Network Analysis in Healthcare

- **Course:** CS5891/CS3891
- **Instructor:** You Chen, Ph.D. (you.chen@vanderbilt.edu)
- **TA:** Yubo Feng (yubo.feng@Vanderbilt.Edu)
- **Semester:** Fall 2021
- **Time:** Monday & Wednesday, 3:30 – 5:00 pm
- **Location:** Featheringill Hall, Room 211
- **Website:** http://www.ohpenlab.org/courses/
- **Office Hours:** Upon Appointment
- **Academic session**: 08/25/2021 - 12/10/2021

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https://hiplab.mc.vanderbilt.edu/~ychen/

Course overview

- A new course - no textbook for the course
- Scientific paper–driven
- A tour of network analysis in health via various scientific studies
- Assignments – six reading summaries plus a network analysis project
- Goal – open a door for students entering network science and learn how to apply network analysis in health

- [Syllabus](#)

Topics covered

- Sociometric factors – basic network science
- Network analysis in learning health systems
- Network analysis in prediction
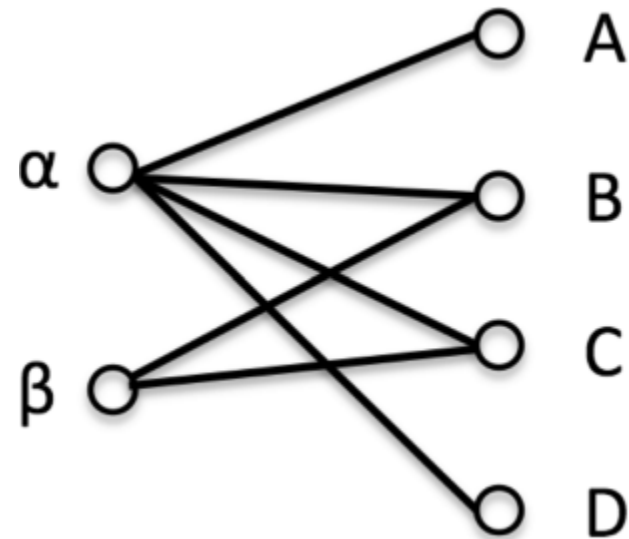- Network analysis in drug repurposing and drug-drug interactions

Learning health system
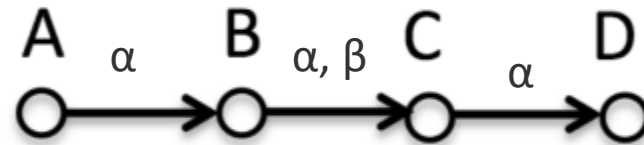
Patient referral paths

Physician-patient encounter records

A: family practice
B: internal medicine
C: Cardiology
D: Vascular surgery

Patient

Physician

Net patient flow:
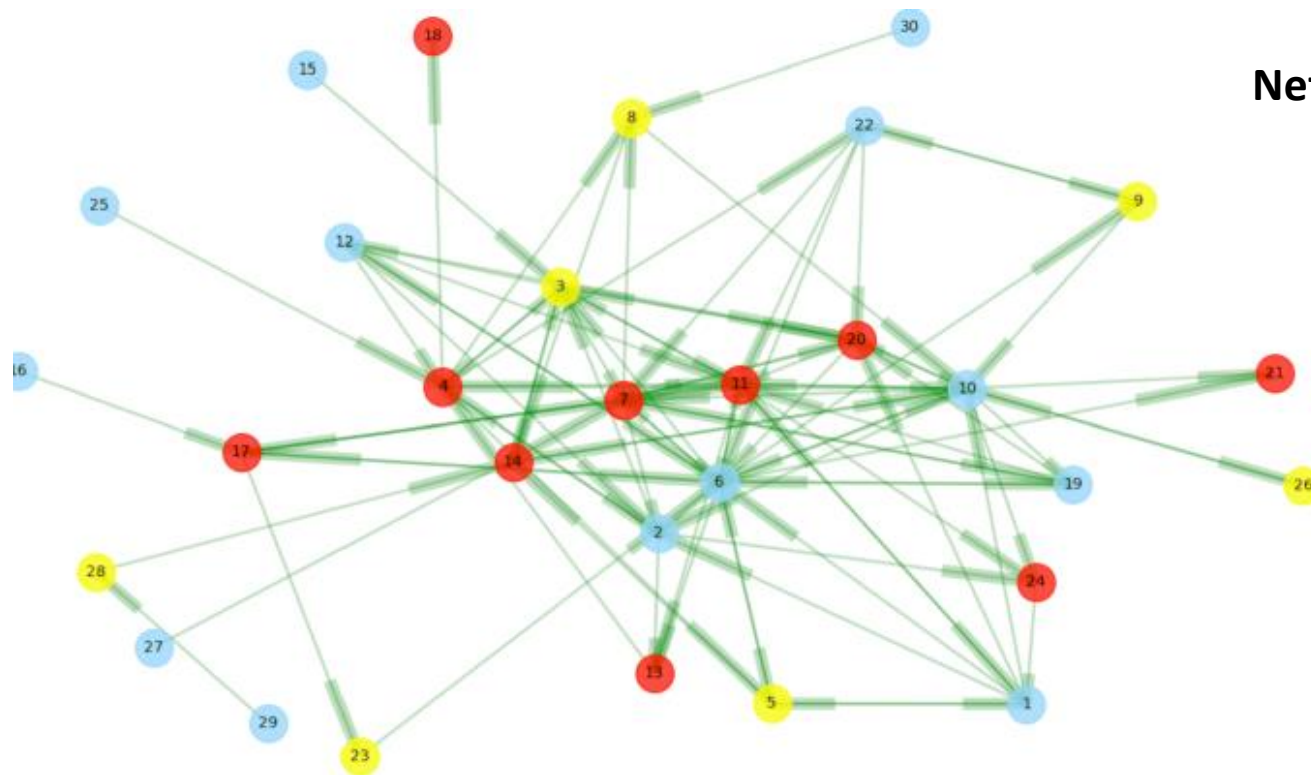# of referrals in - # of referrals out

It encodes the flow of patients and information between physicians in a healthcare system or across healthcare systems

It related to treatment outcomes and effectiveness of medical resources utilization

α: A(2011-01-01)->B(2011-01-10)->C(2011-02-01) ->D(2011-03-01)
β: B(2011-03-01)->C(2011-03-20)

A referral network with 30 physicians and 101 directed edges in a single hospital
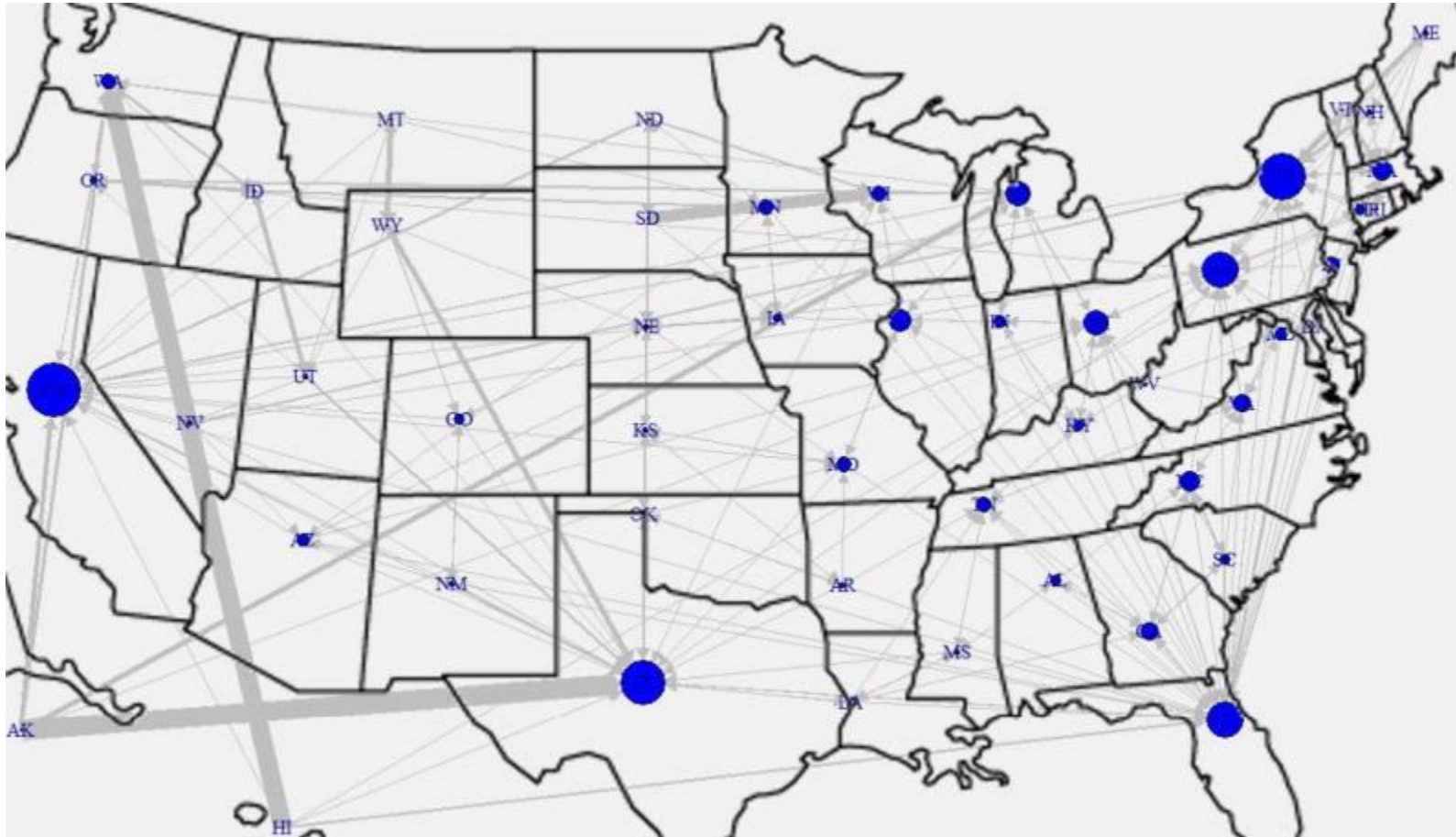

Net patient flow: # of referrals in - # of referrals out

- ● positive
- ● zero
- ● negative

- Targets of referrals are marked with shadow on directed edges

Source: An C, et.al. Referral paths in the US physician network. Applied network science. 2018 Dec;3(1):1-24.

