Case Study: Admission Prediction with a Multilayer Perceptron

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Machine Learning Summer School

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INTRODUCTION

Hospital admission

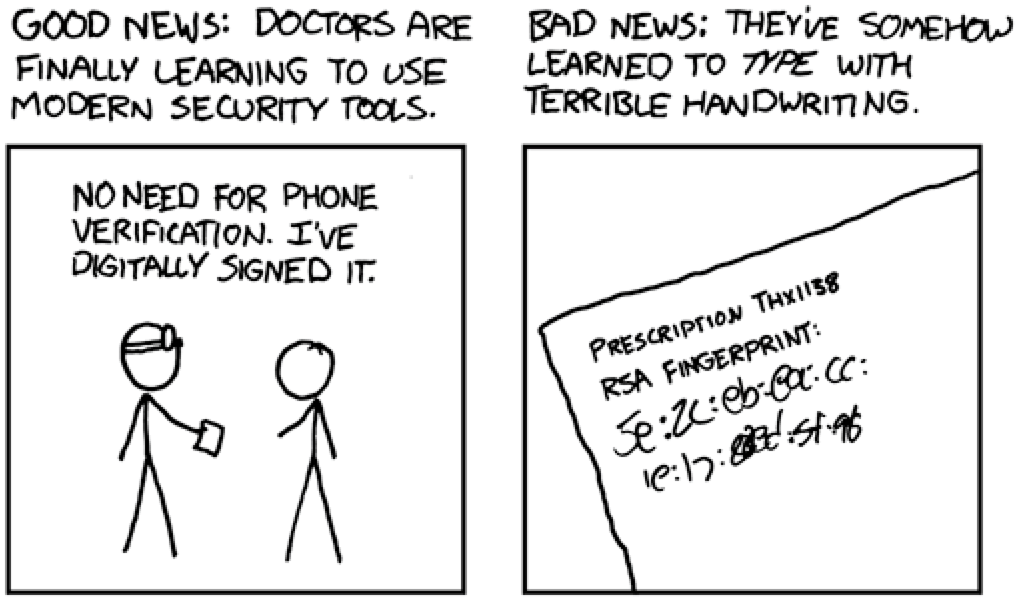
- 35,000,000 admissions every year in the U.S.
- Hospital admissions are risky and expensive:
    - 700,000 hospital-acquired infections per year
    - $18,000 per stay
- Preventing hospital admission can save lives & lower healthcare costs

Where does health data come from?

- Electronic health records
- Insurance claims
- Clinical trials
- Patient and disease registries
- Health surveys
- Phone apps
- Wearable electronics

Electronic Health Records (EHR)

