Linking two temporal big data domains: The clinical and the omics worlds

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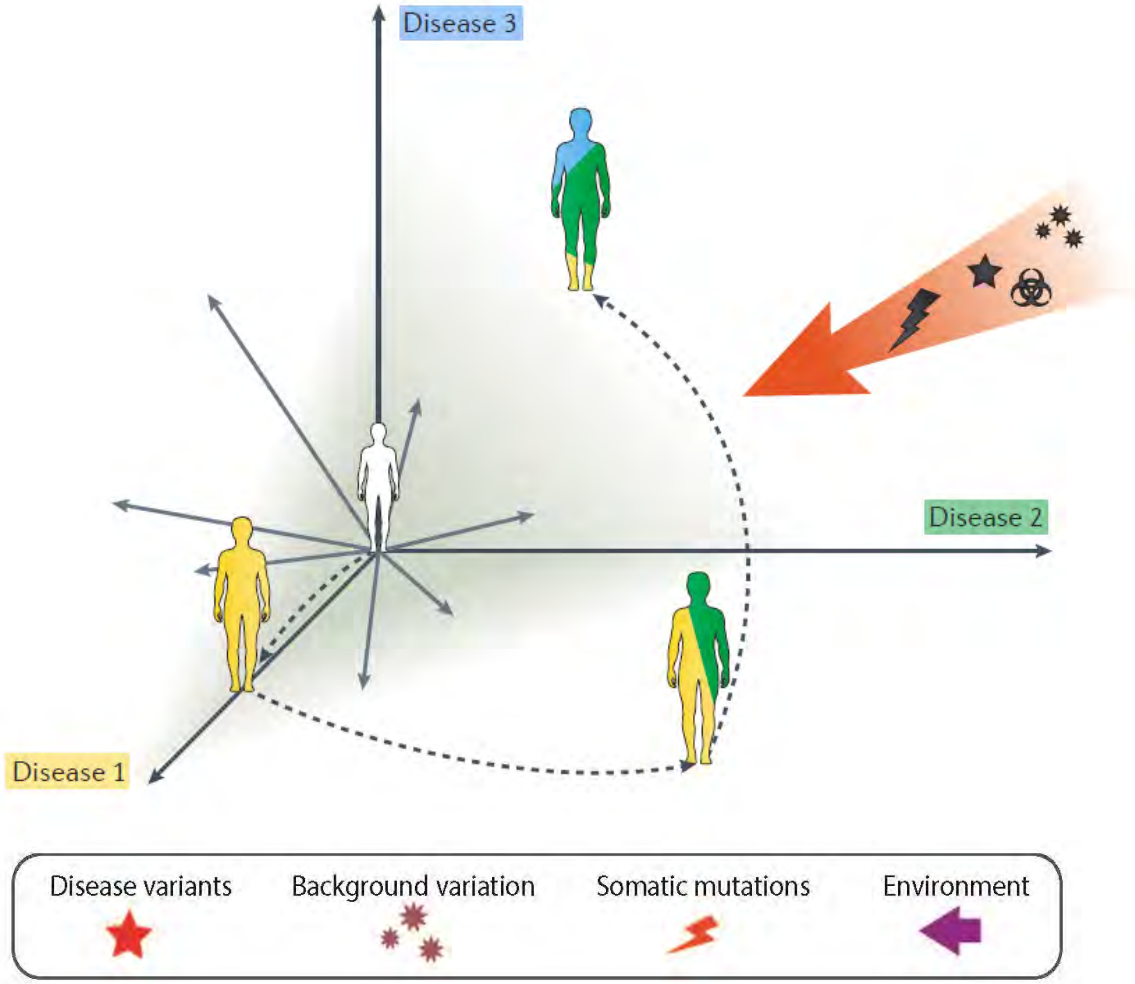
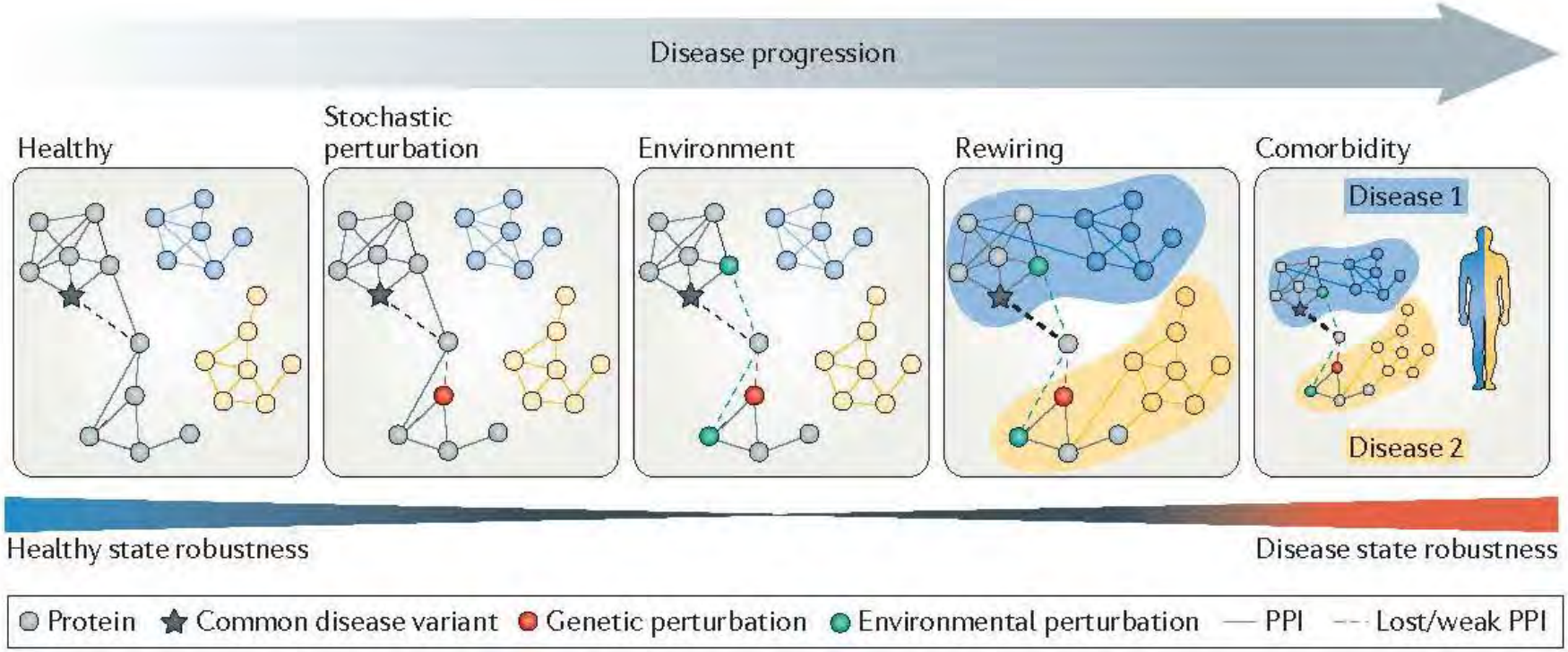
Lifelong multimorbidity journeys in disease space



Hu, Thomas & Brunak
Nature Rev. Genetics 2016,

Rewiring



Hu, Thomas & Brunak
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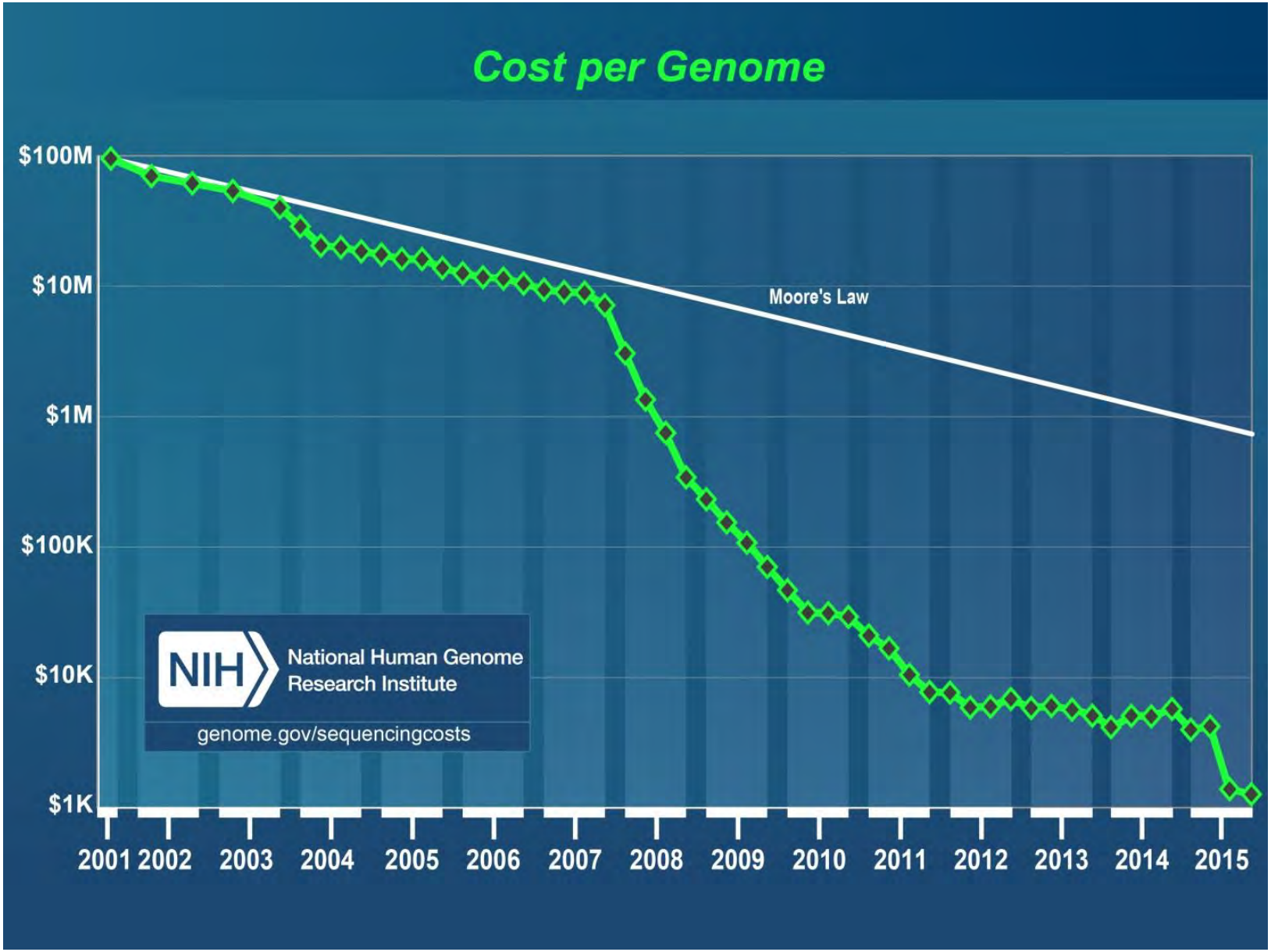
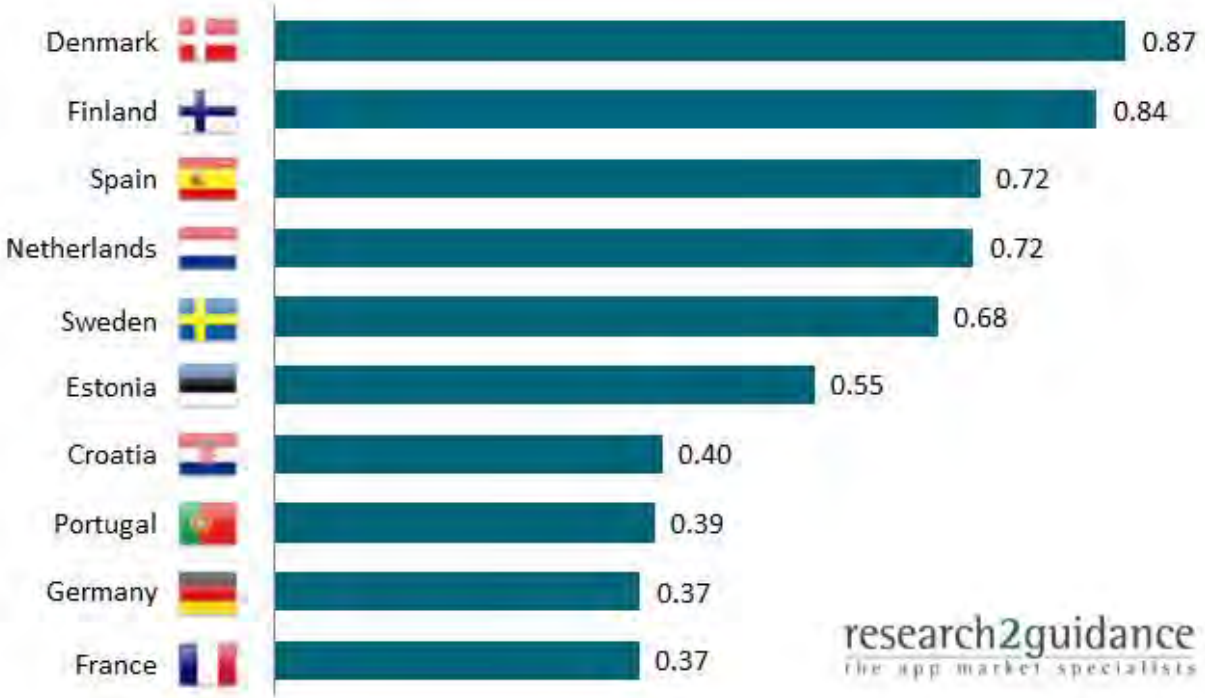

Cost per Genome
$100M
$10M
$1M
$100K
$10K
$1K
Moore's Law
NIH
National Human Genome Research Institute
genome.gov/sequencingcosts
2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015