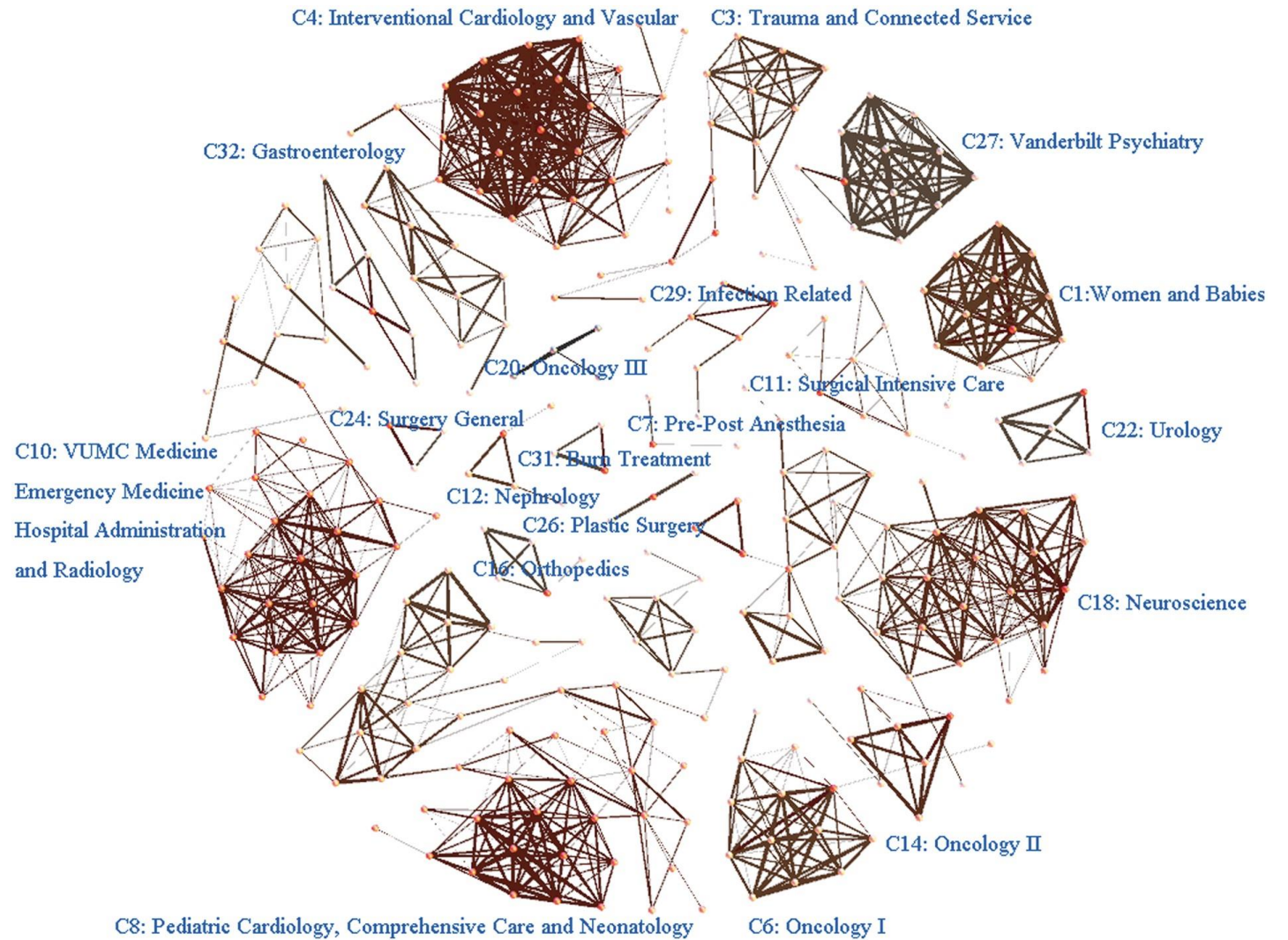# U.S. patient referral network

Directed edges of each state's top five out-of-state referrals

Intra-hospital collaboration - networks of departments at VUMC

Labels in figure:
- C4: Interventional Cardiology and Vascular
- C3: Trauma and Connected Service
- C27: Vanderbilt Psychiatry
- C32: Gastroenterology
- C29: Infection Related
- C1: Women and Babies
- C20: Oncology III
- C11: Surgical Intensive Care
- C24: Surgery General
- C7: Pre-Post Anesthesia
- C22: Urology
- C10: VUMC Medicine Emergency Medicine Hospital Administration and Radiology
- C31: Burn Treatment
- C12: Nephrology
- C26: Plastic Surgery
- C18: Neuroscience
- C16: Orthopedics
- C14: Oncology II
- C8: Pediatric Cardiology, Comprehensive Care and Neonatology
- C6: Oncology I

Chen Y, et.al. Identifying collaborative care teams through electronic medical record utilization patterns. Journal of the American Medical Informatics Association. 2017;24(e1):e111-20.

Hierarchical structure
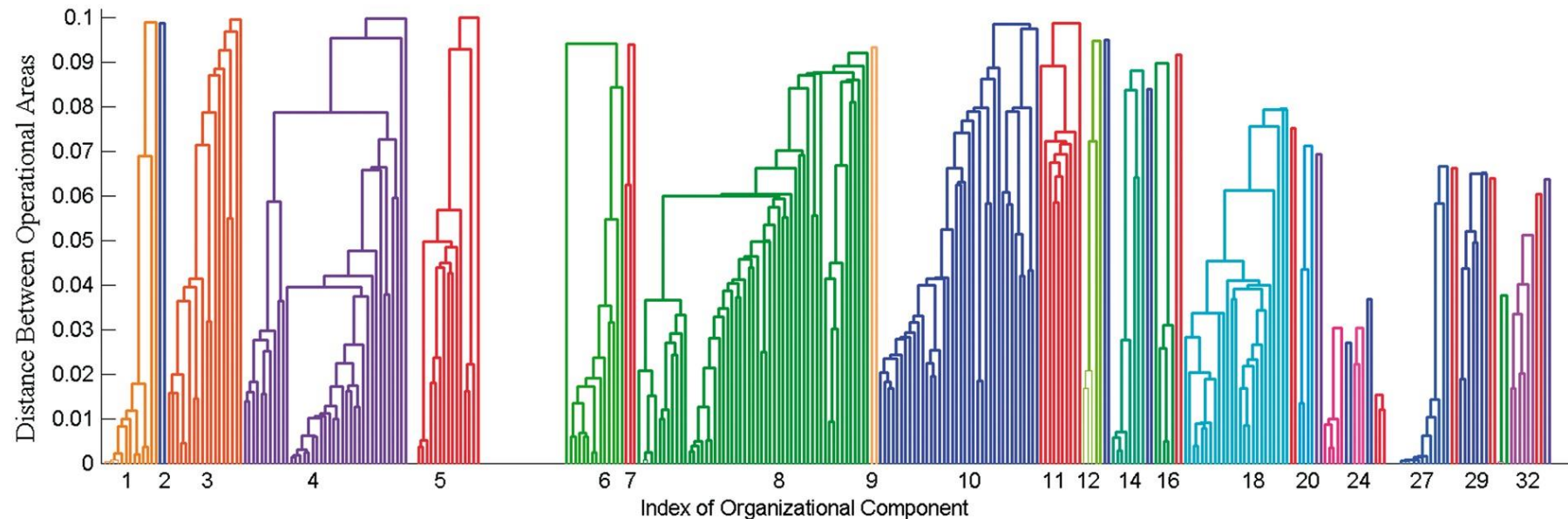
1: Women and Babies; 2: Dancing Injured Service; 3: Trauma and Connected Services; 4: Interventional Cardiology and Vascular Institute;