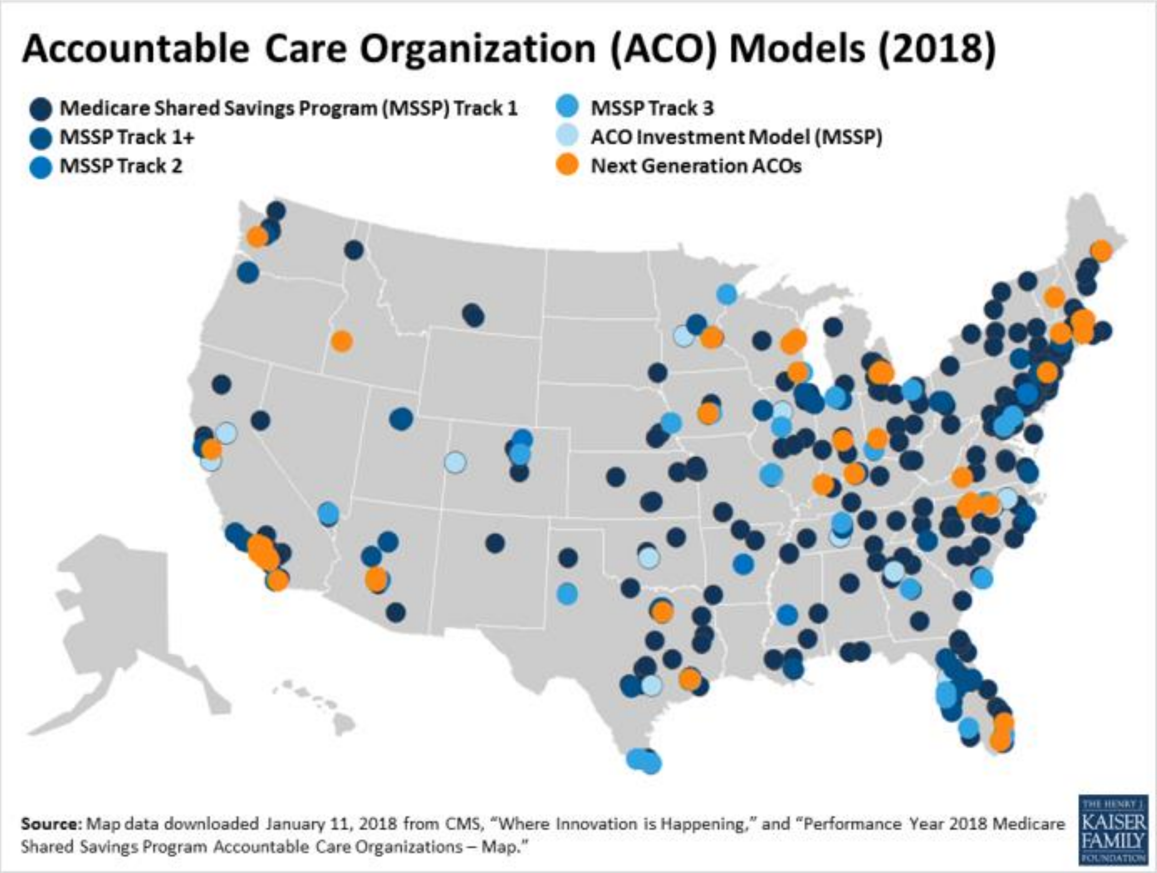
- 99% of large hospitals use EHRs
- What does an EHR store?
  - Values
    - Diagnosis codes
    - Procedure codes
    - Medication lists
    - Lab results
    - Vital signs
  - Text (medical notes)
  - Images