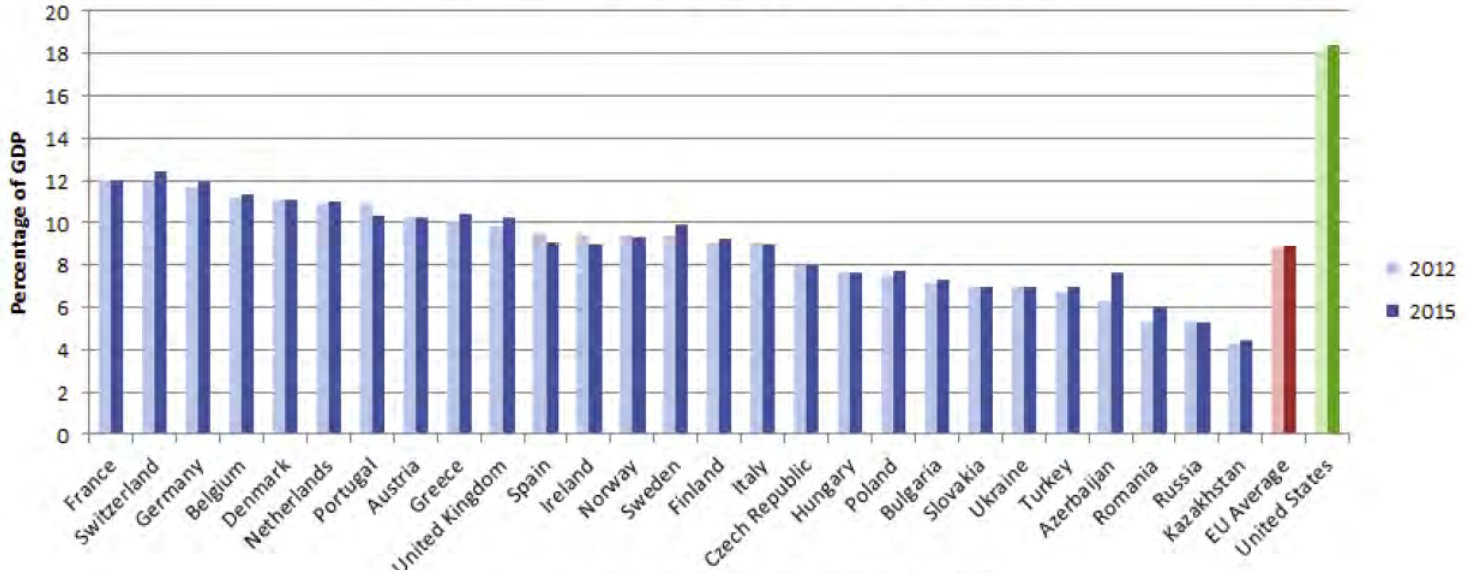
DENMARK IS THE LEADING COUNTRY IN EHEALTH ADOPTION

Top 10 EU countries by eHealth adoptions of patients and doctors

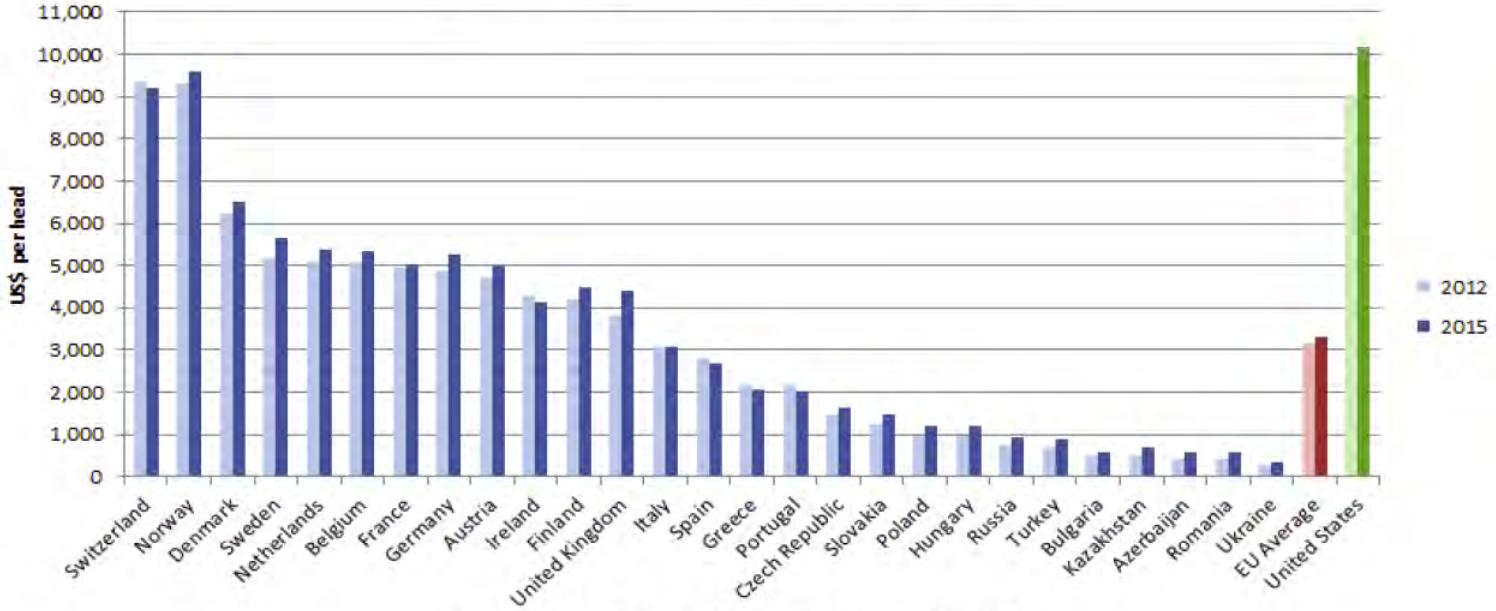


eHealth adoption – doctors transferring prescription electronically, doctors electronically exchanging medical patient data with other healthcare professionals , patients making appointment via website, patients seeking online information about health

Healthcare spending as percentage of GDP



Healthcare spending per head (US$)



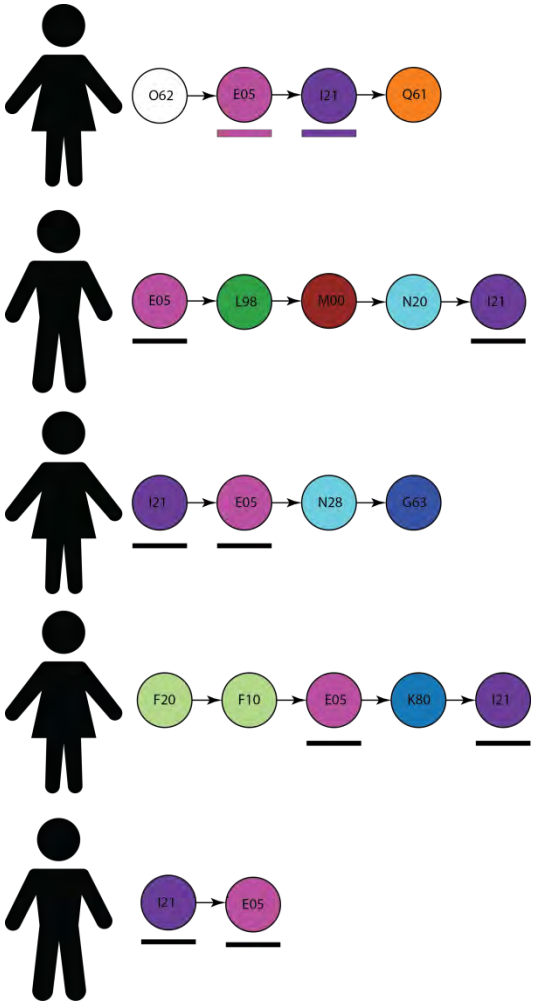
Source: The Economist Intelligence Unit (2012)

Disease risk

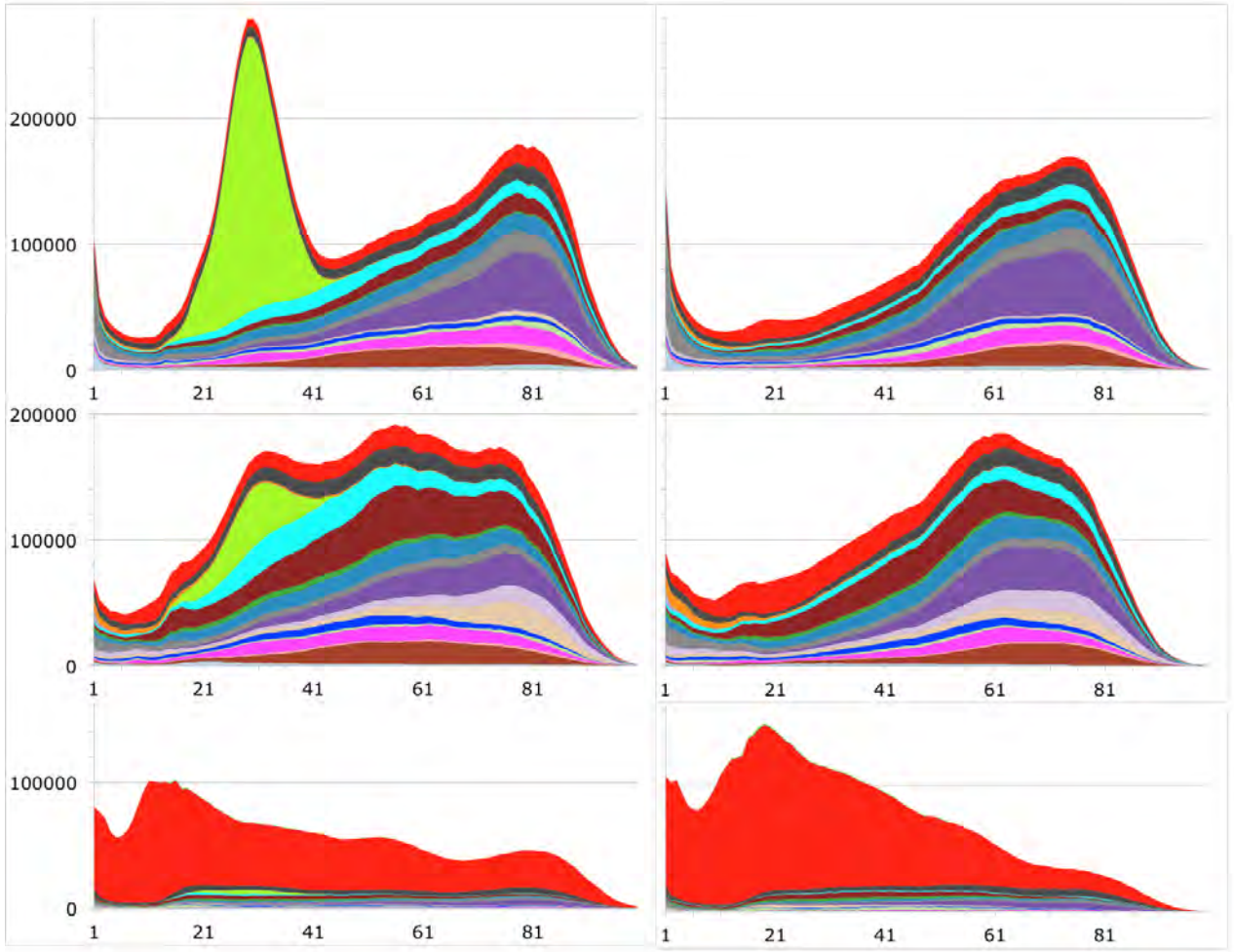
– journey versus destination

Cancer
Diabetes
Obesity
Mental disorders

Diagnosis trajectories across 6.2 million Danish individuals (ICD-10 era, 1994-2015)



National Patient Registry (6.2M Danes) ICD10 diagnoses as a function of age

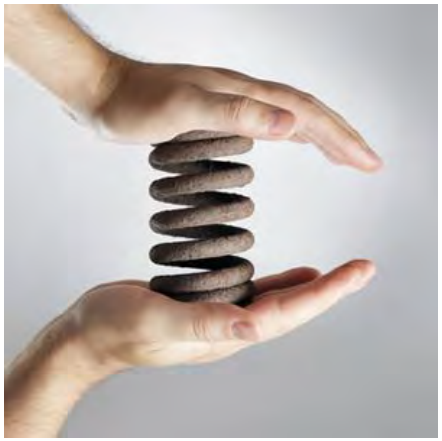


ICD 10 chapter coloring

1: Certain infectious and parasitic diseases
2: Neoplasms
3: Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism
4: Endocrine, nutritional and metabolic diseases
5: Mental and behavioural disorders
6: Diseases of the nervous system
7: Diseases of the eye and adnexa
8: Diseases of the ear and mastoid process
9: Diseases of the circulatory system
10: Diseases of the respiratory system
11: Diseases of the digestive system
12: Diseases of the skin and subcutaneous tissue
13: Diseases of the musculoskeletal system and connective tissue
14: Diseases of the genitourinary system
15: Pregnancy, childbirth and the puerperium
16: Certain conditions originating in the perinatal period
17: Congenital malformations, deformations and chromosomal abnormalities
18: Symptoms, signs and abnormal clinical and aboratory findings, not elsewhere classified
19: Injury, poisoning and certain other consequences of external causes
20: External causes of morbidity and mortality

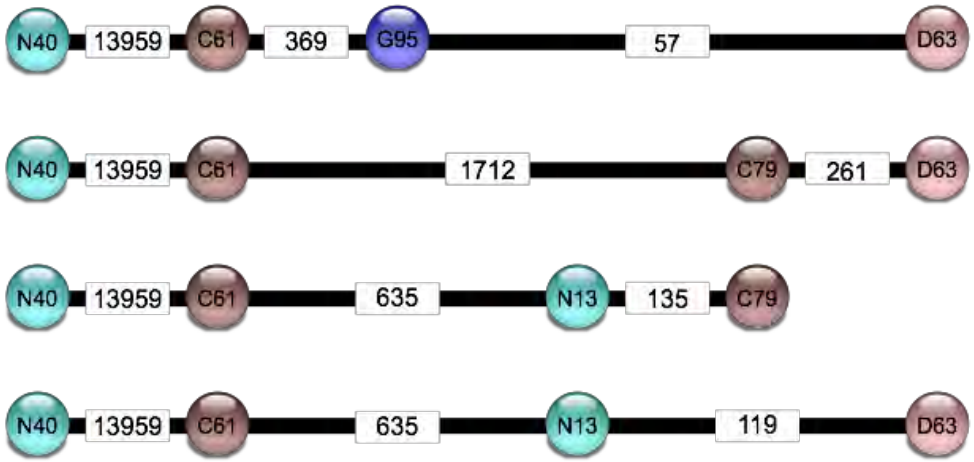
AB Jensen et al.,
Nature Comm., 2014

6-7 million trajectories



?