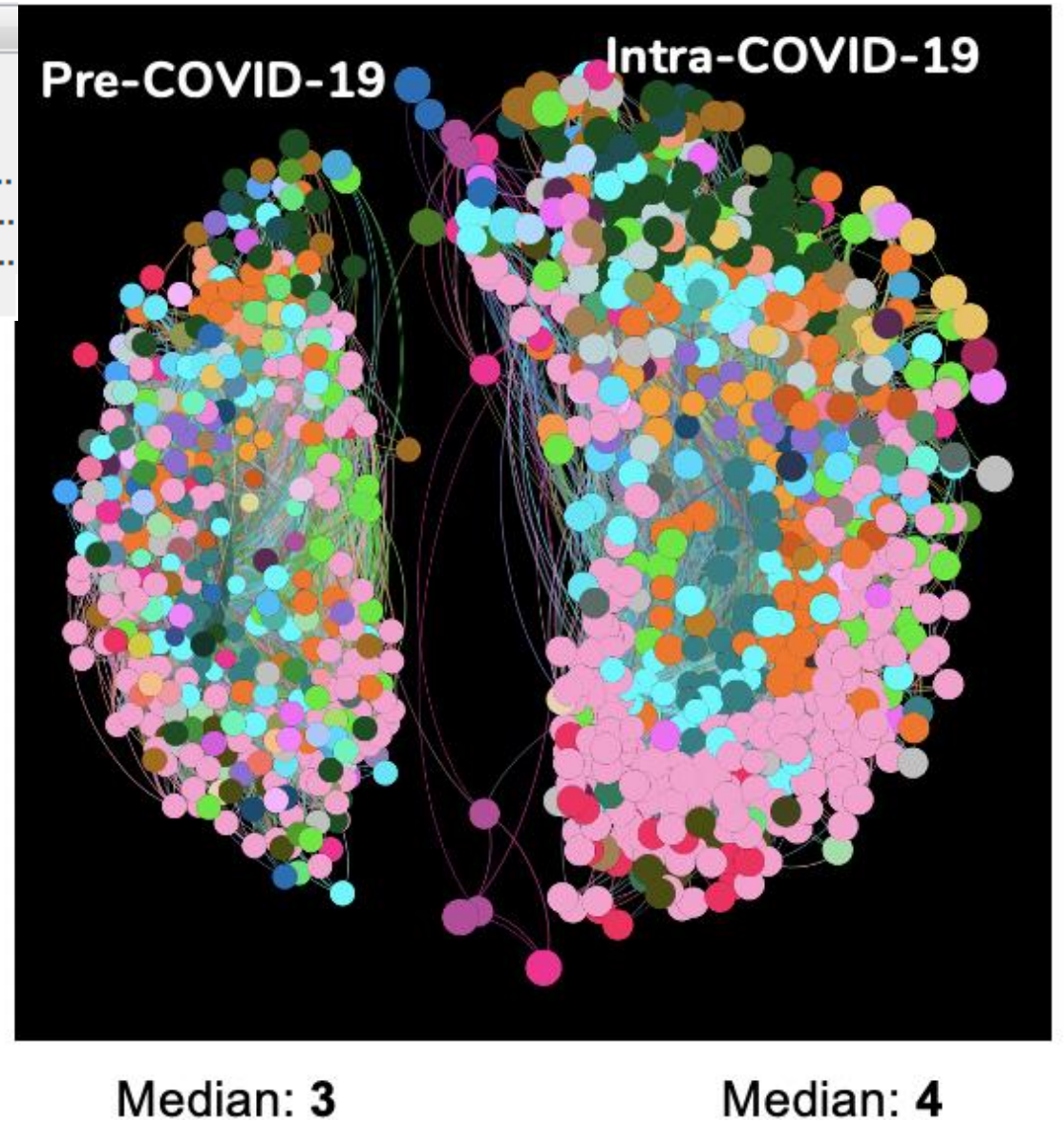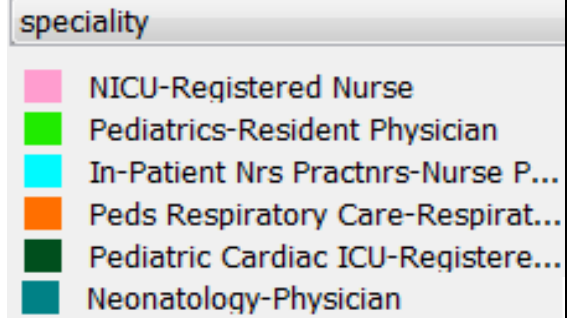5: Pediatrics Surgery; 6: Oncology I; 7: Pre-Post Anesthesia; 8: Pediatric Cardiology, Comprehensive Care and Neonatology;

9: Prevention of Skin Diseases; 10: VUMC Medicine, Emergency Medicine, VUH Administrative and Research, and Radiology; 11: Surgical Intensive Care Unit;

12: Nephrology; 13: Otolaryngology; 14: Oncology II; 15: Virology Lab; 16: Orthopedics; 17: Pediatric Infections; 18: Neuroscience; 19: Infection Monitoring;

20: Oncology III; 21: Endocrinology; 22: Urology; 23: Outpatient Surgical Related; 24: Surgery, General; 25: Pathology; 26: Plastic Surgery; 27: Vanderbilt Psychiatry;

28: Ophthalmology; 29: Infection Related; 30: Rheumatology Clinic; 31: Burn Treatment; 32: Gastroenterology; 33: Human Nutrition; 34: VMG Support Systems

Changes in collaboration structures in the neonatal intensive unit

speciality

- NICU-Registered Nurse
- Pediatrics-Resident Physician
- In-Patient Nrs Practnrs-Nurse P...
- Peds Respiratory Care-Respirat...
- Pediatric Cardiac ICU-Registere...
- Neonatology-Physician

Pre-COVID-19   Intra-COVID-19

Median: 3   Median: 4

Mannering H, et.al. Assessing Neonatal Intensive Care Unit Structures and Outcomes Before and During the COVID-19 Pandemic. JMIR, 2021
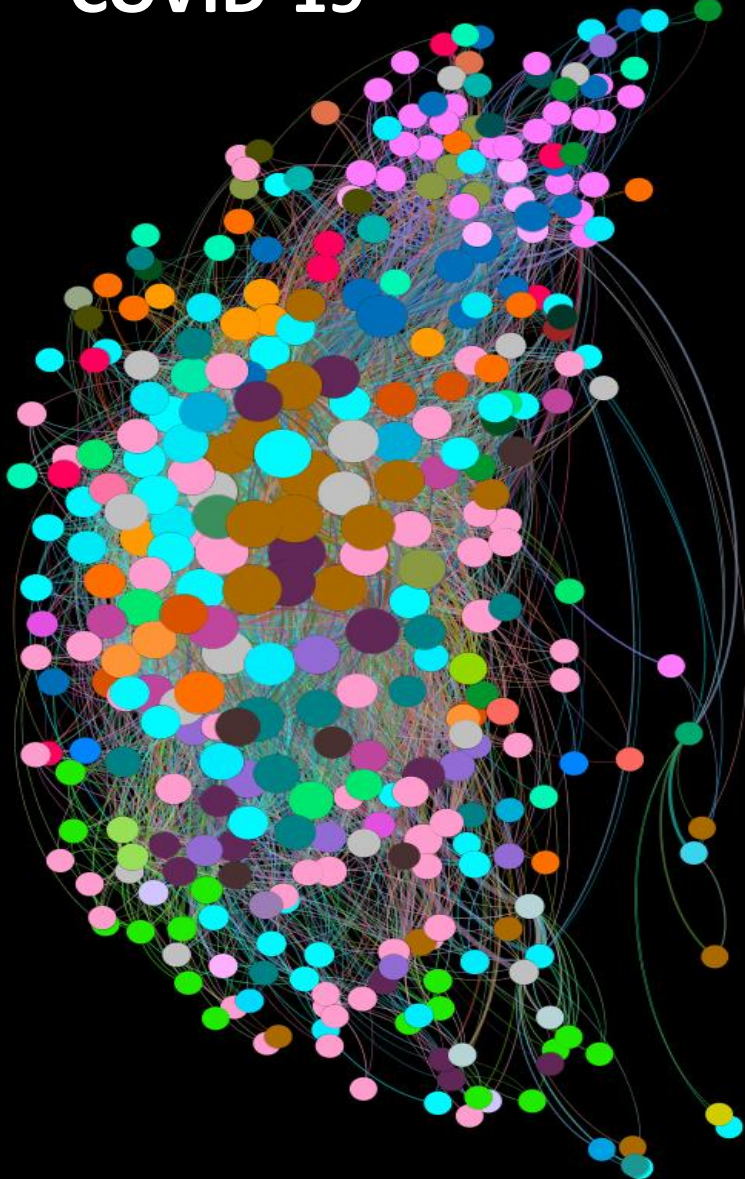
COVID-19 / **Non-COVID19**
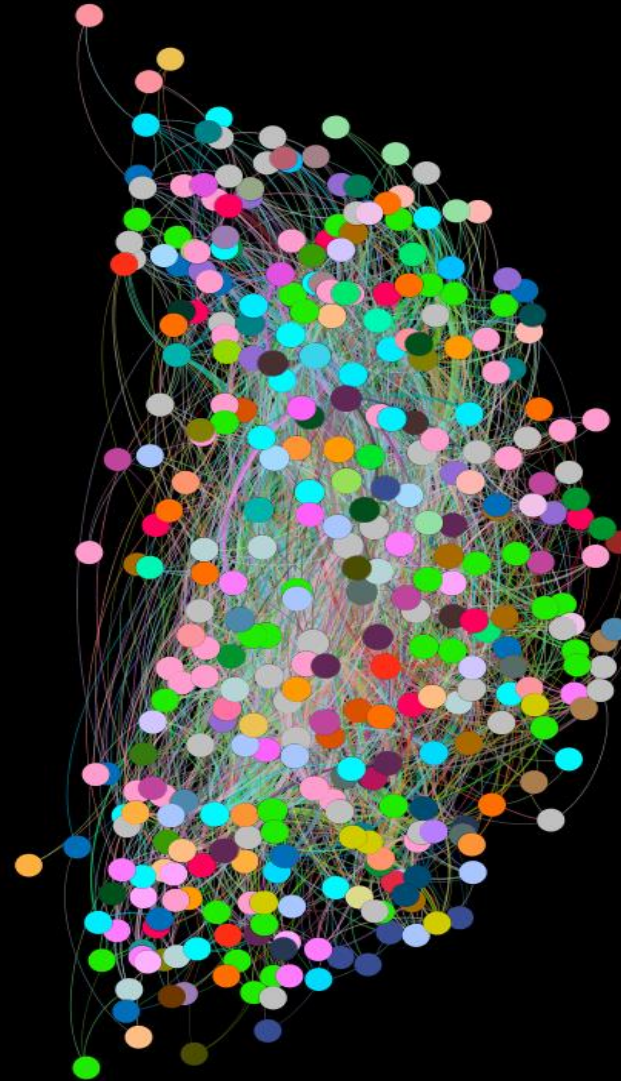
Healthcare workers are much more highly densely connected (active in EHRs) in the COVID-19 network than in the Non-COVID-19 network

Legend:
- MICU-Registered Nurse
- Medicine-Housestaff-Resident Physician
- Respiratory Care-Respiratory Therapist
- Radiology-Physician
- Emergency Services-Registered Nurse
- Internal Medicine-Physician
- Cardiovascular Medicine-Physician
- Hospital Nurse Practitioners-Nurse Practitio.
- Med Center East-Registered Nurse
- Emergency Medicine-Physician

Yan C, et.al. Collaboration Structures in COVID-19 Critical Care: Retrospective Network Analysis Study. JMIR human factors. 2021;8(1):e25724.

