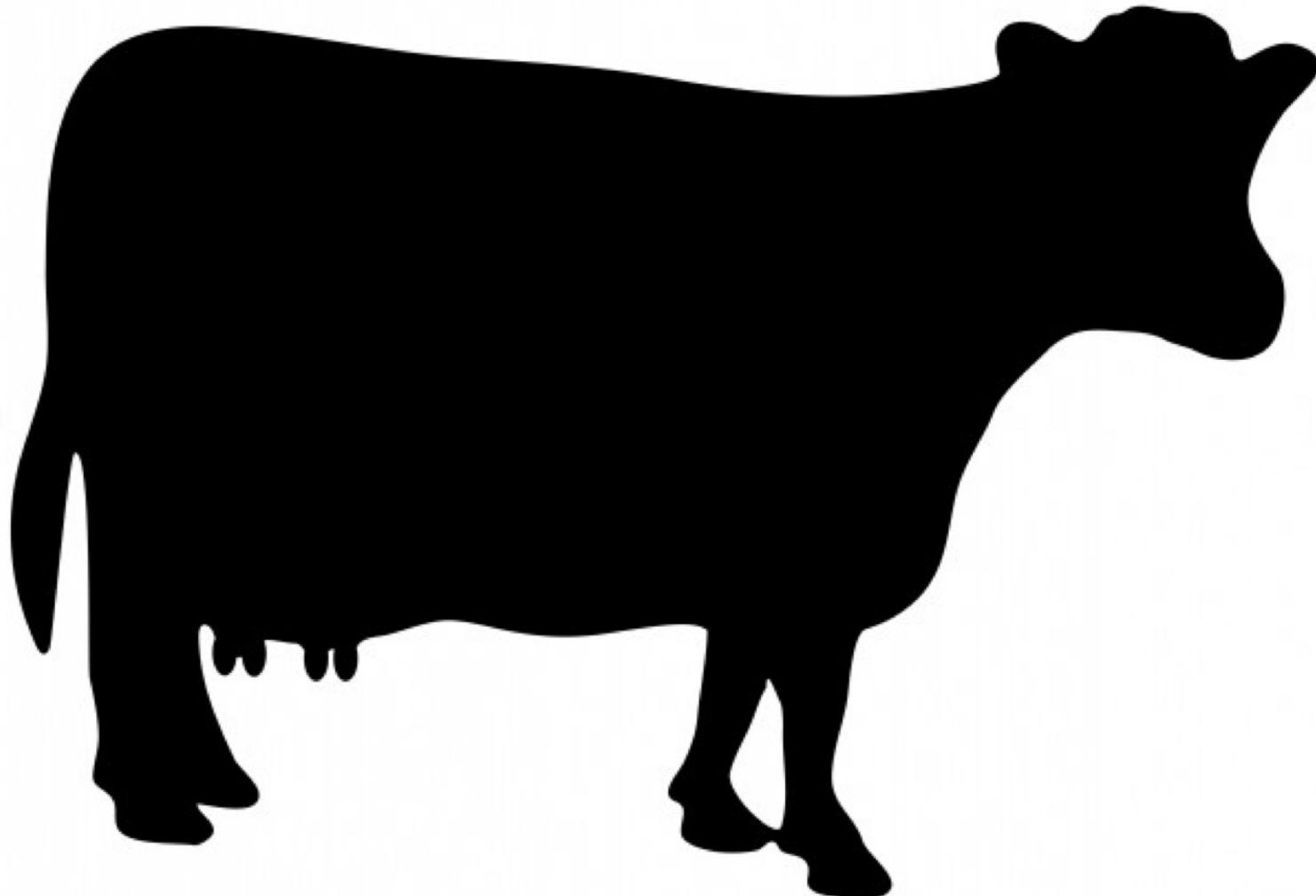
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Multilayer Animal Disease Network for cows

- 2,000,000 cows
- 150,000 genomes
- farm/herd/family....
- history of food intake
- complete health care records/diagnoses/treatment/vaccines/dosage
- 80 diseases
- metabolic information
- sensor data
- tissue samples



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Silke Aichberger, MUW

Anna Chmiel, MUW

Gottfried Endel, Hauptverband

Sarah Etter, MUW

Nina Haug, MUW

Caspar Matzhold, MUW

Ellenor Mittendorfer-Rutz, Karolinska

Thomas Niederkrotenthaler, MUW

Michaela Kaleta, MUW

Alexandra Kautzky-Willer, MUW

Peter Klimek, MUW, Complexity Science Hub

Miriam Leitner, MUW

Michael Leutner, MUW

Ruggiero Lo Sardo, MUW

Irmgard Schiller-Frühwirth, Hauptverband

Johannes Sorger, Complexity Science Hub

Stefan Thurner, MUW, Complexity Science Hub