6.2 million individual trajectories condensed into 1,171 “recurrent” ones



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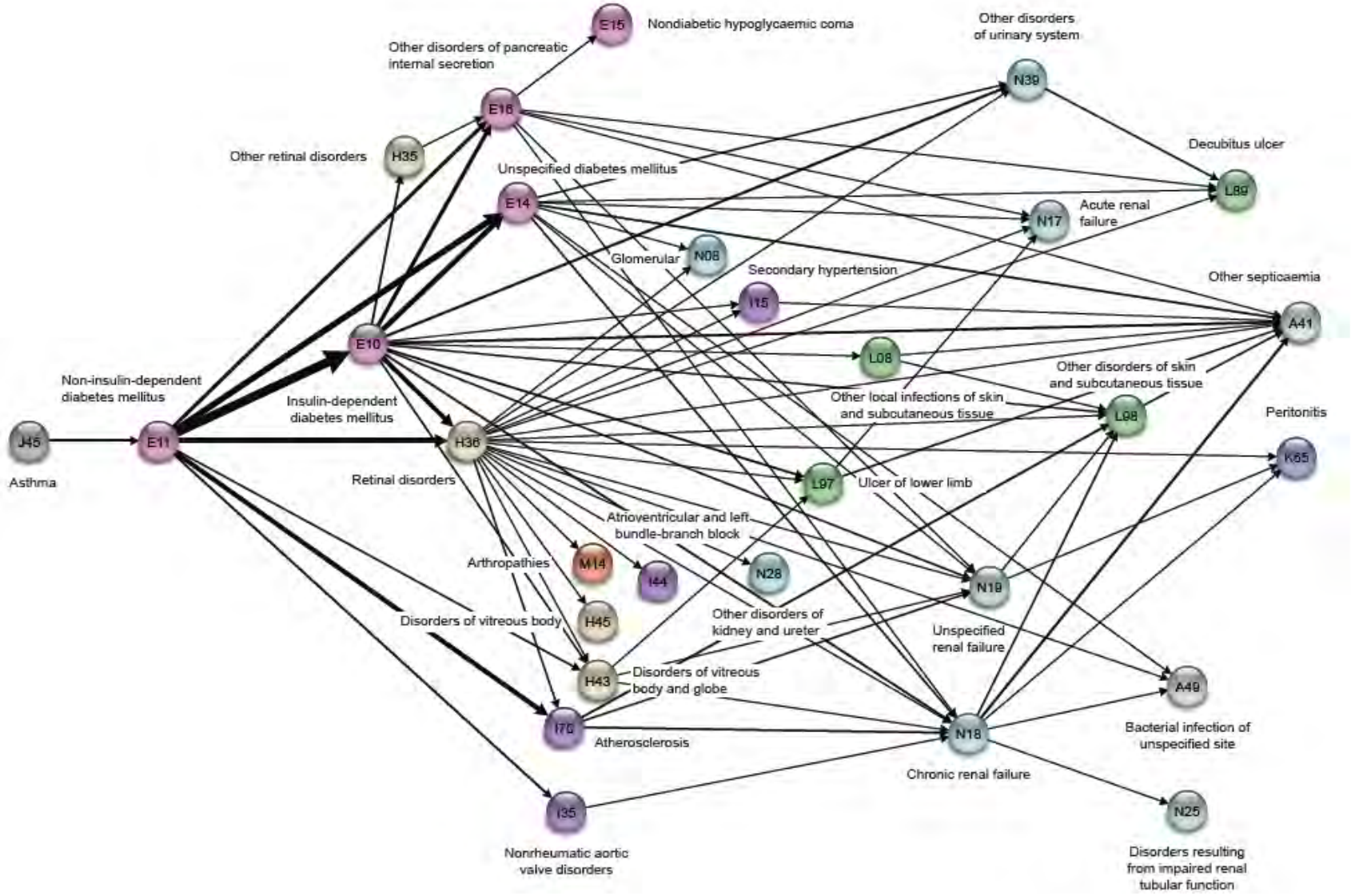
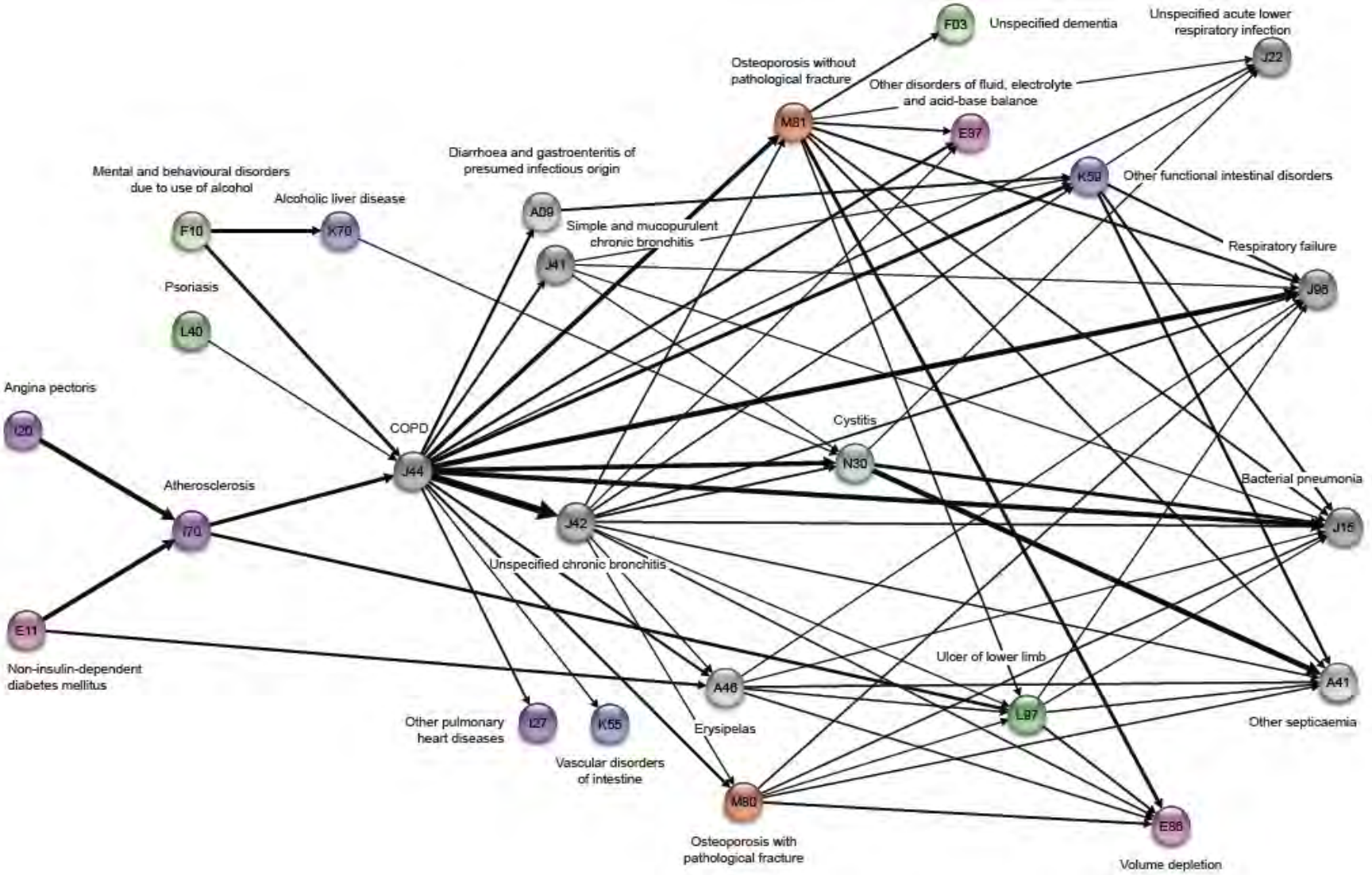
AB Jensen et al.,
Nature Comm., 2014

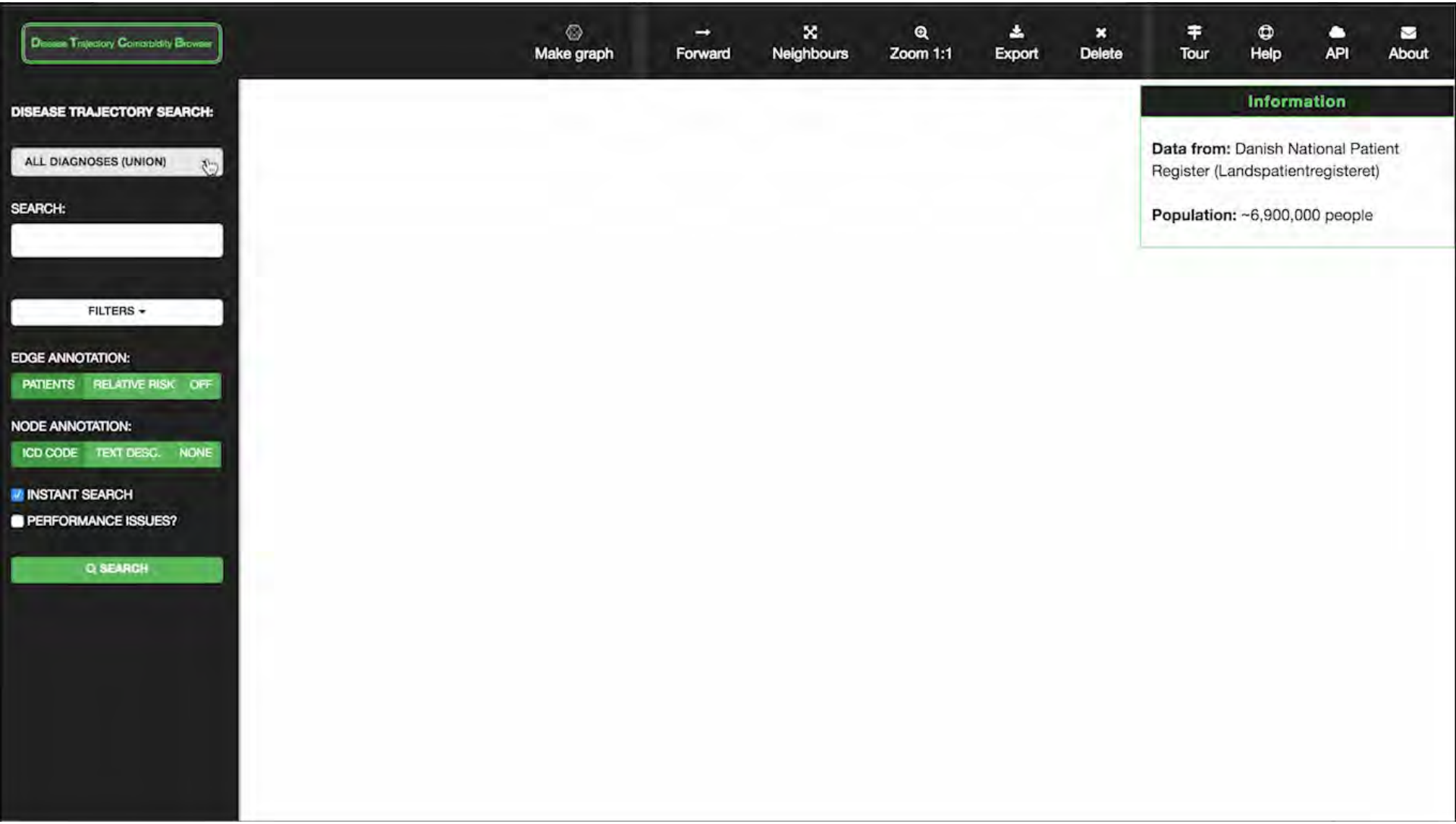
Diabetes trajectory network



COPD trajectory cluster

with five preceding diagnoses leading to COPD and some of the possible outcomes




Disease Trajectory Comorbidity Browser
Make graph
Forward
Neighbours
Zoom 1:1
Export
Delete
Tour
Help
API
About
DISEASE TRAJECTORY SEARCH:
ALL DIAGNOSES (UNION)
SEARCH:
FILTERS
EDGE ANNOTATION:
PATIENTS
RELATIVE RISK
OFF
NODE ANNOTATION:
ICD CODE
TEXT DESC.
NONE
INSTANT SEARCH
PERFORMANCE ISSUES?
SEARCH
Information
Data from: Danish National Patient Register (Landspatientregisteret)
Population: ~6,900,000 people

Nature Genetics, 48:510-518, 2016

nature genetics

Analysis of five chronic inflammatory diseases identifies 27 new associations and highlights disease-specific patterns at shared loci

David Ellinghaus[1,49], Luke Jostins[2], Sarah L Spain[2], Adrian Cortes[3,4], Jörn Bethune[1], Buhm Han[5], Yu Rang Park[6], Soumya Raychaudhuri[7–10], Jennie G Pouget[11,12], Matthias Hübenthal[1], Trine Folseraas[13–16], Yunpeng Wang[17], Tonu Esko[18–20], Andres Metspalu[18], Harm-Jan Westra[7–10], Lude Franke[21], Tune H Pers[7,20,22,23], Rinse K Weersma[24], Valerie Collij[24], Mauro D'Amato[25,26], Jonas Halfvarson[27], Anders Boeck Jensen[28], Wolfgang Lieb[29,30], Franziska Degenhardt[31,32], Andreas J Forstner[31,32], Andrea Hofmann[31,32], The International IBD Genetics Consortium (IIBDGC)[33], International Genetics of Ankylosing Spondylitis Consortium (IGAS)[33], International PSC Study Group (IPSCSG)[33], Genetic Analysis of Psoriasis Consortium (GAPC)[33], Psoriasis Association Genetics Extension (PAGE)[33], Stefan Schreiber[1,34], Ulrich Mrowietz[35], Brian D Juran[36], Konstantinos N Lazaridis[36], Søren Brunak[28], Anders M Dale[17,37], Richard C Trembath[38], Stephan Weidinger[35], Michael Weichenthal[35], Eva Ellinghaus[1], James T Elder[39,40], Jonathan N W N Barker[41], Ole A Andreassen[42,43], Dermot P McGovern[44,45], Tom H Karlsen[13–16], Jeffrey C Barrett[2], Miles Parkes[46], Matthew A Brown[47,48,50] & Andre Franke[1,50]

We simultaneously investigated the genetic landscape of ankylosing spondylitis, Crohn's disease, psoriasis, primary sclerosing cholangitis and ulcerative colitis to investigate pleiotropy and the relationship between these clinically related diseases. Using high-density genotype data from more than 86,000 individuals of European ancestry, we identified 244 independent multidisease signals, including 27 new genome-wide significant susceptibility loci and 3 unreported shared risk loci. Complex pleiotropy was supported when contrasting multidisease signals with expression data sets from human, rat and mouse together with epigenetic and expressed enhancer profiles. The comorbidities among the five immune diseases were best explained by biological pleiotropy rather than heterogeneity (a subgroup of cases genetically identical to those with another disease, possibly owing to diagnostic misclassification, molecular subtypes or excessive comorbidity). In particular, the strong comorbidity between primary sclerosing cholangitis and inflammatory bowel disease is likely the result of a unique disease, which is genetically distinct from classical inflammatory bowel disease phenotypes.