Internal medicine physicians and nurse practitioners in the COVID-19 connect with each other; while those in the Non-COVID-19 are separated

Residents

Residents

COVID-19

Non-COVID-19
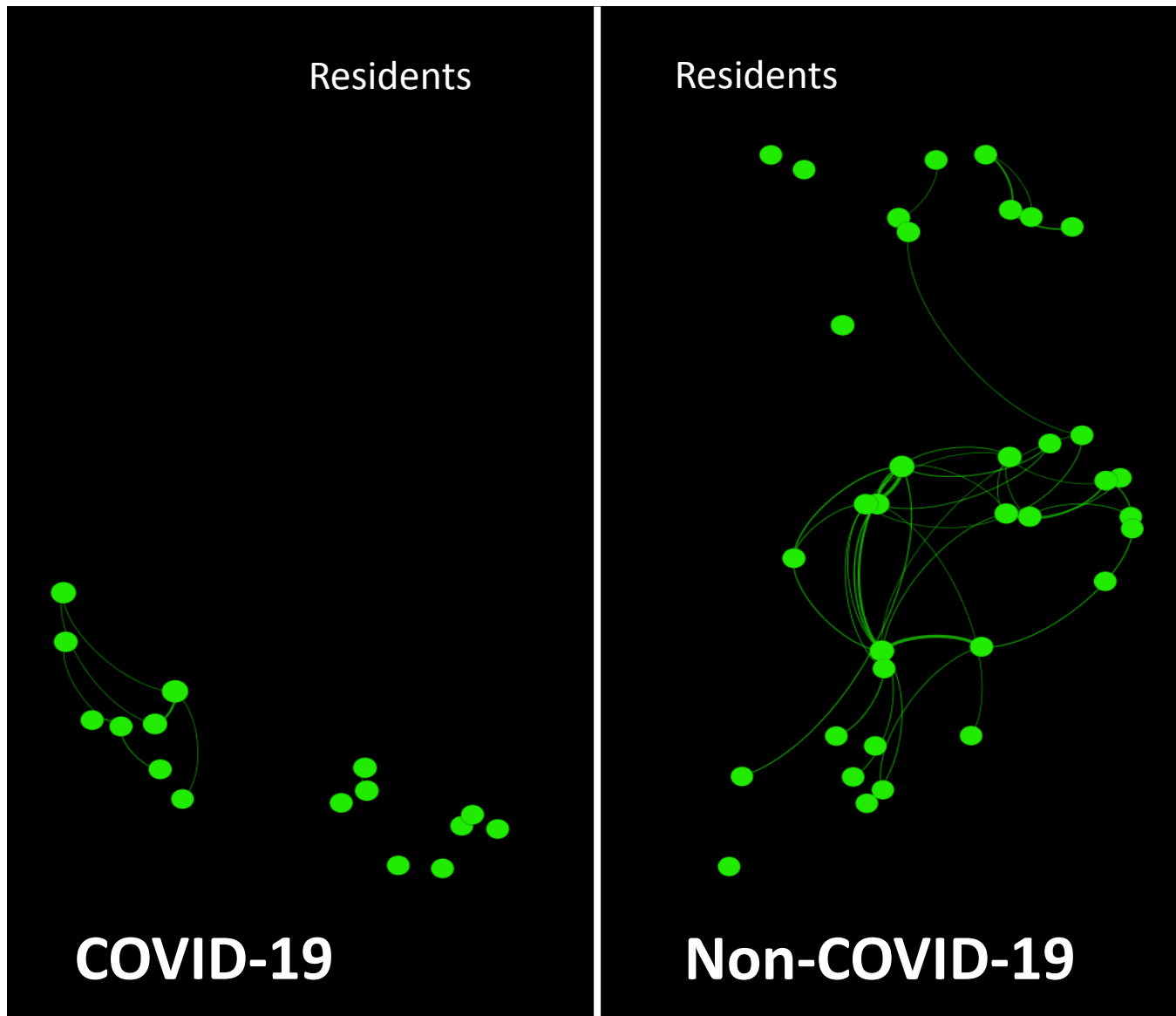
VUMC put full-time non-trainee healthcare workers in the management of critically ill COVID-19 patients, mirroring the national graduate medical education protections of residents placed at the outset of the COVID-19 pandemic

Collaboration structures and clinical outcomes

Nursing handoff structures are associated with family satisfaction
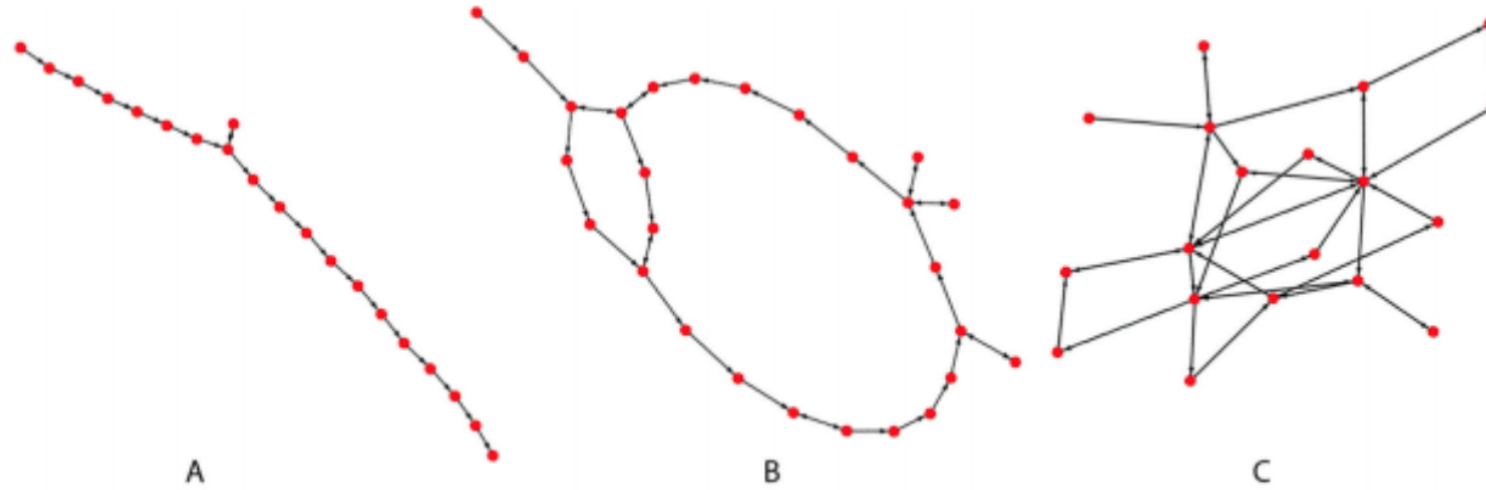
NICU nurse handoff structure

A   B   C

Higher family satisfaction

Critical care nursing team structures are associated with mortality risk

Nodes with white color are nurses who had received and disseminated useful information from a wide range of sources to their colleagues