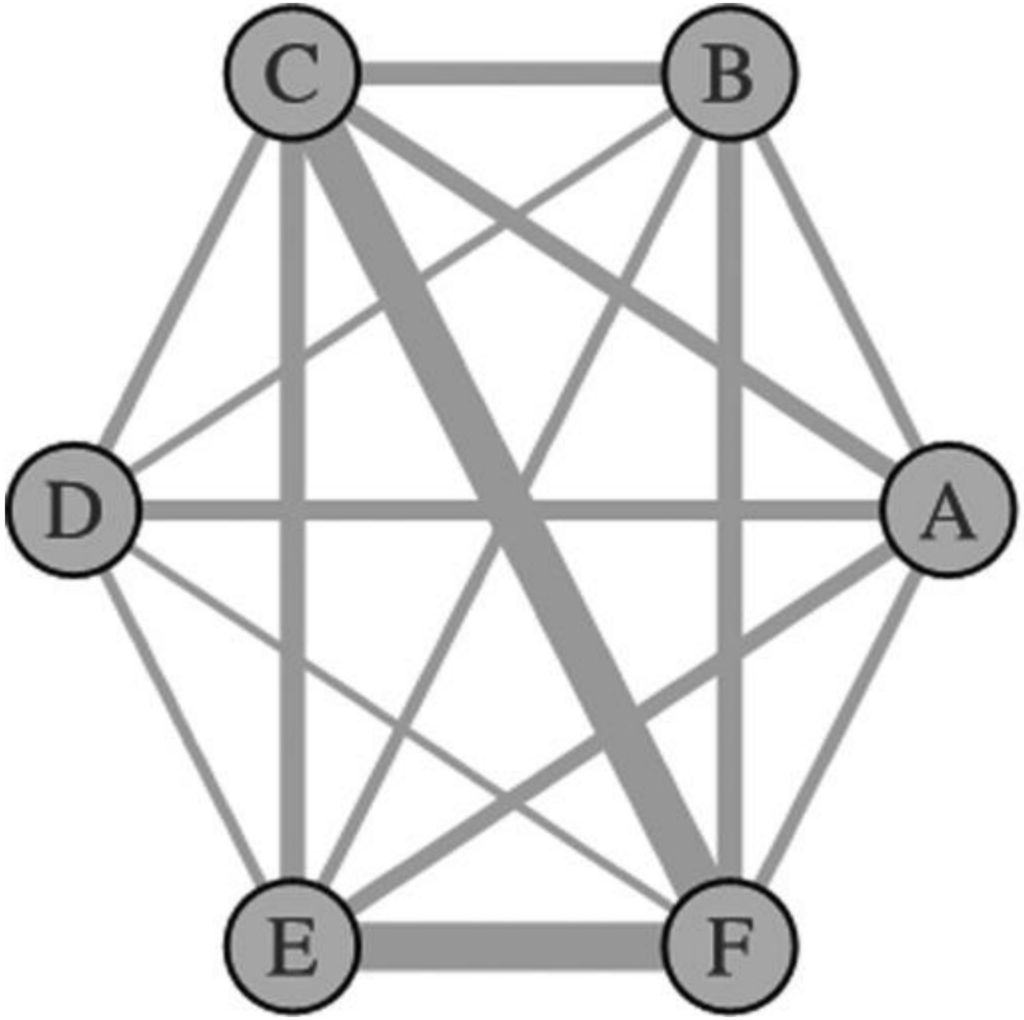
https://www.xkcd.com/asmarterplanet//

Insurance claims

- Bill for health services that the hospital sends to the insurance company for payment
- Duke receives insurance claims records for all patients in the Medicare Shared Savings Program (MSSP)
- Includes diagnoses, procedures, and medications from all medical facilities where the patient received care



Patients go to multiple hospitals



Frequency of patients receiving care from multiple emergency departments in Manhattan in 2011.

Kern et al. “Patients’ Use of Multiple Hospitals in a Major U.S. City: Implications for Population Management.” Popul Health Manag. 2017 Apr 1; 20(2): 99–102.

Duke admission prediction project

- Goal: use 12 months of patient data to predict risk of hospital admission in the next 6 months
- Data Preparation
  - Input: EHR data + insurance claims
  - Output: risk probability
- Model: multilayer perceptron
- Action: Duke Care Managers implement interventions to improve health of high-risk patients

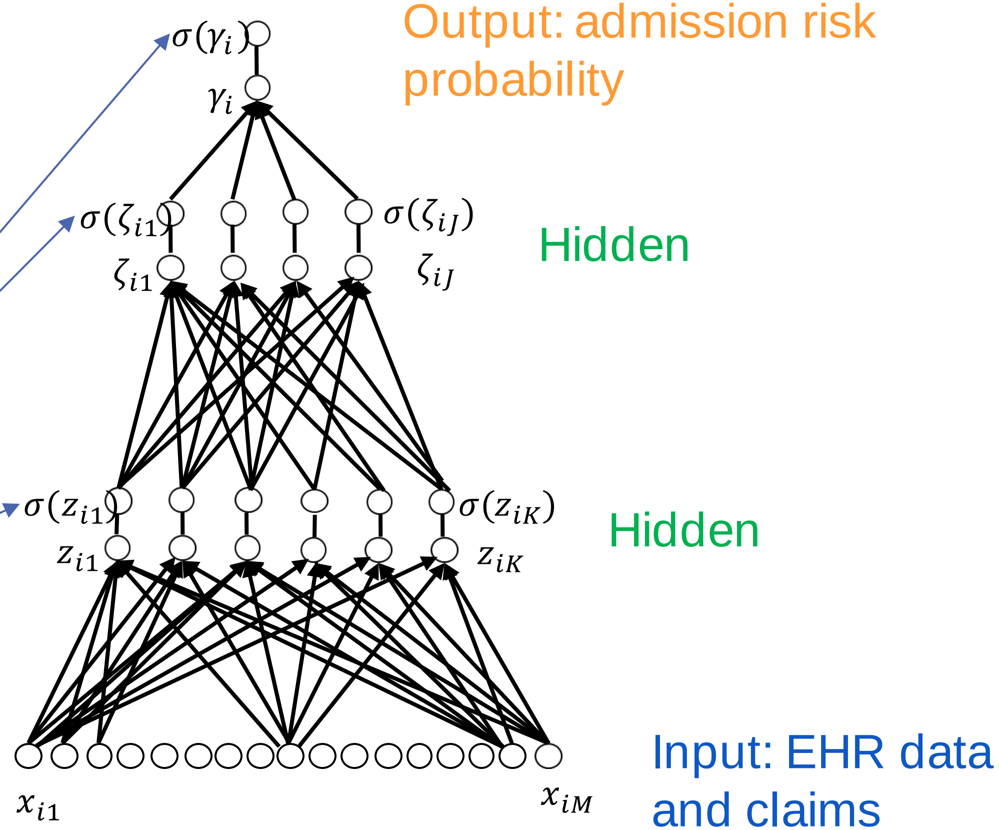
https://www.flickr.com/photos/myfuturedotcom/6052491503