Genome-wide association studies (GWAS) have shown overlap in the genetic susceptibility to human diseases that affect a range of

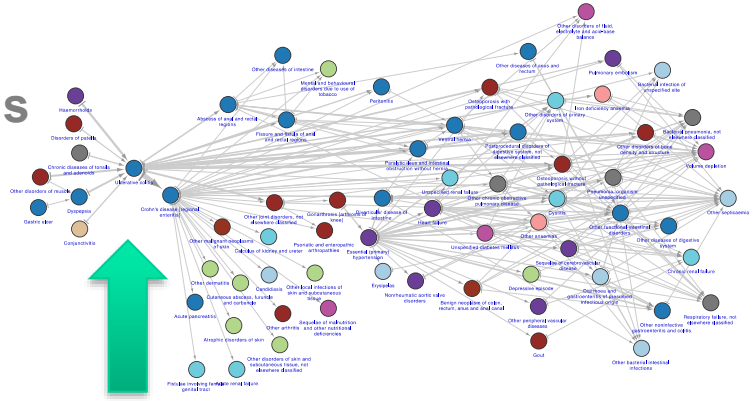
In this study, we combined Immunochip genotype data for 52,262 cases and 34,213 controls of European ancestry, currently the largest available

Immunochip genotype data: 52,262 cases

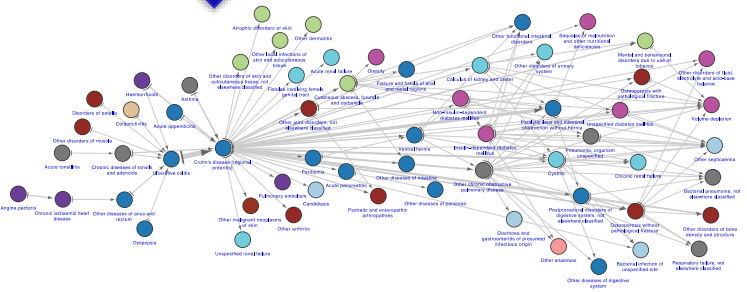
Ankylosing spondylitis (8,726)
Crohn's disease (19,085)
Psoriasis (6,530)
Primary sclerosing cholangitis (3,408)
Ulcerative colitis (14,413)

34,213 healthy controls

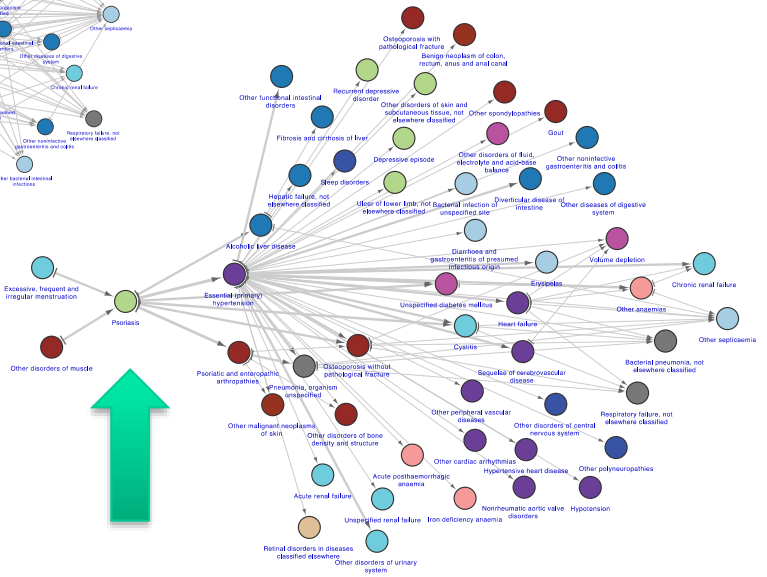
Ulcerative colitis



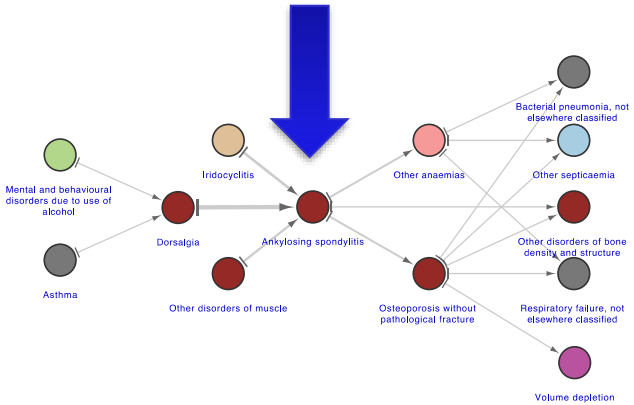
Crohn's disease



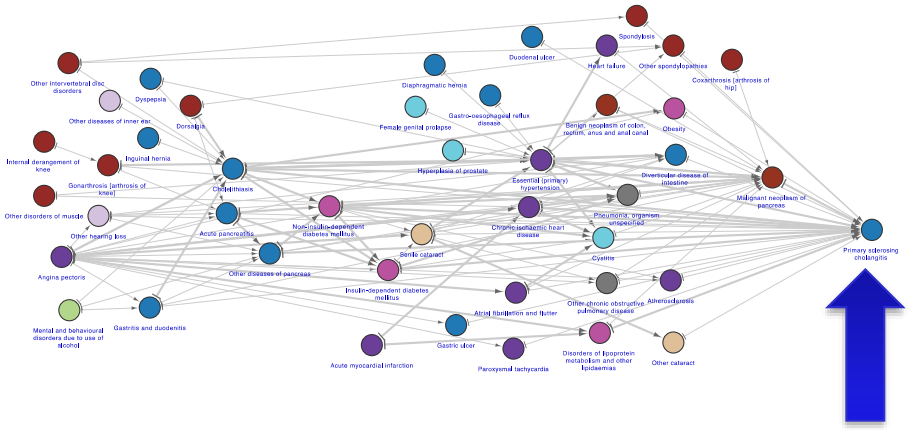
Psoriasis



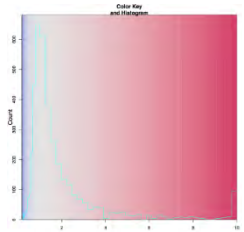
Ankylosing spondylitis



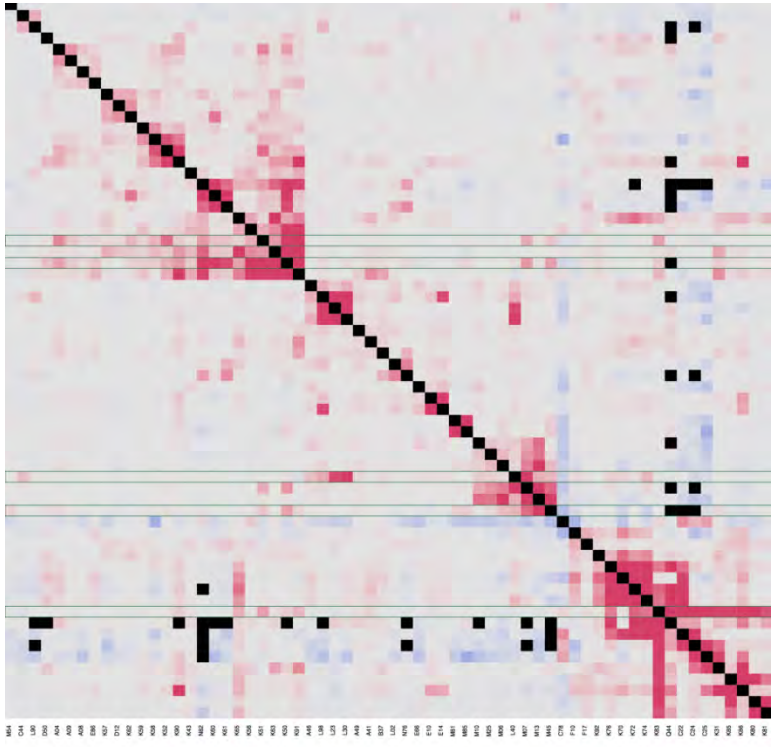
Sclerosing cholangitis



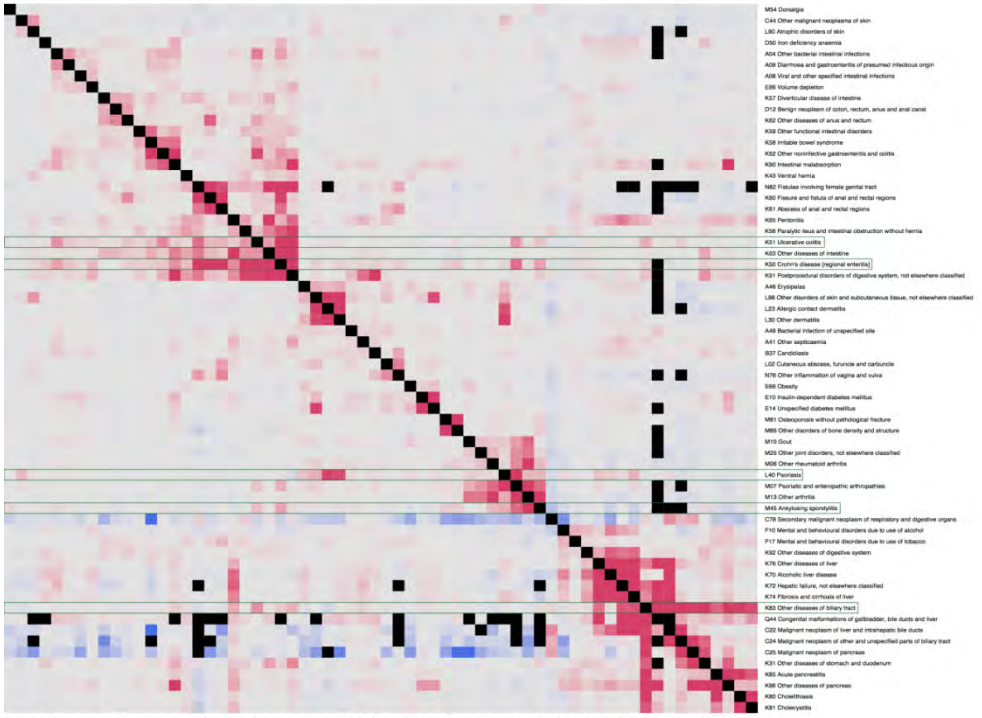
Temporal disease associations



A and B



A before B



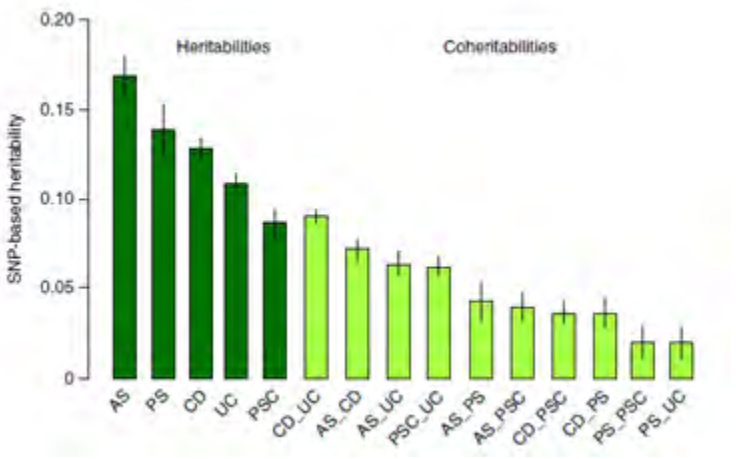
Shared or distinct genetic etiology?

Pleiotropy (sharing of risk alleles by disease A and disease B) or **Heterogeneity** (a subgroup of disease A cases has a higher load of risk alleles for disease B)?

Genetic and healthdata overlap analyses shows

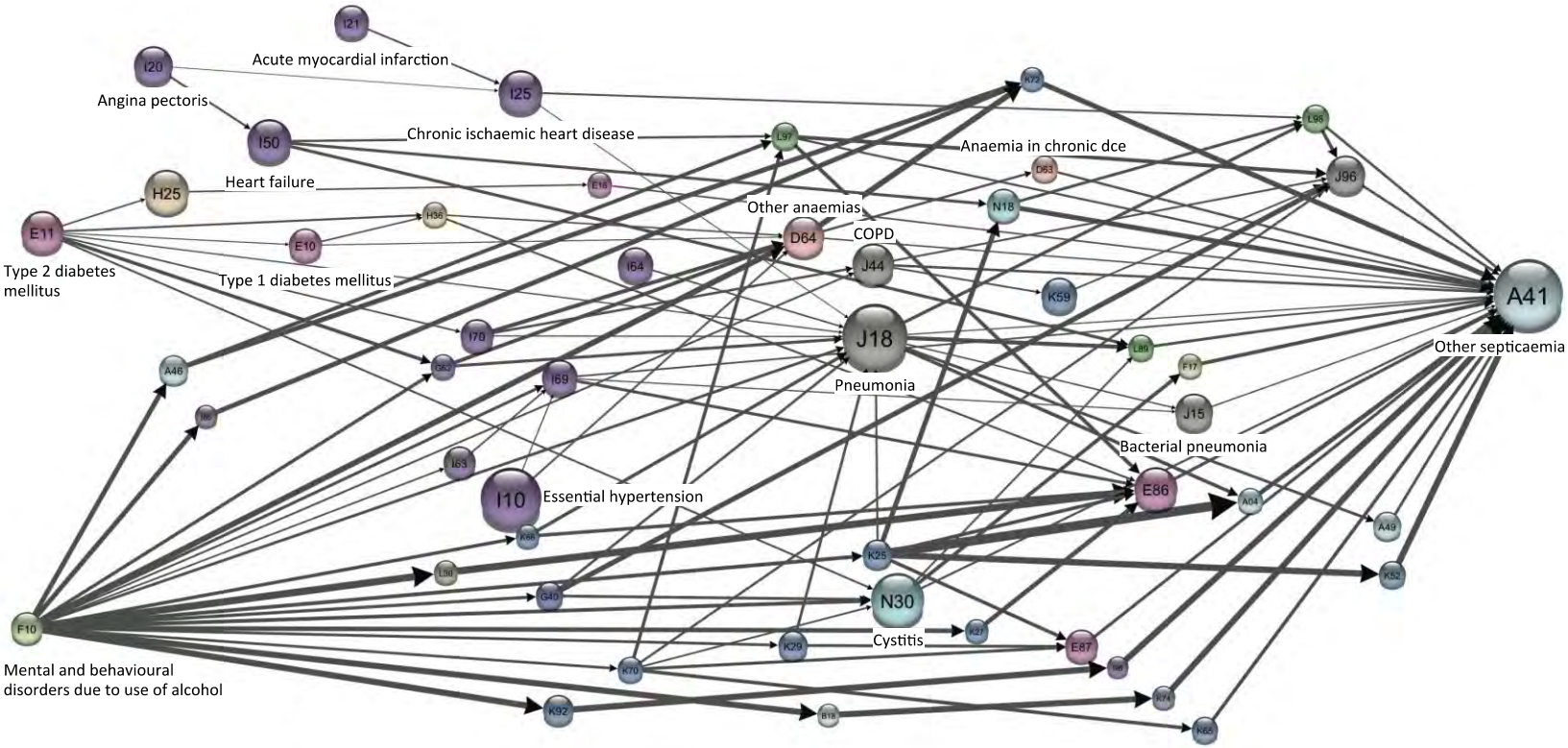
- **that shared pathophysiological pathways are the basis for clinical co-occurrence**
- that patients with concomitant syndromes are genetically distinct from patients without concomitant syndromes.