Kelly Costa D, et.al. The structure of critical care nursing teams and patient outcomes: a network analysis. American journal of respiratory and critical care medicine. 2020 Feb 15;201(4):483-5.
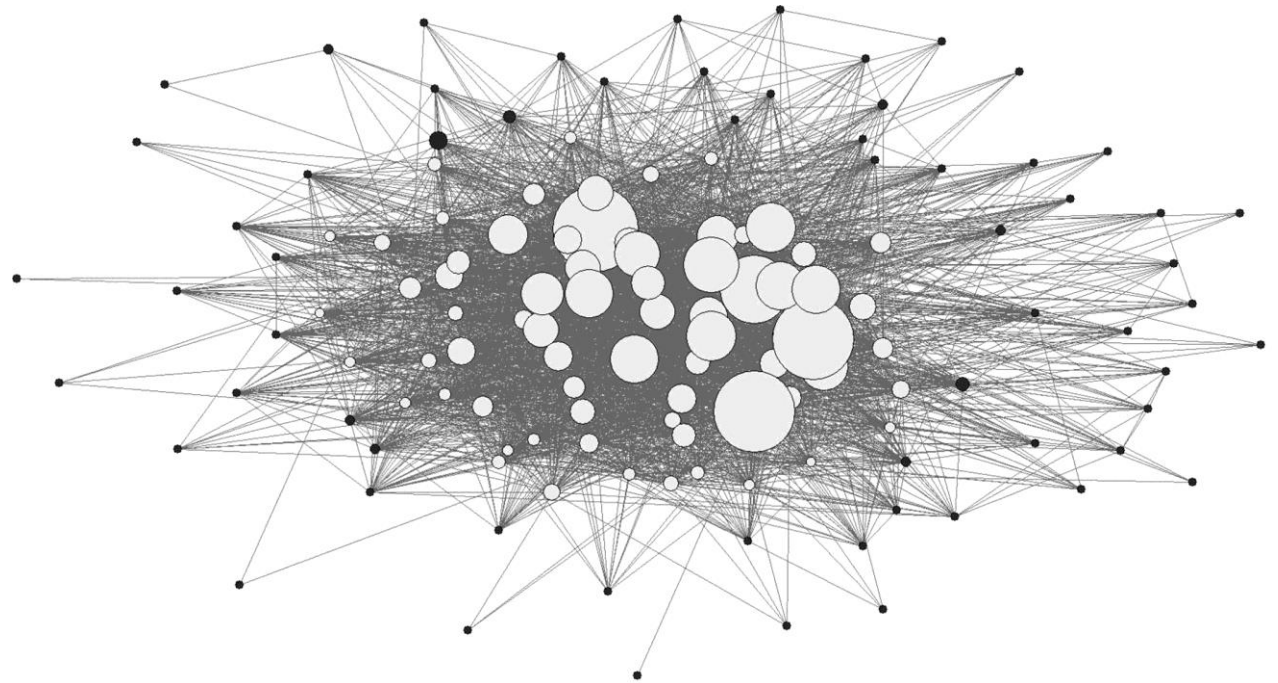
Relating network structure to length of stay

Out-degree average > 1.7   Out-degree average < 1.7

Length of stay

Low out-degree group

High out-degree group
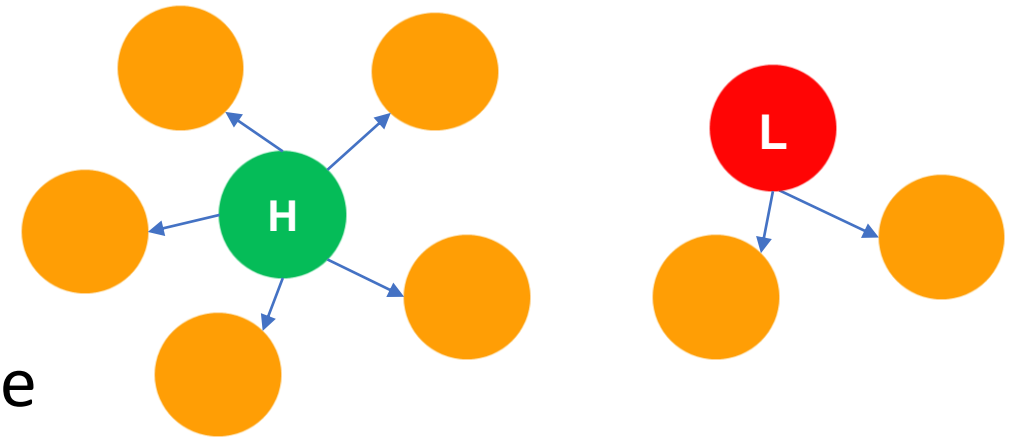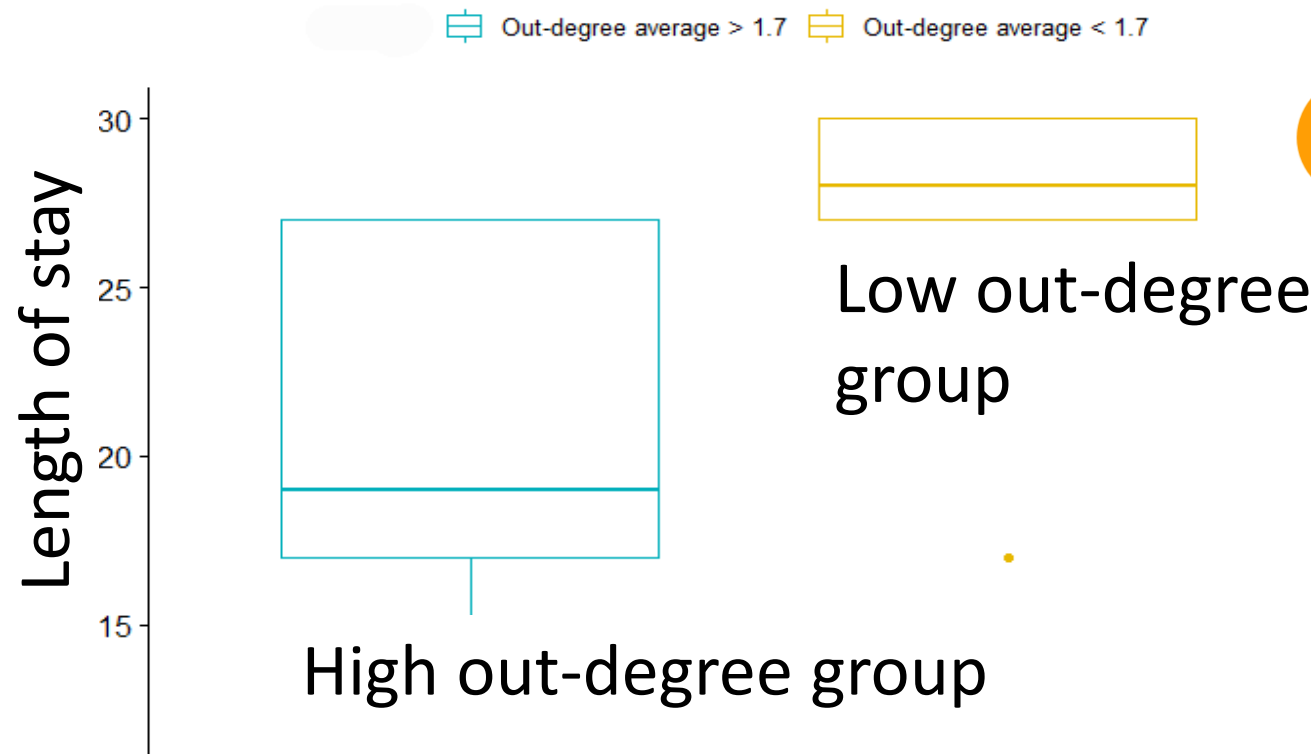
Higher out-degree group is associated with shorter length of stay

Kim C, et.al. Provider networks in the neonatal intensive care unit associate with length of stay. In2019 IEEE 5th International Conference on Collaboration and Internet Computing (CIC) 2019 Dec 12 (pp. 127-134). IEEE.

Cancer survivors whose providers have more patients in common tend to have higher quality and lower cost care

Provider A

Care density of solid line patient: (AB+BC+AC)/3 = 2

Provider B
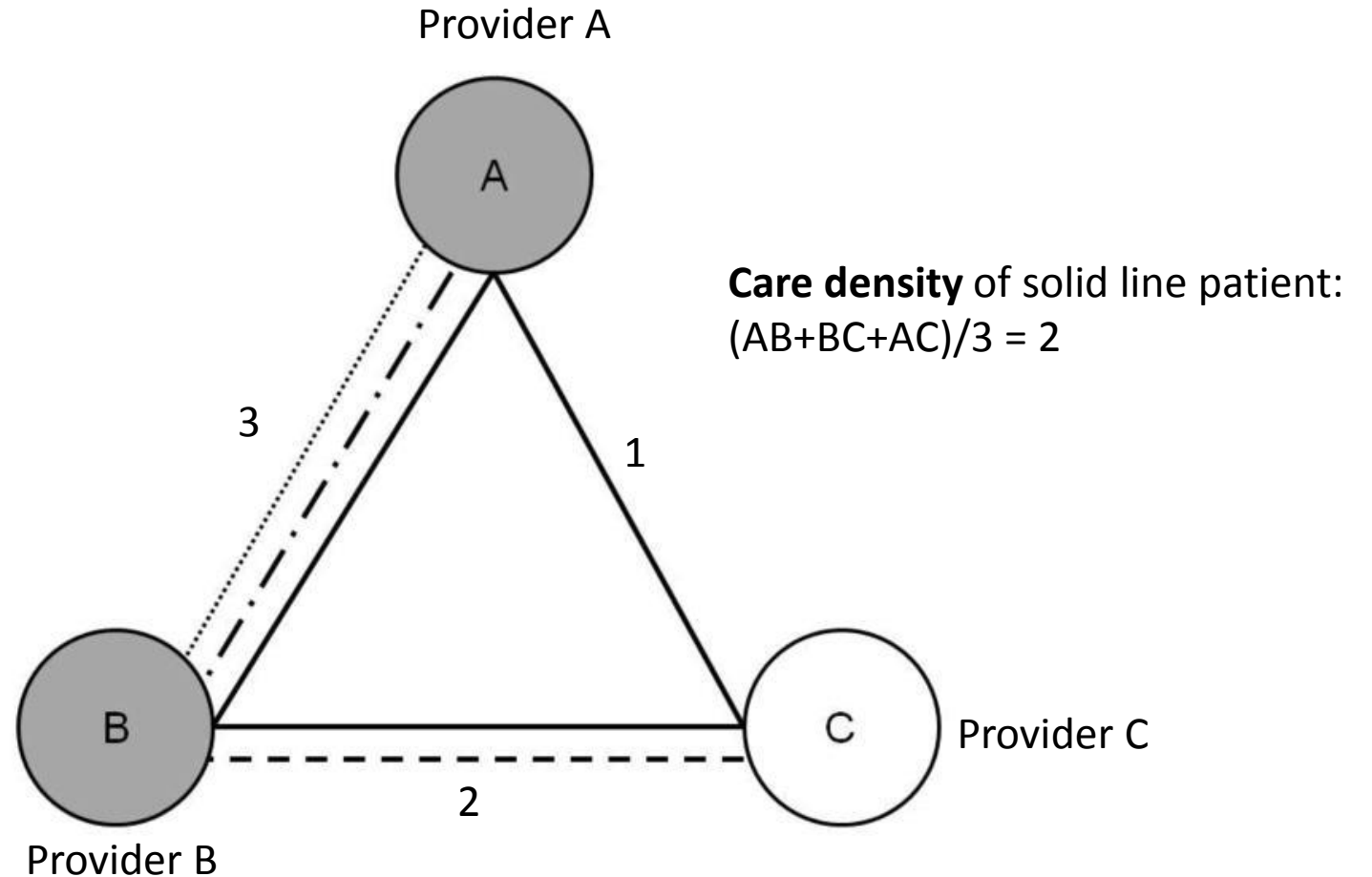
Provider C

Patients with high care density—indicating high levels of patient-sharing among their providers—

had significantly lower rates of hospitalization and lower inpatient and outpatient costs

Pollack CE, Frick KD, Herbert RJ, Blackford AL, Neville BA, Wolff AC, Carducci MA, Earle CC, Snyder CF. It's who you know: patient-sharing, quality, and costs of cancer survivorship care. Journal of Cancer Survivorship. 2014 Jun 1;8(2):156-66.