Immunochip-wide pleiotropy estimates

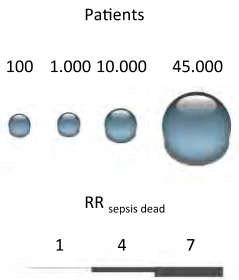


Ellinghaus et al. Nature Genetics, 48:510-518, 2016

Sepsis survival across pre-history
(120,000 patients, 56 significant trajectories)

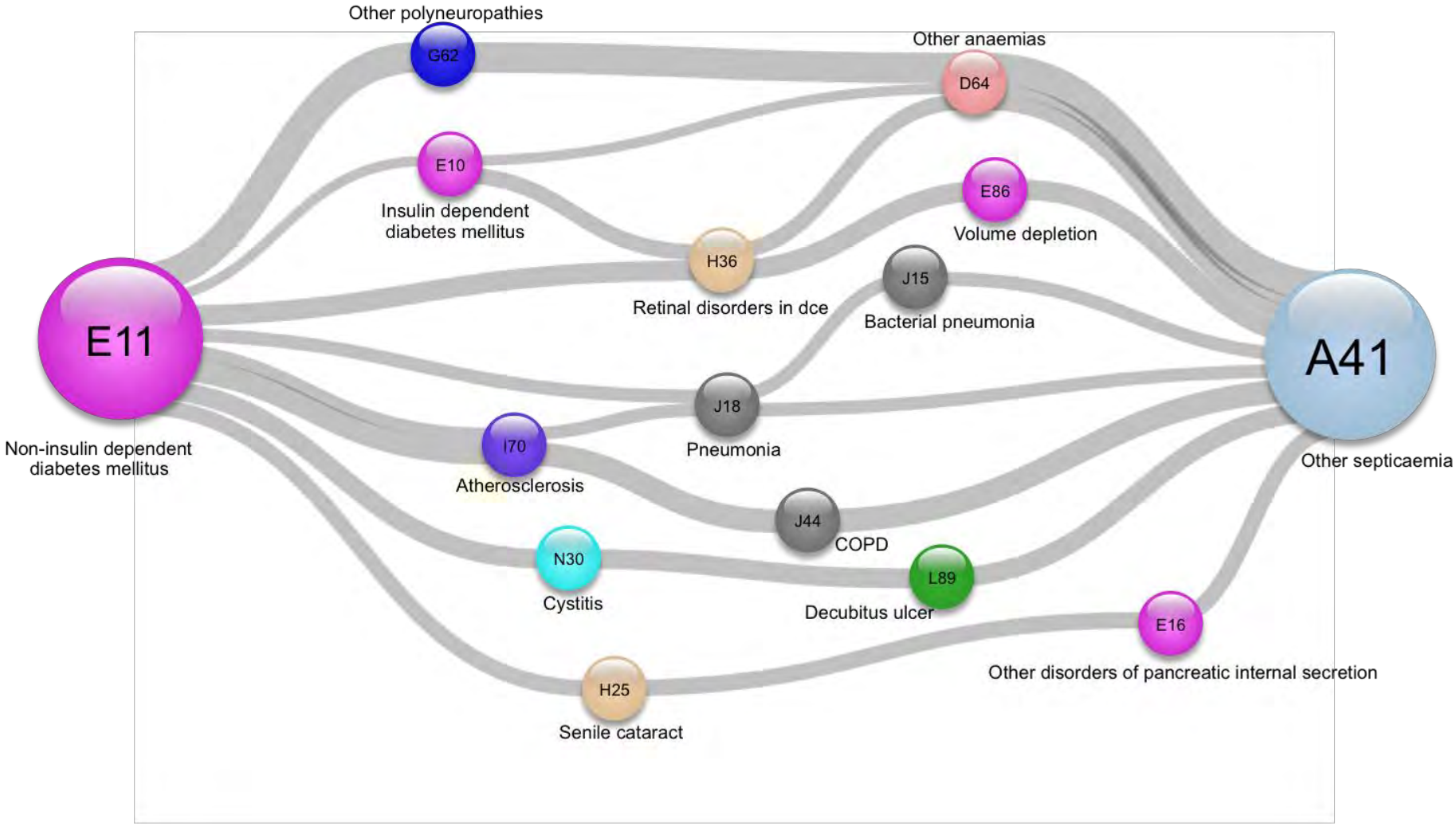


A04	Other bacterial intestinal infections
A46	Erysipelas
A49	Bacterial infection of unspecified site
B18	Chronic viral hepatitis
E16	Other disorders of pancreatic internal secretion
E87	Other disorders of fluid, electrolyte and acid-base balance
G40	Epilepsy
G62	Other polyneuropathies
H25	Senile cataract
H36	Retinal disorders in diseases classified elsewhere
I63	Cerebral infarction
I69	Sequelae of cerebrovascular disease
I70	Atherosclerosis
I85	Oesophageal varices
I98	Other disorders of circulatory system in diseases classified elsewhere
J96	Respiratory failure, not elsewhere classified
K25	Gastric ulcer
K27	Peptic ulcer, site unspecified
K29	Gastritis and duodenitis
K52	Other noninfective gastroenteritis and colitis
K59	Other functional intestinal disorders
K65	Peritonitis
K70	Alcoholic liver disease
K72	Hepatic failure, not elsewhere classified
K74	Fibrosis and cirrhosis of liver
K86	Other diseases of pancreas
K92	Other diseases of digestive system
L30	Other dermatitis
L89	Decubitus ulcer
L97	Ulcer of lower limb, not elsewhere classified
N18	Chronic renal failure

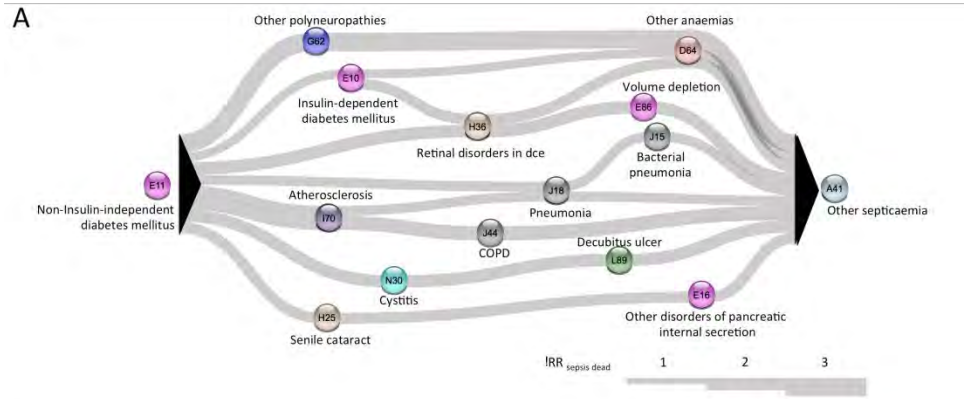


Beck et al, 2016

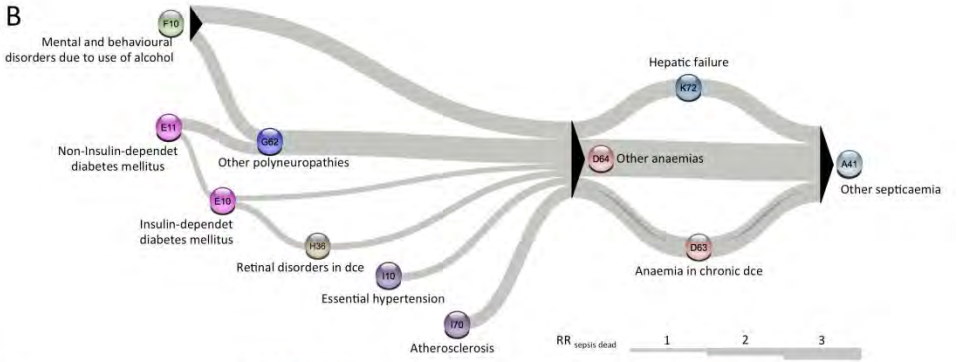
From diabetes to sepsis

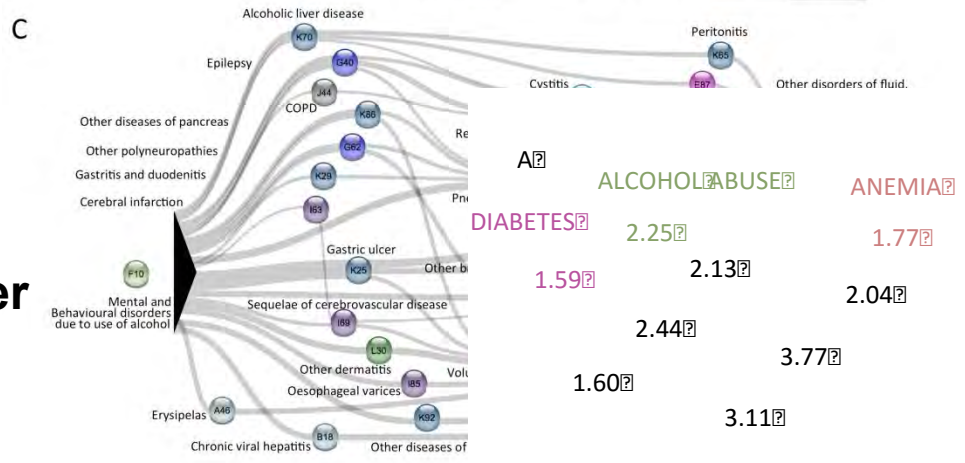


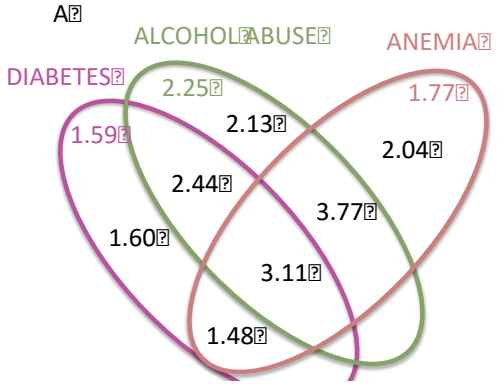
Diabetes



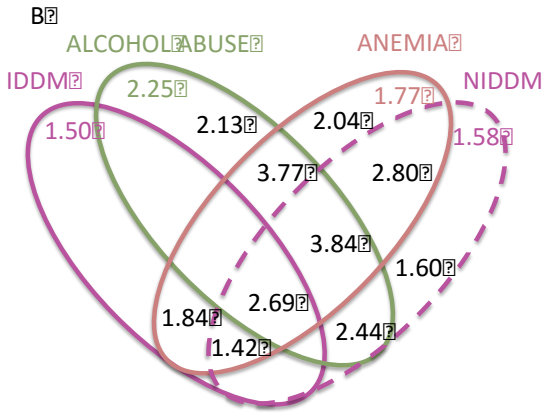
Anaemia







Mental disorder



The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL IMPLICATIONS OF BASIC RESEARCH

A Wake-up Call for Type 2 Diabetes?

Shanta J. Persaud, Ph.D., and Peter M. Jones, Ph.D.

N Engl J Med 2016; 375:1090-1092 | September 15, 2016 | DOI: 10.1056/NEJMcibr1607950

This study examines an established association between a variant in a melatonin-receptor gene and type 2 diabetes, yielding insights into how the variant confers susceptibility to the disease.

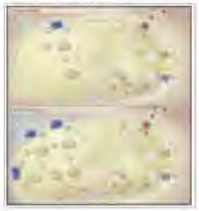
Disclosure forms provided by the authors are available at NEJM.org.

SOURCE INFORMATION

From the Diabetes Research Group, Division of Diabetes and Nutritional Sciences, King's College London, London.

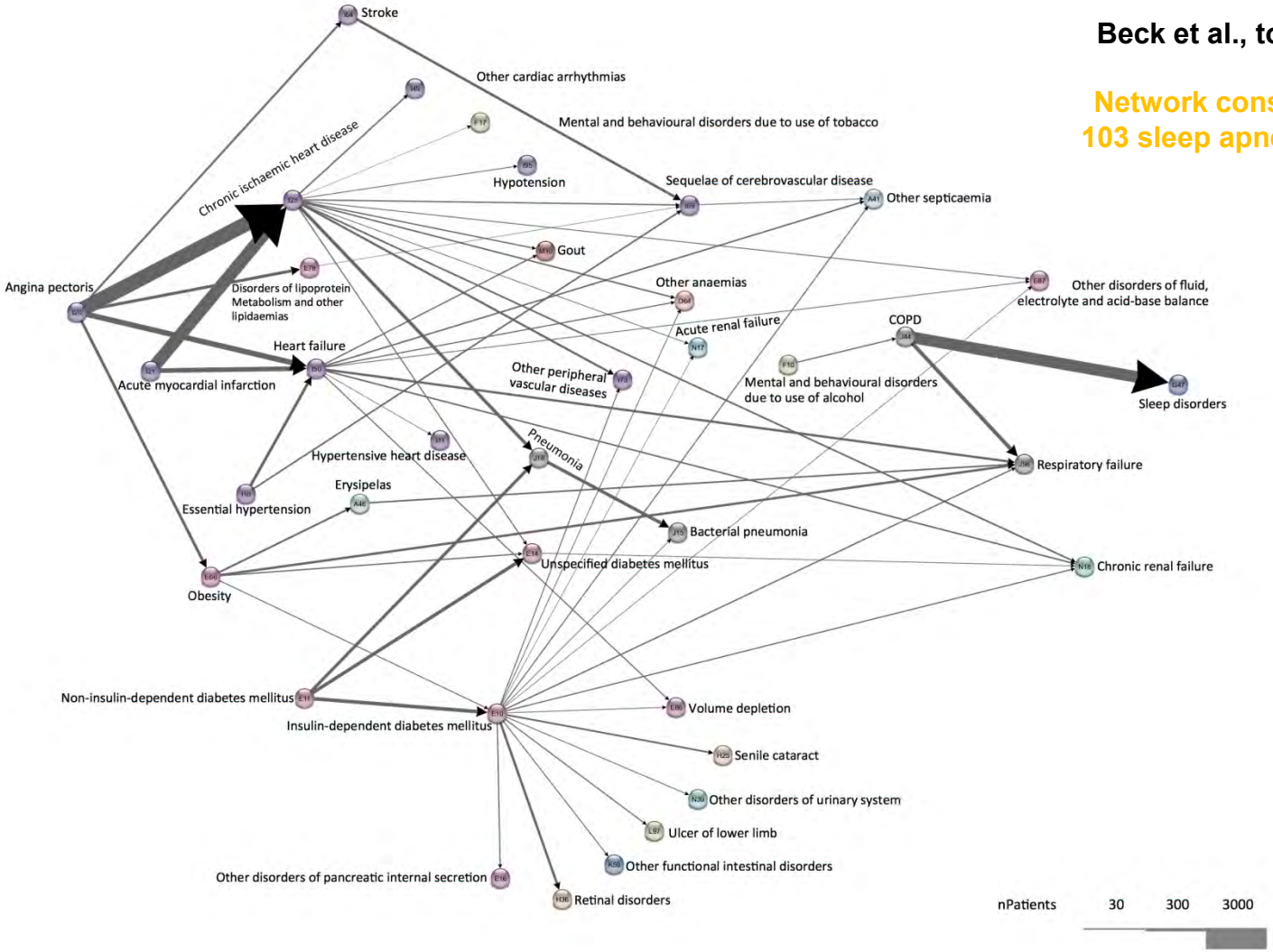
MEDIA IN THIS ARTICLE

FIGURE 1



Effect of Variant *MTNR1B* on Melatonin Signaling in Islet Beta Cells.

Sleep Apnea and Diabetes

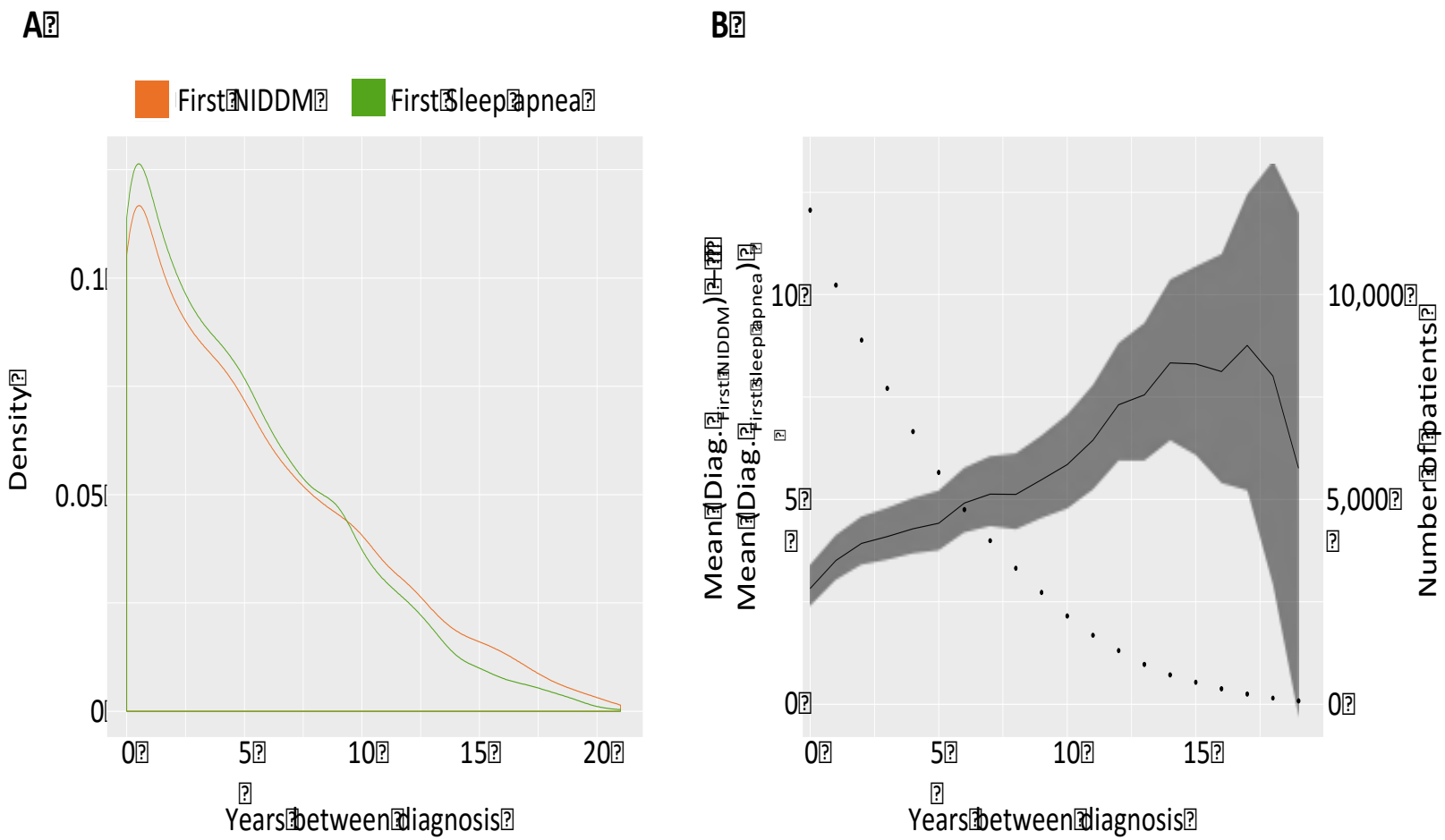


Beck et al., to appear 2017

Network constructed from 103 sleep apnea trajectories

No significant diagnosis direction, but patients diagnosed with diabetes before sleep apnea have significantly more comorbidities than patients diagnosed with sleep apnea before diabetes.

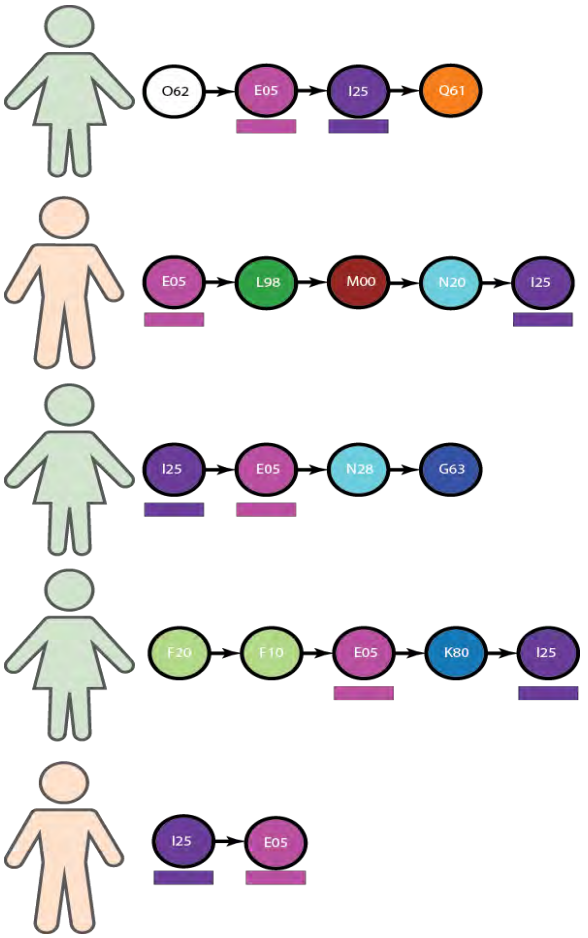
Excess number of comorbidities if diabetes is first



(A) Distribution of years between NIDDM and sleep apnea for patients diagnosed with NIDDM first (orange) and for patients diagnosed with sleep apnea first (green). (B) The plot shows the excess number of comorbidities for patients diagnosed with NIDDM first compared to those diagnosed with sleep apnea first (black line) with the 95% confidence interval (grey area). The dots indicate the number of patients having the minimum years between the two diagnoses.

Gender medicine:
Gender specific disease trajectories

- Males and females have some differences in physiology which may predispose or protect against certain diseases and their comorbidities

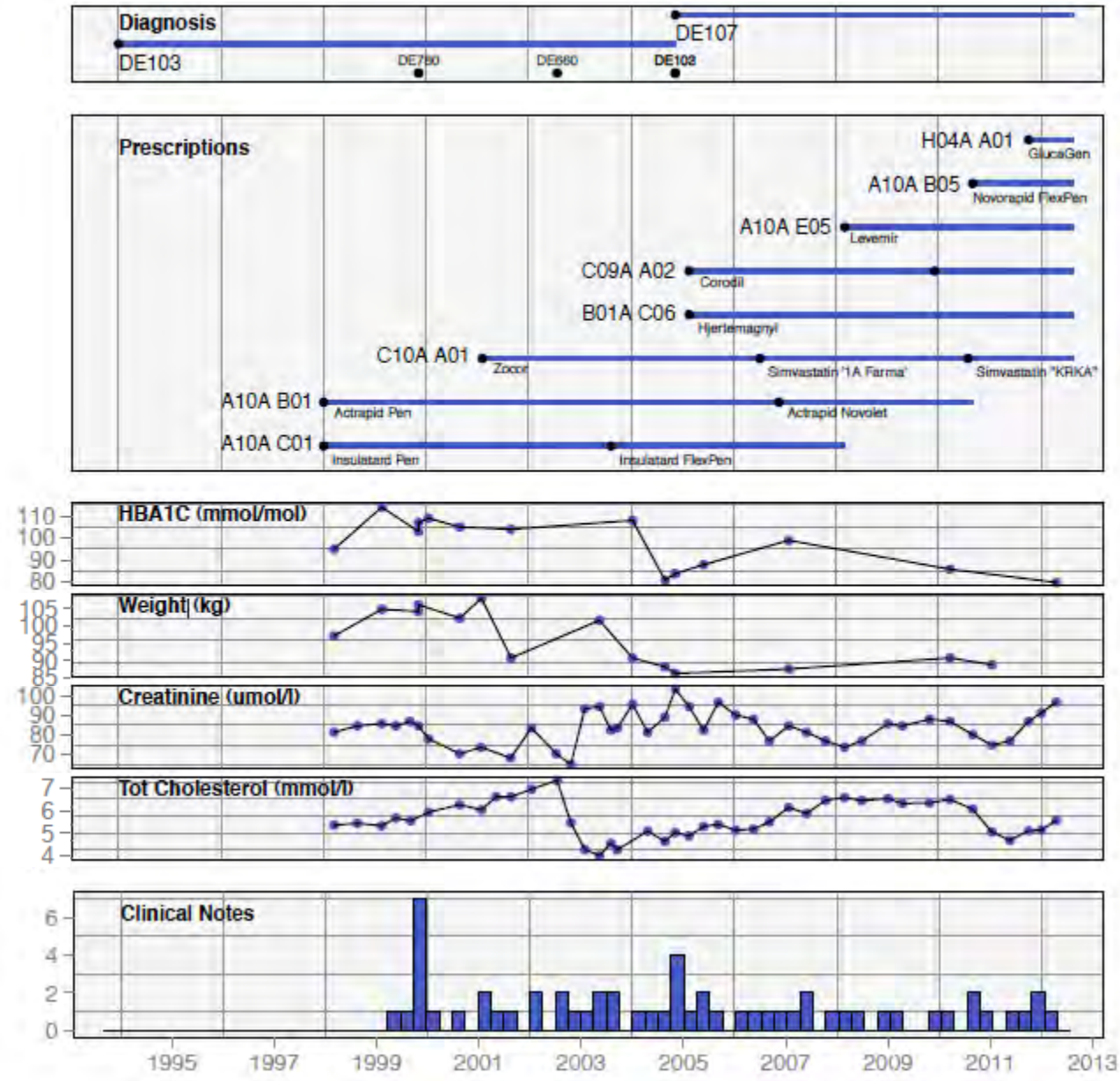


Diagnoses

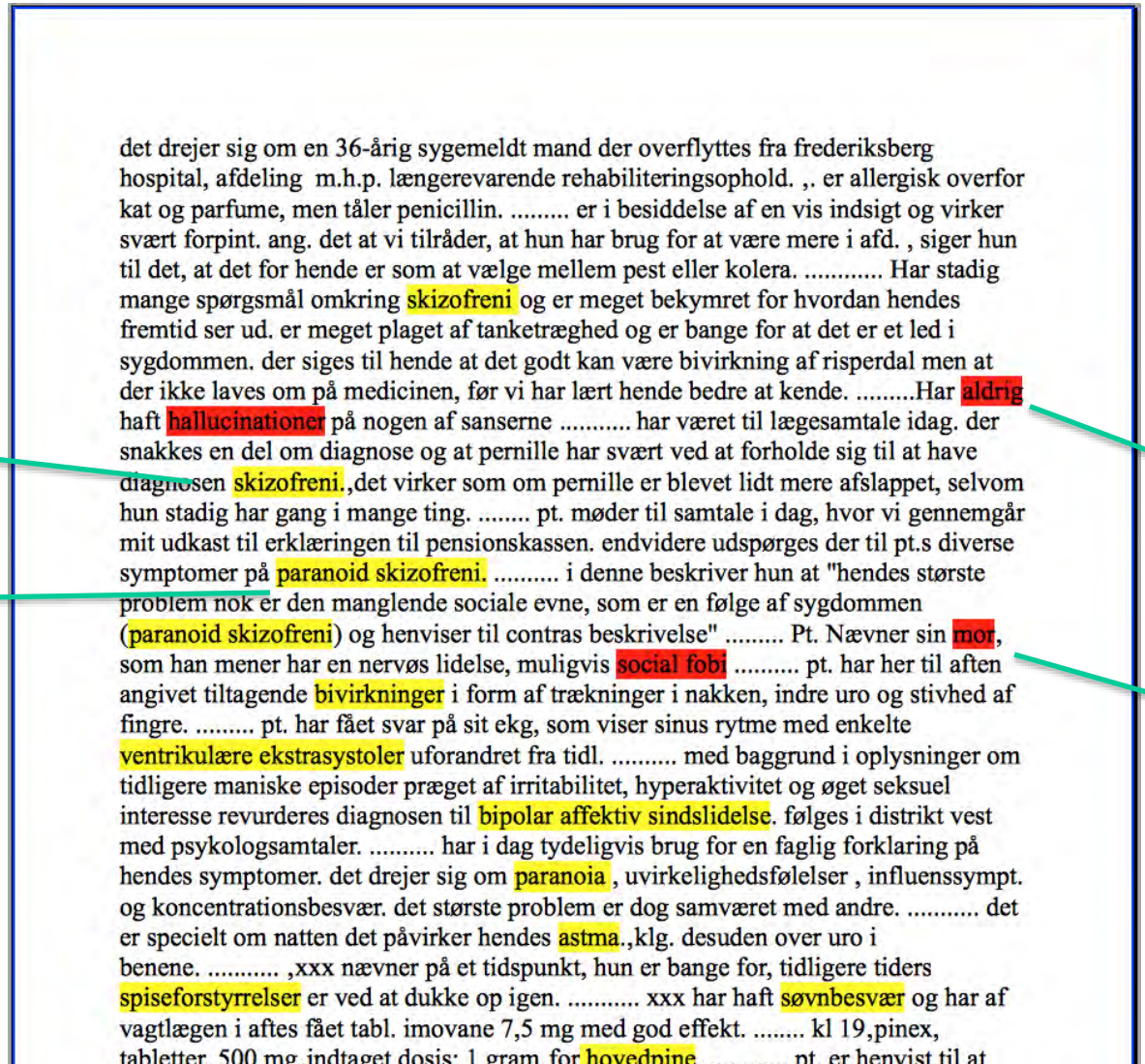
Drugs

Lab tests

Text



Deep-phenotyping by text mining of ICD10 terms in patient records



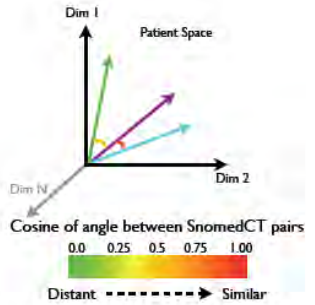
det drejer sig om en 36-årig sygemeldt mand der overflyttes fra frederiksberg hospital, afdeling m.h.p. længerevarende rehabiliteringsophold. ,. er allergisk overfor kat og parfume, men tåler penicillin. ..... er i besiddelse af en vis indsigt og virker svært forpint. ang. det at vi tilråder, at hun har brug for at være mere i afd. , siger hun til det, at det for hende er som at vælge mellem pest eller kolera. ..... Har stadig mange spørgsmål omkring skizofreni og er meget bekymret for hvordan hendes fremtid ser ud. er meget plaget af tanketrægthed og er bange for at det er et led i sygdommen. der siges til hende at det godt kan være bivirkning af risperdal men at der ikke laves om på medicinen, før vi har lært hende bedre at kende. .....Har aldrig haft hallucinationer på nogen af sanserne ..... har været til lægesamtale idag. der snakkes en del om diagnose og at pernille har svært ved at forholde sig til at have diagnosen skizofreni. ,det virker som om pernille er blevet lidt mere afslappet, selvom hun stadig har gang i mange ting. ..... pt. møder til samtale i dag, hvor vi gennemgår mit udkast til erklæringen til pensionskassen. endvidere udspørges der til pt.s diverse symptomer på paranoid skizofreni. ..... i denne beskriver hun at "hendes største problem nok er den manglende sociale evne, som er en følge af sygdommen (paranoid skizofreni) og henviser til contras beskrivelse" ..... Pt. Nævner sin mor, som han mener har en nervøs lidelse, muligvis social fobi ..... pt. har her til aften angivet tiltagende bivirkninger i form af trækninger i nakken, indre uro og stivhed af fingre. ..... pt. har fået svar på sit ekg, som viser sinus rytme med enkelte ventrikulære ekstrasystoler uforandret fra tidl. ..... med baggrund i oplysninger om tidligere maniske episoder præget af irritabilitet, hyperaktivitet og øget seksuel interesse revurderes diagnosen til bipolar affektiv sindslidelse. følges i distrikt vest med psykologsamtaler. ..... har i dag tydeligvis brug for en faglig forklaring på hendes symptomer. det drejer sig om paranoia , uvirkelighedsfølelser , influenssympt. og koncentrationsbesvær. det største problem er dog samværet med andre. ..... det er specielt om natten det påvirker hendes astma.,klg. desuden over uro i benene. ..... ,xxx nævner på et tidspunkt, hun er bange for, tidligere tiders spiseforstyrrelser er ved at dukke op igen. ..... xxx har haft søvnbesvær og har af vagtlægen i aftes fået tabl. imovane 7,5 mg med god effekt. ..... kl 19,pinex, tabletter, 500 mg, indtaget dosis: 1 gram, for hovedpine. ..... pt. er henvist til at