Prediction

Headaches (severe)

Anxiety, nervousness "Impending doom"

Abdominal or chest pain

Excess sweating

Pallor

Racing heart

Severe malignant hypertension

Nausea/vomiting

Weight loss

Tremors

New onset diabetes

"Spells" may be spontaneous or precipitated by change in body position, anxiety, medications

PHEOCHROMOCYTOMA

DARK   COLOR   CELL   TUMOR

RARE ADRENAL GLAND TUMOR

CELLS DARKEN

Symptoms

Disease

Human Symptoms Disease Network

Knowledge base

PubMed

Given symptoms, can we predict/diagnose diseases?
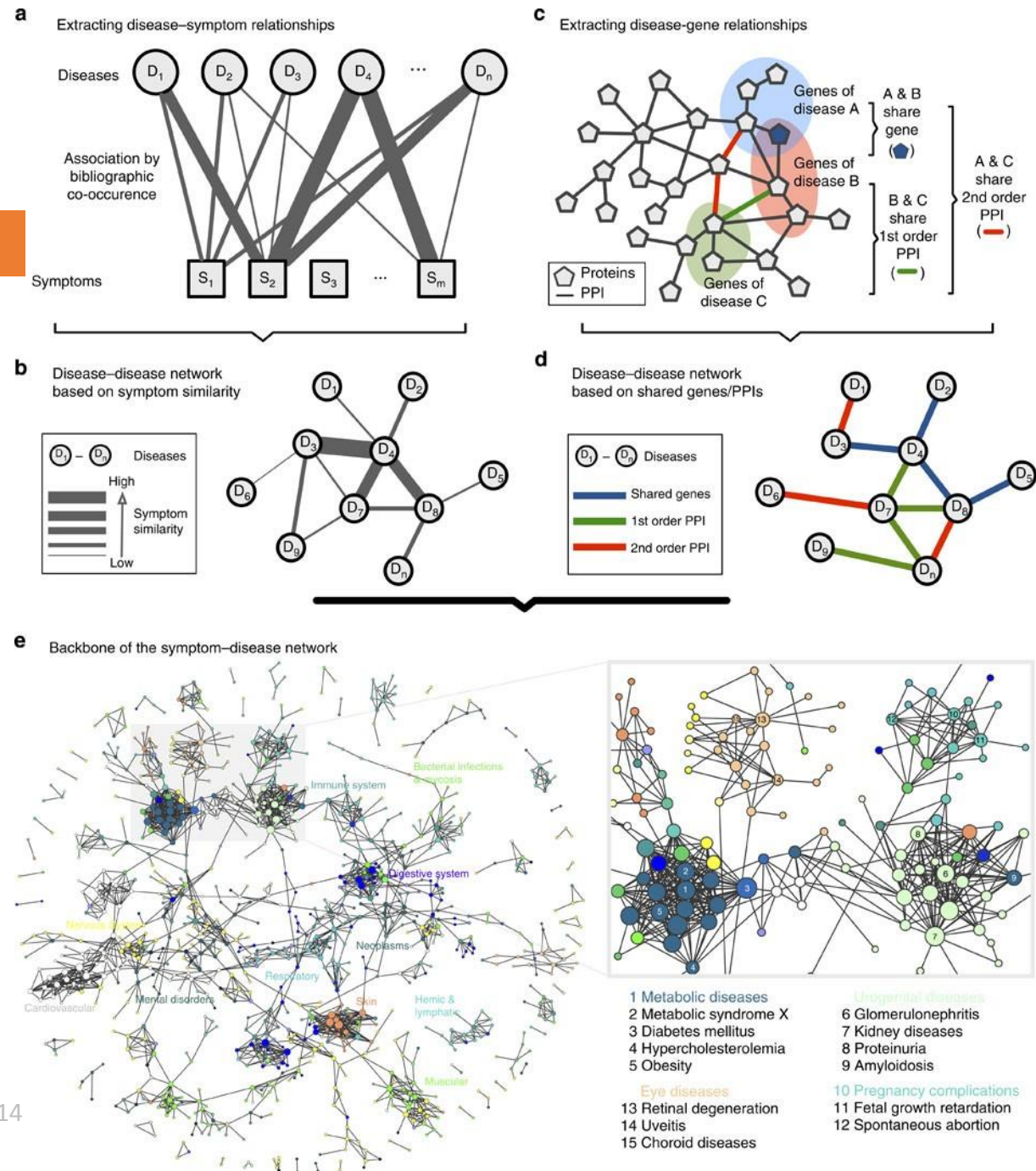
PheWAS GWAS studies

Disease-Disease networks

Refined symptom –disease networks – new edges added

a. Extracting disease–symptom relationships

Diseases — D₁ D₂ D₃ D₄ ... Dₙ

Association by bibliographic co-occurence

Symptoms — S₁ S₂ S₃ ... Sₘ

b. Disease–disease network based on symptom similarity

D₁ - Dₙ Diseases
High / Low Symptom similarity

c. Extracting disease-gene relationships

Genes of disease A — A & B share gene
Genes of disease B
B & C share 1st order PPI
A & C share 2nd order PPI
Proteins — PPI
Genes of disease C

d. Disease–disease network based on shared genes/PPIs

D₁ - Dₙ Diseases
Shared genes
1st order PPI
2nd order PPI

e. Backbone of the symptom–disease network

1 Metabolic diseases
2 Metabolic syndrome X
3 Diabetes mellitus
4 Hypercholesterolemia
5 Obesity
6 Glomerulonephritis
7 Kidney diseases
8 Proteinuria
9 Amyloidosis
10 Pregnancy complications
11 Fetal growth retardation
12 Spontaneous abortion
13 Retinal degeneration
14 Uveitis
15 Choroid diseases

Zhou X, et.al. Human symptoms–disease network. Nature communications. 2014 Jun 26;5(1):1-0.

Temporal disease trajectories

- The directed graph describes a normal progression from having hyperplasia of prostate diagnosed to having prostate cancer, cancer metastasis and anaemia