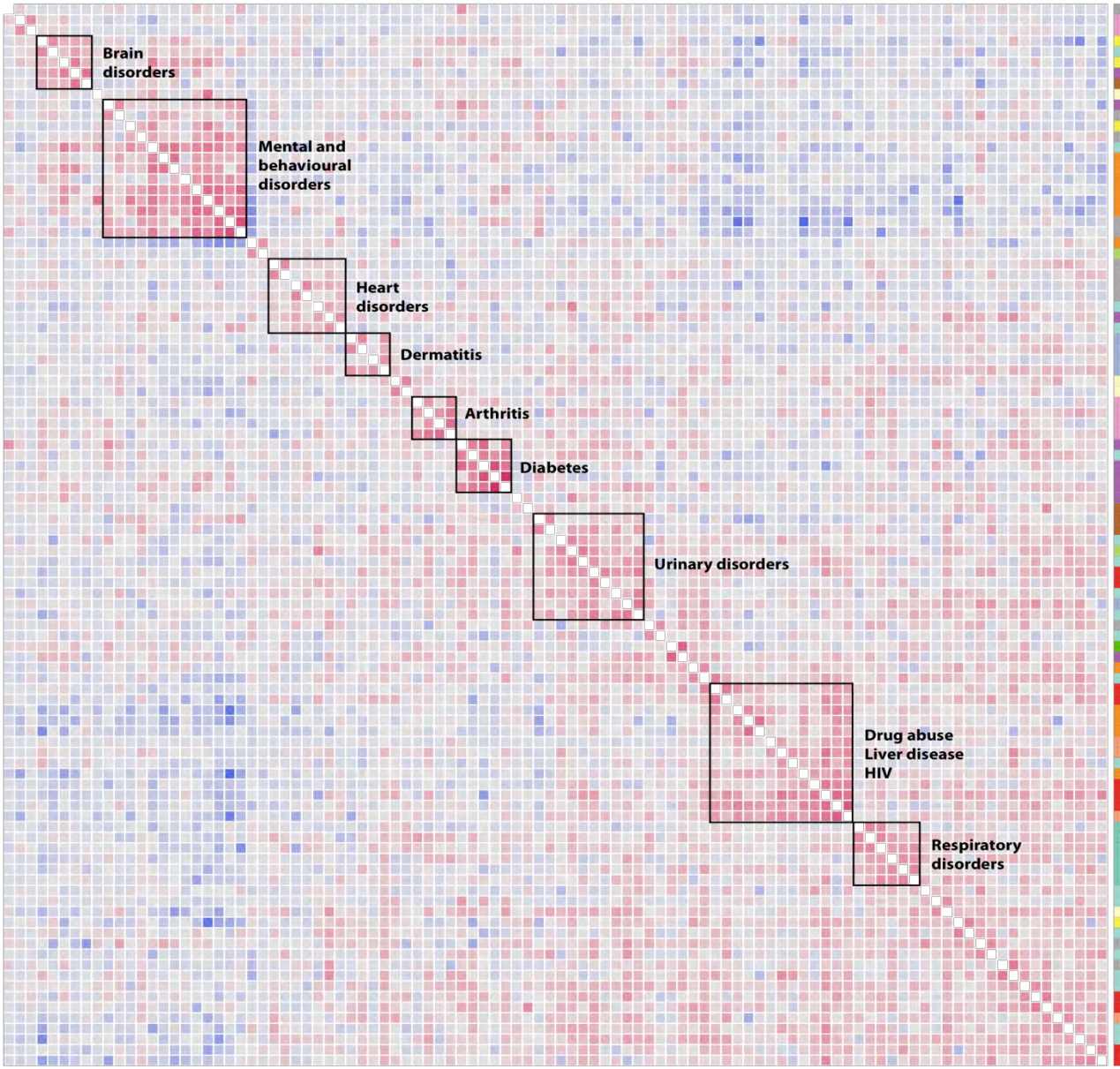
F20

F200

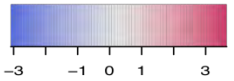
Negation

Family

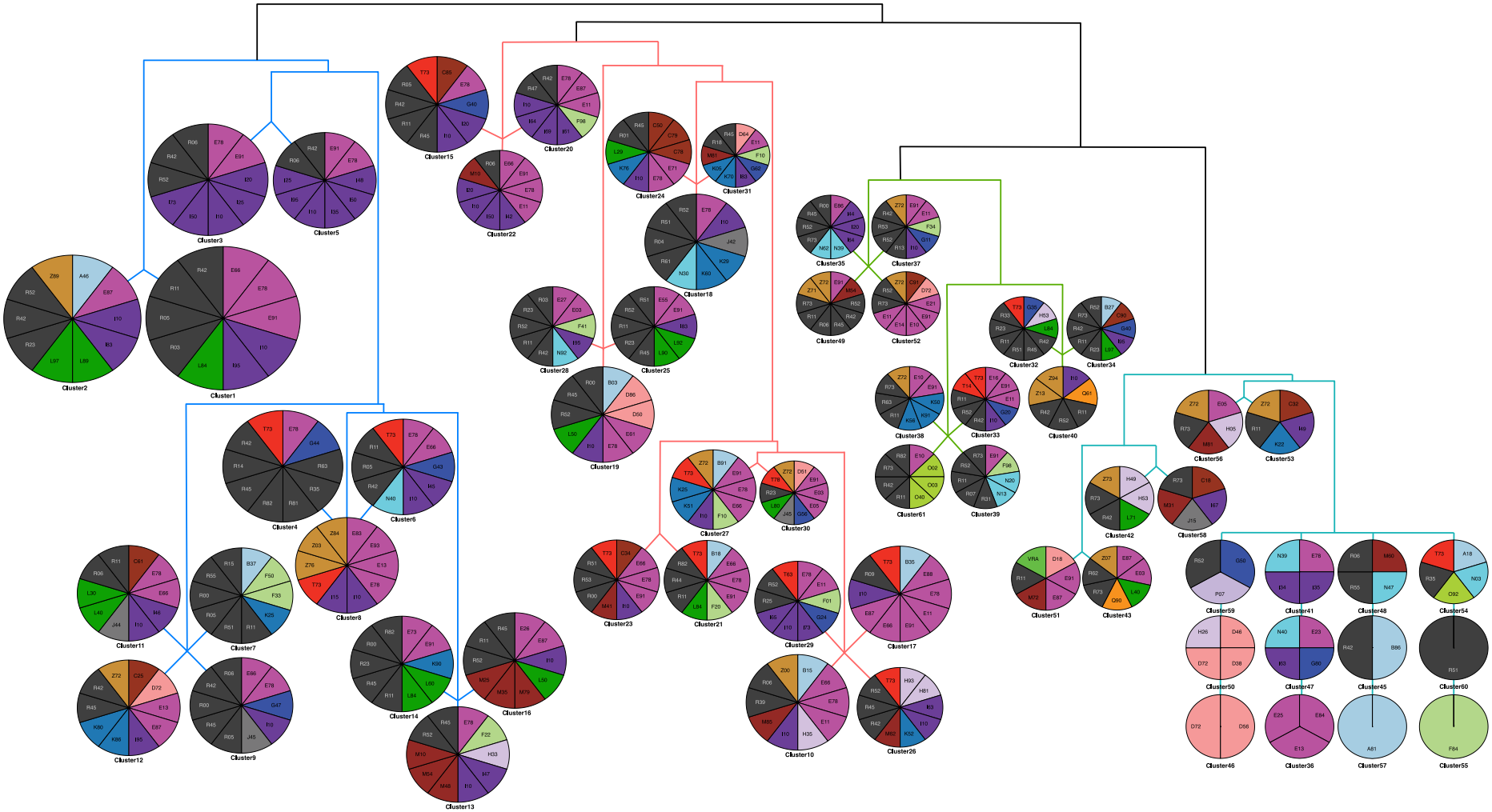




I11 HYPERTENSIVE HEART DISEASE
M10 GOUT
M14 ARTHROPATHIES IN OTHER DISEASES CLASSIFIED ELSEWHERE
G62 OTHER POLYNEUROPATHIES
R27 OTHER LACK OF COORDINATION
G93 OTHER DISORDERS OF BRAIN
E51 THIAMINE DEFICIENCY
H55 NYSTAGMUS AND OTHER IRREGULAR EYE MOVEMENTS
T90 SEQUELAE OF INJURIES OF HEAD
E78 DISORDERS OF LIPOPROTEIN METABOLISM AND OTHER LIPIDAEMIAS
I25 CHRONIC ISCHAEMIC HEART DISEASE
G91 HYDROCEPHALUS
I61 INTRACEREBRAL HAEMORRHAGE
R41 OTHER SYMPTOMS AND SIGNS INVOLVING COGNITIVE FUNCTIONS AND AWARENESS
F04 ORGANIC AMNESIC SYNDROME, NOT INDUCED BY ALCOHOL AND OTHER PSYCHOACTIVE SUBSTANCES
F18 MENTAL AND BEHAVIOURAL DISORDERS DUE TO USE OF VOLATILE SOLVENTS
F62 ENDURING PERSONALITY CHANGES, NOT ATTRIBUTABLE TO BRAIN DAMAGE AND DISEASE
F06 OTHER MENTAL DISORDERS DUE TO BRAIN DAMAGE AND DYSFUNCTION AND TO PHYSICAL DISEASE
F07 PERSONALITY AND BEHAVIOURAL DISORDERS DUE TO BRAIN DISEASE, DAMAGE AND DYSFUNCTION
F01 VASCULAR DEMENTIA
I64 STROKE, NOT SPECIFIED AS HAEMORRHAGE OR INFARCTION
I69 SEQUELAE OF CEREBROVASCULAR DISEASE
F50 EATING DISORDERS
N91 ABSENT, SCANTY AND RARE MENSTRUATION
I44 ATRIOVENTRICULAR AND LEFT BUNDLE-BRANCH BLOCK
I45 OTHER CONDUCTION DISORDERS
I48 ATRIAL FIBRILLATION AND FLUTTER
I49 OTHER CARDIAC ARRHYTHMIAS
R32 UNSPECIFIED URINARY INCONTINENCE
E87 OTHER DISORDERS OF FLUID, ELECTROLYTE AND ACID-BASE BALANCE
R00 ABNORMALITIES OF HEART BEAT
L21 SEBORRHOEIC DERMATITIS
L40 PSORIASIS
L20 ATOPIC DERMATITIS
L30 OTHER DERMATITIS
T14 INJURY OF UNSPECIFIED BODY REGION
T63 TOXIC EFFECT OF CONTACT WITH VENOMOUS ANIMALS
M06 OTHER RHEUMATOID ARTHRITIS
M11 OTHER CRYSTAL ARTHROPATHIES
M17 GONARTHROSIS [ARTHROSIS OF KNEE]
M19 OTHER ARTHROSIS
E11 NON-INSULIN-DEPENDENT DIABETES MELLITUS
R73 ELEVATED BLOOD GLUCOSE LEVEL
E14 UNSPECIFIED DIABETES MELLITUS
E10 INSULIN-DEPENDENT DIABETES MELLITUS
E16 OTHER DISORDERS OF PANCREATIC INTERNAL SECRETION
E86 VOLUME DEPLETION
H10 CONJUNCTIVITIS
H26 OTHER CATARACT
H40 GLAUCOMA
R30 PAIN ASSOCIATED WITH MICTURITION
N30 CYSTITIS
R31 UNSPECIFIED HAEMATURIA
A41 OTHER SEPTICAEMIA
B37 CANDIDIASIS
R39 OTHER SYMPTOMS AND SIGNS INVOLVING THE URINARY SYSTEM
L89 DECUBITUS ULCER
R33 RETENTION OF URINE
I95 HYPOTENSION
R61 HYPERHIDROSIS
D50 IRON DEFICIENCY ANAEMIA
E61 DEFICIENCY OF OTHER NUTRIENT ELEMENTS
F98 OTHER BEHAVIOURAL AND EMOTIONAL DISORDERS WITH ONSET USUALLY OCCURRING IN CHILDHOOD AND ADOLESC
R11 NAUSEA AND VOMITING
B23 HUMAN IMMUNODEFICIENCY VIRUS [HIV] DISEASE RESULTING IN OTHER CONDITIONS
B24 UNSPECIFIED HUMAN IMMUNODEFICIENCY VIRUS [HIV] DISEASE
F11 MENTAL AND BEHAVIOURAL DISORDERS DUE TO USE OF OPIOIDS
F14 MENTAL AND BEHAVIOURAL DISORDERS DUE TO USE OF COCAINE
F15 MENTAL AND BEHAVIOURAL DISORDERS DUE TO USE OF OTHER STIMULANTS, INCLUDING CAFFEINE
K73 CHRONIC HEPATITIS, NOT ELSEWHERE CLASSIFIED
K76 OTHER DISEASES OF LIVER
R17 UNSPECIFIED JAUNDICE
F19 MENTAL AND BEHAVIOURAL DISORDERS DUE TO MULTIPLE DRUG USE AND USE OF OTHER PSYCHOACTIVE SUBSTANC
B15 ACUTE HEPATITIS A
B17 OTHER ACUTE VIRAL HEPATITIS
B18 CHRONIC VIRAL HEPATITIS
K77 LIVER DISORDERS IN DISEASES CLASSIFIED ELSEWHERE
J40 BRONCHITIS, NOT SPECIFIED AS ACUTE OR CHRONIC
J42 UNSPECIFIED CHRONIC BRONCHITIS
J45 ASTHMA
J44 OTHER CHRONIC OBSTRUCTIVE PULMONARY DISEASE
J18 PNEUMONIA, ORGANISM UNSPECIFIED
J98 OTHER RESPIRATORY DISORDERS
R09 OTHER SYMPTOMS AND SIGNS INVOLVING THE CIRCULATORY AND RESPIRATORY SYSTEMS
R35 POLYURIA
T73 EFFECTS OF OTHER DEPRIVATION
G24 DYSTONIA
R25 ABNORMAL INVOLUNTARY MOVEMENTS
I46 CARDIAC ARREST
R02 GANGRENE, NOT ELSEWHERE CLASSIFIED
I50 HEART FAILURE
R18 ASCITES
R60 OEDEMA, NOT ELSEWHERE CLASSIFIED
A46 ERYSIPELAS
B95 STREPTOCOCCUS AND STAPHYLOCOCCUS AS THE CAUSE OF DISEASES CLASSIFIED TO OTHER CHAPTERS
K59 OTHER FUNCTIONAL INTESTINAL DISORDERS
R10 ABDOMINAL AND PELVIC PAIN
R50 FEVER OF OTHER AND UNKNOWN ORIGIN
A49 BACTERIAL INFECTION OF UNSPECIFIED SITE
B34 VIRAL INFECTION OF UNSPECIFIED SITE



Roche et al. PLoS Comp. Biol. 2011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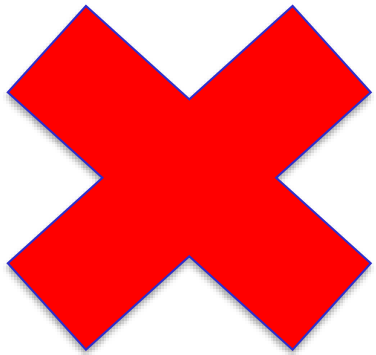
Which disease-disease and symptom correlations are treatment related?