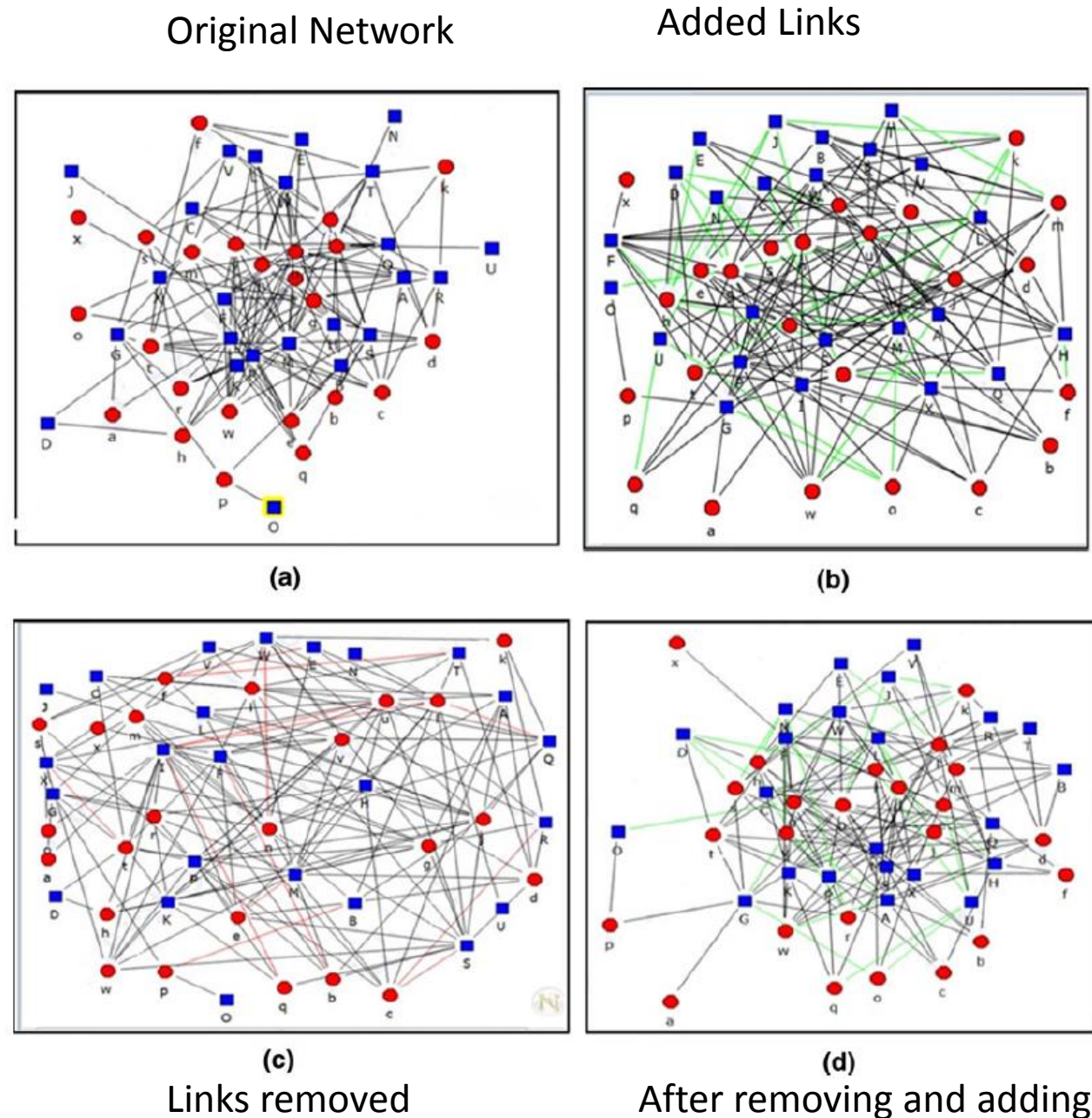Jensen AB, et.al. Temporal disease trajectories condensed from population-wide registry data covering 6.2 million patients. Nature communications. 2014 Jun 24;5(1):1-0.
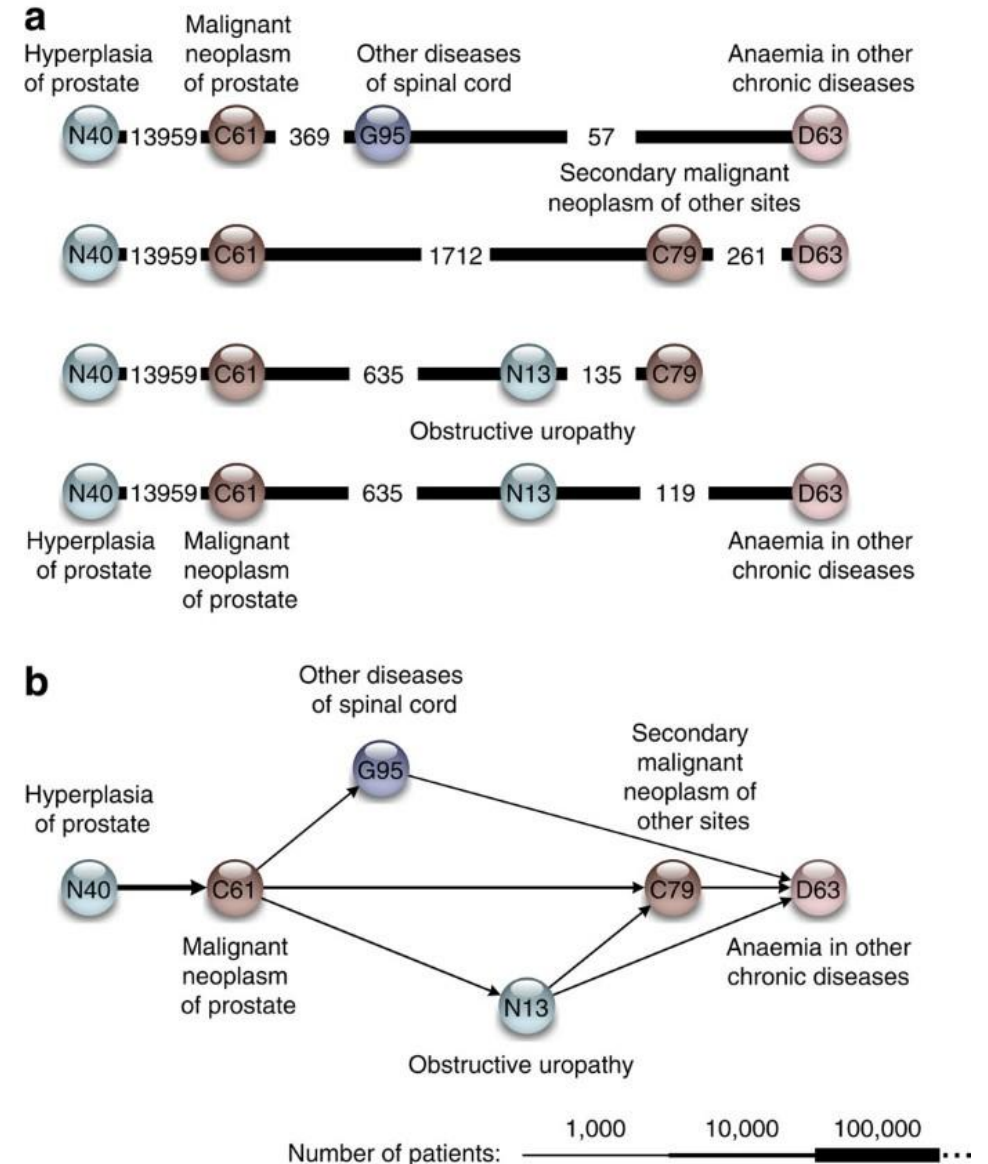
Link prediction – medical referral systems

Which specialists are more likely to receive future referrals, and which specialists are more likely to lose their links with the general practitioners in the same network

Original Network

Added Links

(a)

(b)

(c)
Links removed

(d)
After removing and adding

Almansoori W, et.al. Link prediction and classification in social networks and its application in healthcare and systems biology. Network Modeling Analysis in Health Informatics and Bioinformatics. 2012 Jun 1;1(1-2):27-36.

Link prediction – reconstructing protein-protein interaction networks

Topological profiles for node 6 and node 8

Compute topological profiles for each node

Original network

Compute topological similarities between nodes

Reconstruct network by linking nodes with high similarities

Reconstructed network

Topological similarity between node 6 and node 8

Lei C, Ruan J. A novel link prediction algorithm for reconstructing protein–protein interaction networks by topological similarity. Bioinformatics. 2013 Feb 1;29(3):355-64.

Drug repositioning and drug-drug interactions

Discovering novel drug-disease associations

Oh M, Ahn J, Yoon Y. A network-based classification model for deriving novel drug-disease associations and assessing their molecular actions. PLoS One. 2014 Oct 30;9(10):e111668.
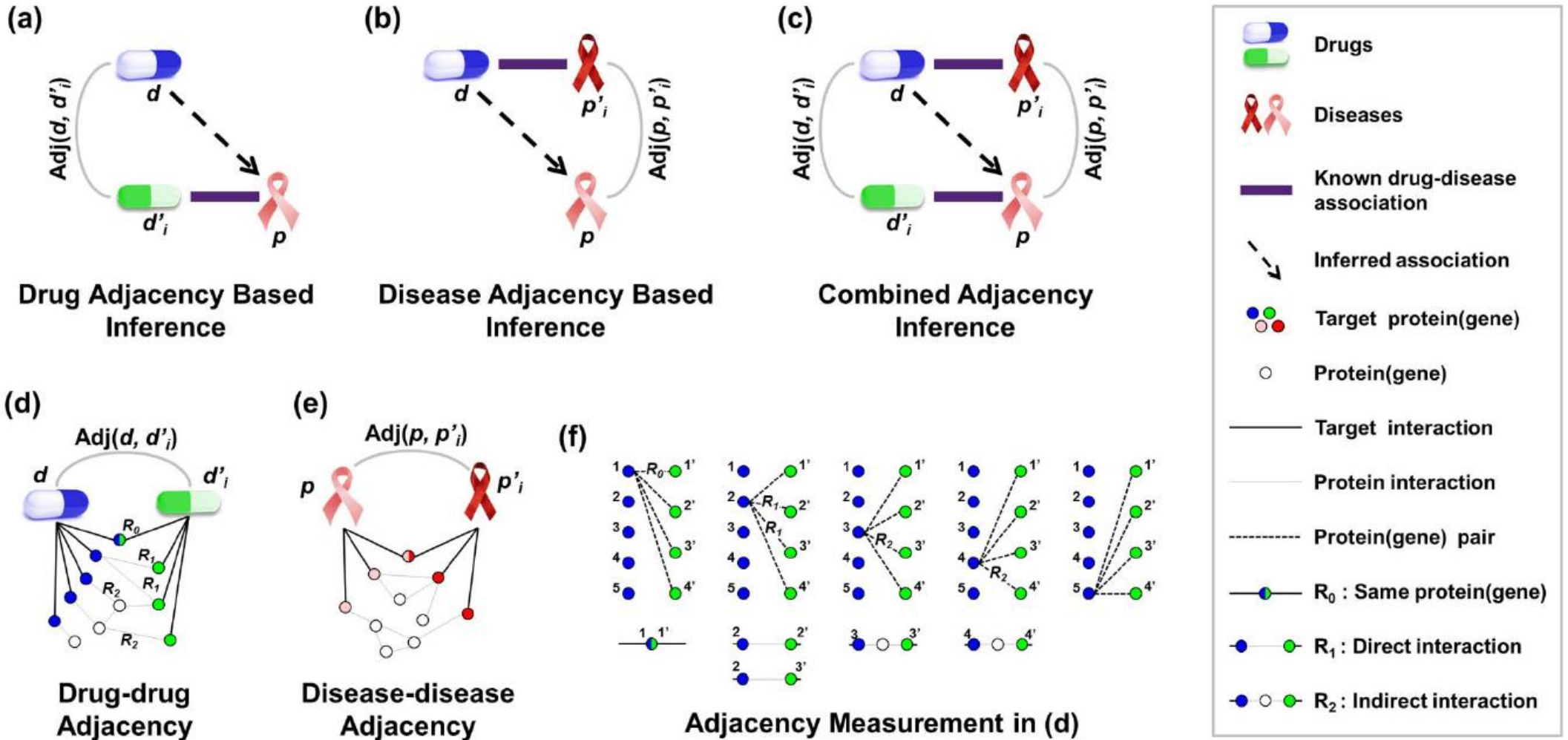
Predicting drug-drug interactions – similarity score