Text mining of drug names, ADE/ADRs, diagnoses, …

Removed ADR - no corresponding structured data

Behandlet med Zyprexa 5 mg fra 3. til 24.6.99 og 10 mg fra 24. til 29.6.99 med nogen effekt på tankeforstyrrelser, men seponeret pga appetitøgning. Herefter Risperdal 2 mg stigende til 4 mg i perioden 29.6. til 12.7.99, men seponeret på grund af uro i kroppen og "ostek-lokkefornemmelse". Herefter Orap 2 mg fra 2.8. stigende til 3 mg fra 30.8.99 med god effekt på tankeekko og tankemylder. Behandlet med Zoloft 50 mg fra maj 98 til maj 99 med noget virkning på depressive symptomer, men seponeret på grund af natlig svedtendens. Siden 14.7.99 Efexor 75 mg med nogen effekt på antallet og sværhedsgraden af kortvarige depressive episoder.

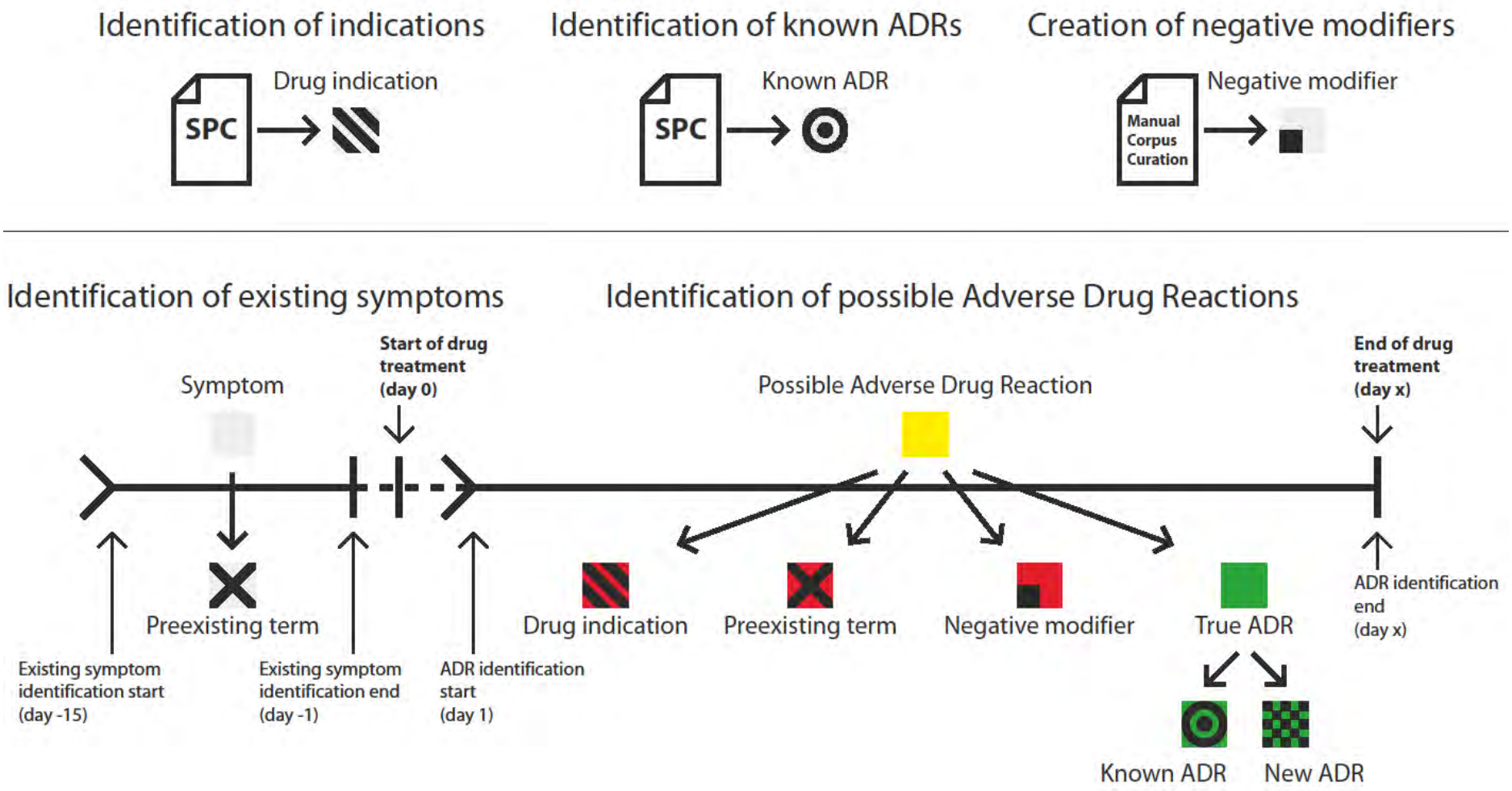
se venligst under allergier. Desuden forsøgt beh med Zyprexa, sep grundet vægtøgning, træthed og manglende effekt. Risperdal ord med nogen effekt tillagt dogmatil (1999). Efterfølgende aurorix beh seponeret i 1999. Startede istedet remeron. Aktuel medicindois, jvf ud-skrivningsnotat fra U12 samt EPJmedicinliste.

tbl. leponex 100+0+0+200 mg,tbl. nivotril 0,5 +0+1+ 0 mg,tbl. amitriptylin 0+0+0+30 mg,tbl. klomipramin 0+0+0+25 mg,tbl. imoclone 7,5 mg nocte,tbl. nivotril 2 mg p.n. max x 1 dgl. tbl. marevan a 2,5 mg efter skema,tbl. magnesia 1 g p.n. laxoberal dr. 7,5 mg /ml 15 dr. p.n. mix. link 150 mg /ml 15 ml p.n. max x 3 dgl. Figensaft 20+0+20+0 ml,Pt. er aktuelt,CAVE,tricykliske antidepressiva. Dette kan dog ikke bekræftes og pt. har tidl. fået imipramin, som han har tålt godt, hvorfor der er ansøgt om ophævelser af denne cave på højere niveau. Har tidl. fået zyprexa som blev sep. grundet vægtøgning, træthed og manglende effekt.

Removed ADR - negation and subject identification

...Jeg mener fortsat, at han har brug for medicin, da han i går fx var meget vred og følte sig utryg og angst og har haft svært ved at sove. Dette synes pt. at accepterer. Jeg tilbyder herefter Zyprexa i stedet for Risperdal, pt. afviser dette, da han ved medpatient har fået denne medicin og har fået øget appetit, dette vil han ikke. Har ikke tidligere fået antipsykotisk medicin. Accepterer herefter Cisordinol, startende på en lille dosis. Accepterer også angstdæmpende medicin i dagtiden. Angiver, at når han bliver vred kan han godt styre det. Synes det hjalp i går noget at få Nozinan. Virker fortsat garderet. Siger intet uopfordret. Sparsomt sygdomsindsigt. Er ikke vredladen. Er i dag [illegible] heller latent aggressiv...

Text mining Adverse Drug Reactions
(using 7,500 drug names and 21,000 ADRs)

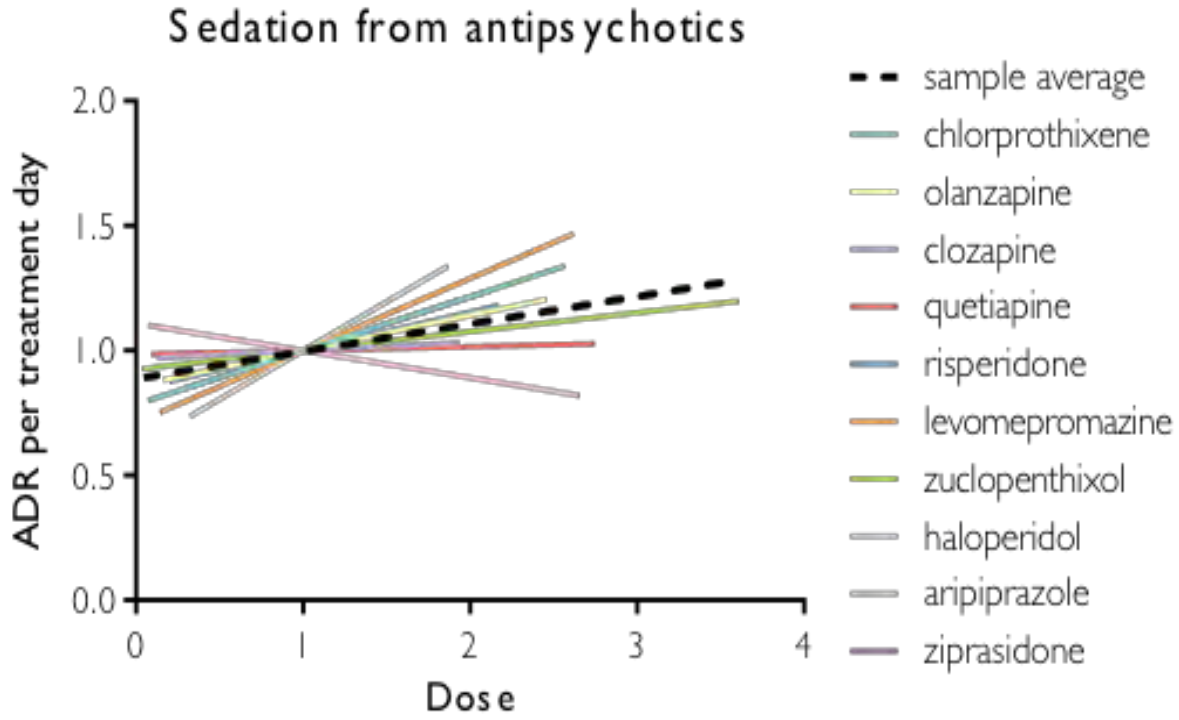


Eriksson et al. Drug Safety 2014

Data from two Danish regions

ADR-dose dependencies

Dosages from structured medication data

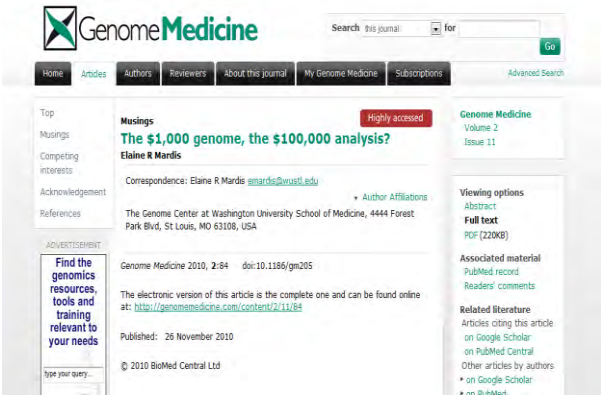


ADRs and doses are normalized on multiples of the minimum dose prescribed of each drug.

Plot for 21 days steady dosage data is visualized, sample average slope 0.1105 (95% CI, 0.03085-0.1901), non-zero slope p-value was 0,0074, all individual drug slopes are positive except for haloperidol.

Eriksson et al. Drug Safety 2014

Δ population health data



- **Health data driven:**
  - **Redefine phenotypes as trajectories**
  - **Enable prediction using predictable trajectories?**

- **Include what is not in patient records in new ways:**
  - **Diet,**
  - **Income, …**
  - **Education, grades in exams, …**
  - **Behavior, risk-taking, …**

Personlig Medicin og Individualiseret Behandling

Oplæg til en samlet dansk indsats

22. juni 2015

Region Sjælland – vi er til for dig
Syddansk Universitet
Aalborg Universitet
Danske Patienter
Aarhus Universitet
Danske Regioner
Region Hovedstaden
Region Nordjylland
Region Syddanmark
midt regionmidtjylland

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TRANSLATIONAL GENETICS

Mining electronic health records: towards better research applications and clinical care

Peter B. Jensen[1], *Lars J. Jensen*[1] *and Søren Brunak*[1,2]

Abstract | Clinical data describing the phenotypes and treatment of patients represents an underused data source that has much greater research potential than is currently realized. Mining of electronic health records (EHRs) has the potential for establishing new patient-stratification principles and for revealing unknown disease correlations. Integrating EHR data with genetic data will also give a finer understanding of genotype–phenotype relationships. However, a broad range of ethical, legal and technical reasons currently hinder the systematic deposition of these data in EHRs and their mining. Here, we consider the potential for furthering medical research and clinical care using EHR data and the challenges that must be overcome before this is a reality.

Clinical decision support
(CDS). Software systems providing support for decision making to physicians through the application of health knowledge and logical rules to patient data.

Biobanks
Central repositories of biological material that are mainly used for research. They facilitate the re-use of collected samples in different research projects.

Information technology has transformed the way health care is carried out and documented. Presently, the practice of health care generates, exchanges and stores huge amounts of patient-specific information. In addition to the traditional clinical narrative, databases in modern health centres automatically capture structured data relating to all aspects of care, including diagnosis, medication, laboratory test results and radiological imaging data.

This transformation holds great promise for the individual patient as richer information, coupled with clinical decision support (CDS) systems, becomes readily available at the bedside to support informed decision making and to improve patient safety[1,2] ... especially interesting when traditional health-care-sector data is linked with biobanks and genetic data[4].

Despite the great potential, researchers who wish to analyse large amounts of patient data are still faced with technical challenges of integrating scattered, heterogeneous data, in addition to ethical and legal obstacles that limit access to the data[5,6]. It is hoped that large-scale adoption of health information technology (HIT) infrastructure in the form of electronic health records (EHRs) and agreed standards for interoperability and schemes for privacy and consent, will improve this situation (TABLE 1). With incentives for improved public health and the expected health budget savings[7,8], these matters