Park K. Predicting pharmacodynamic drug-drug interactions through signaling propagation interference on protein-protein interaction networks. PloS one. 2015 Oct 15;10(10):e0140816
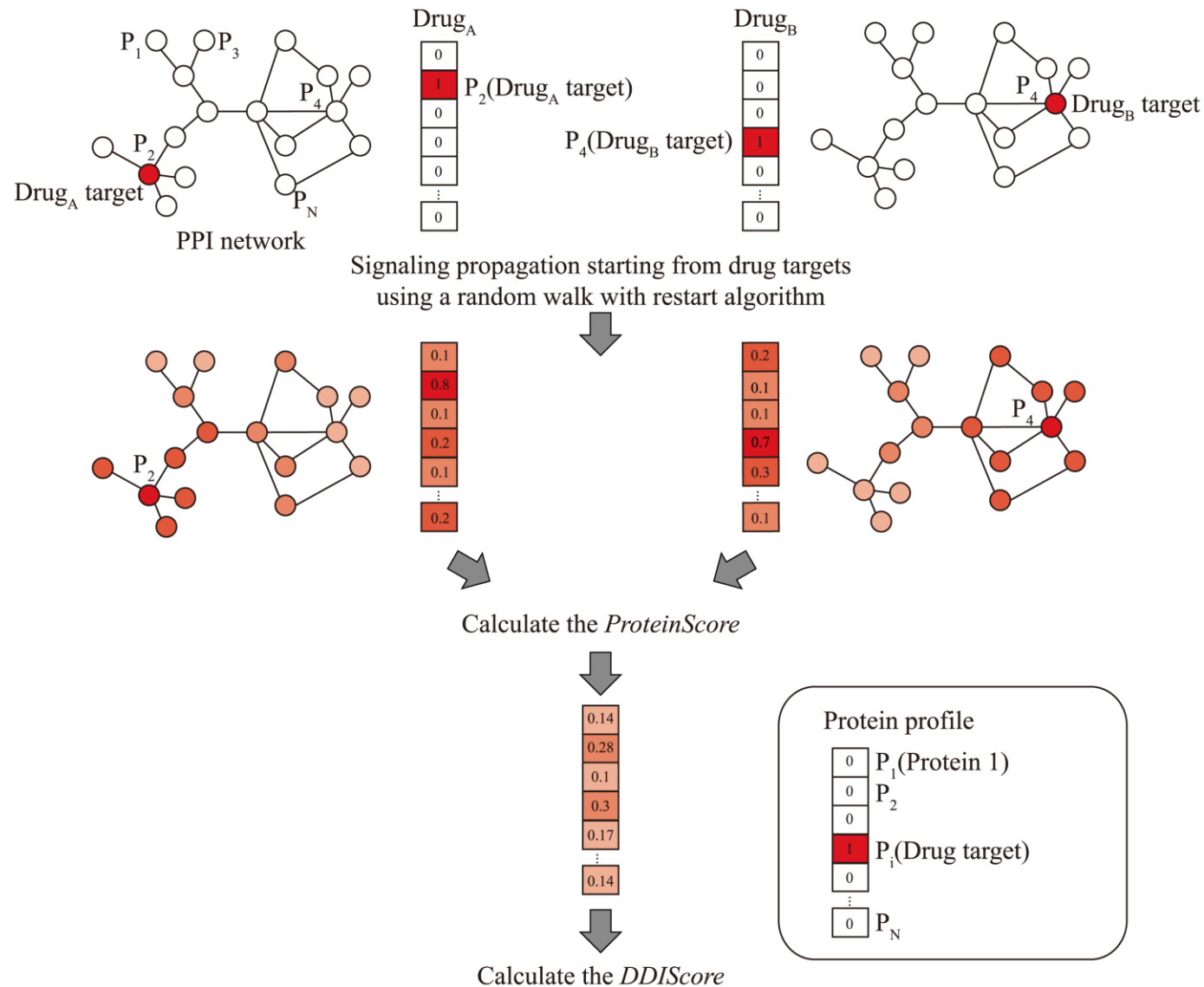
Predicting drug-drug interactions via machine learning
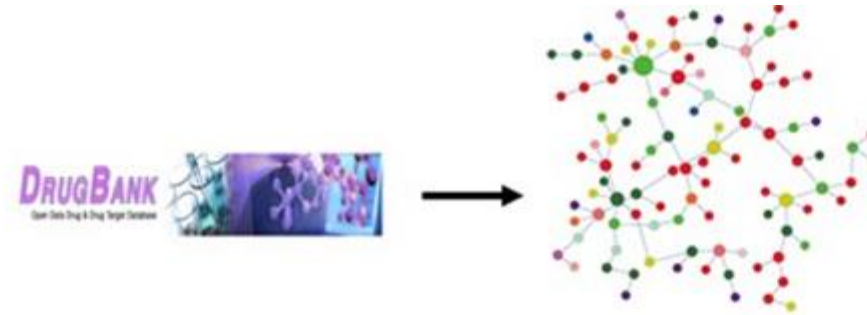
Construction of drug-drug interaction (DDI) network

B

U.S. FDA AERS
SIDER (v2.0)
OFFSIDES
CTD
MetaADEDB
Phenotypic Similarity (S_P)

Therapeutic (ATC) Similarity (S_T)

Clozapine
Structural Similarity (S_s)

Therapeutic Target Database
DRUGBANK
Genomic Similarity (S_G)
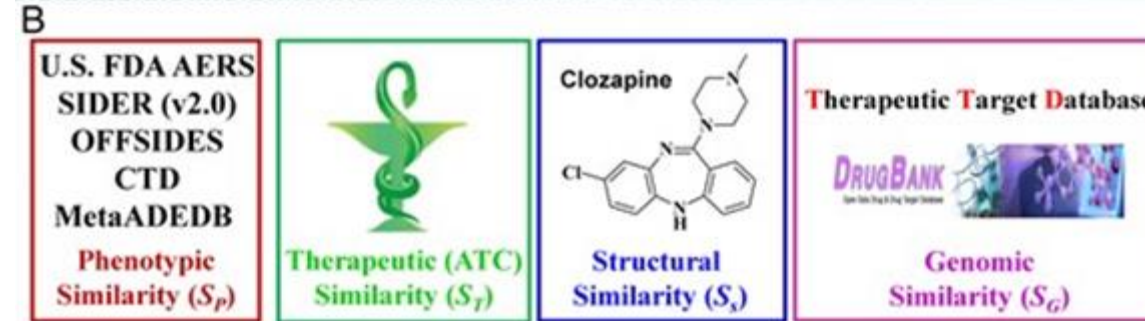
Calculation of drug phenotypic, therapeutic, structural, and genomic similarities

C

DD pairs	S_P	S_T	S_S	S_G	DDI
D_1'-D_1	s_P^1	s_T^1	s_S^1	s_G^1	1
D_2'-D_2	s_P^2	s_T^2	s_S^2	s_G^2	1
D_3'-D_3	s_P^3	s_T^3	s_S^3	s_G^3	0
.	.	.	.	.	.
.	.	.	.	.	.
D_m'-D_m	s_P^m	s_T^m	s_S^m	s_G^m	0

Support Vector Machine
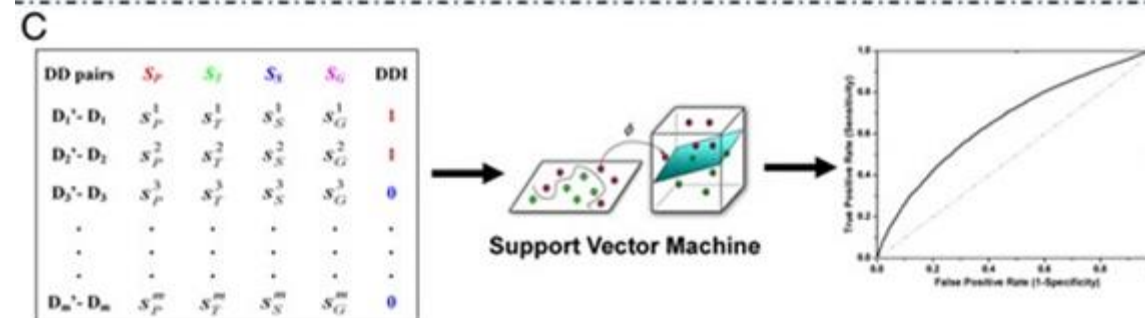
Building heterogeneous network-assisted inference (HNAI) models for DDI prediction

Cheng F, Zhao Z. Machine learning-based prediction of drug–drug interactions by integrating drug phenotypic, therapeutic, chemical, and genomic properties. Journal of the American Medical Informatics Association. 2014 Oct 1;21(e2):e278-86.

A tour of 150 years of interconnected, interdisciplinary research, as represented by Nature's publication record