Multilayer perceptron

- A class of feedforward neural network that has at least three layers: input, hidden, output
- Uses non-linear activations,

  e.g. the sigmoid function:

$$\sigma(z_j) = \frac{e^{z_j}}{1+e^{z_j}}$$



Modified from figure by David Carlson

HEALTH DATA PREPARATION

Challenges with EHR data

(1) High dimensional — Thousands of medical features

(2) Incomplete — e.g., patient sees a doctor in a different hospital system
e.g., patient dies at home

(3) Multiple irregular time scales — Seconds: vital signs
Days: hospital stay
Years: family doctor visits

(4) Noisy — e.g., coding inaccuracies

https://pixabay.com/en/yarn-colors-tangle-thread-986252/

Challenges with EHR data

(1) High dimensional — Use knowledge bases for efficient data representation

(2) Incomplete — Combine EHR data with insurance claims data

(3) Multiple irregular time scales — Discretize time: use all data from 12 months to predict admission risk in the next 6 months

(4) Noisy — Use large data

https://www.flickr.com/photos/alicebyday/25151642179

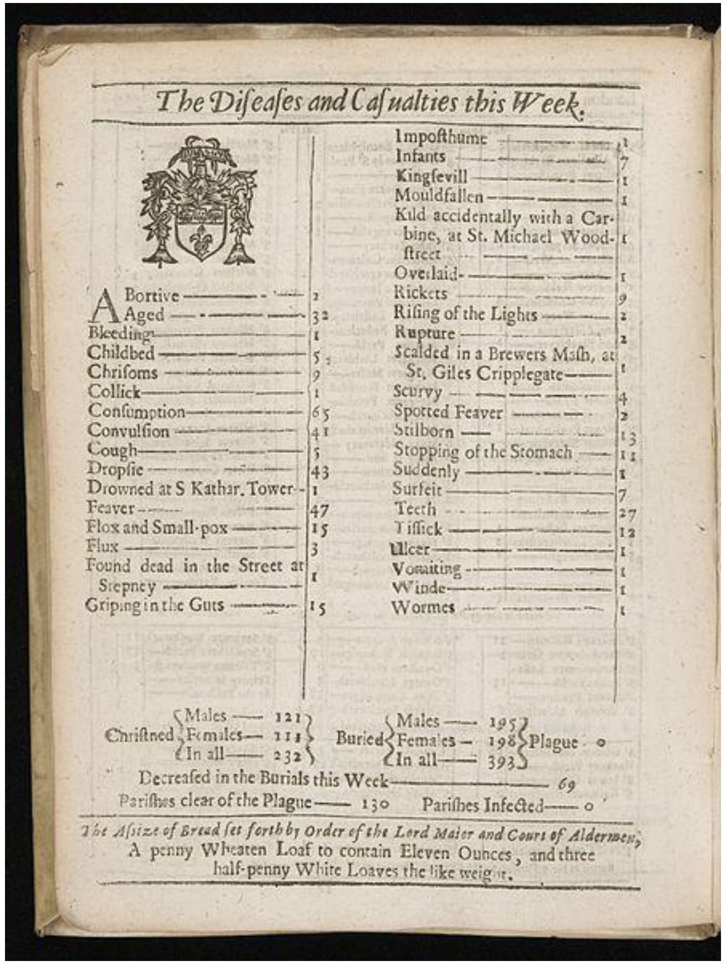
(1) Reducing the dimensionality

Too many ICD diagnosis codes: use CCS codes (knowledge base) to represent as medically meaningful categories

Too many medication names: use medication knowledge base to represent as active ingredients

A history of medical billing & coding

- 1592: London Bills of Mortality
  - Data gathered weekly
  - Arranged into numerical codes and used to measure most frequent causes of death
- 1937: International List of Causes of Death
- 1977: International Classification of Diseases (ICD) expanded beyond causes of death, to include illnesses and injuries
- Current system: ICD-10



The Diseases and Casualties this Week.

Abortive	2	Imposthume	1
Aged	32	Infants	7
Bleeding	1	Kingsevill	1
Childbed	5	Mouldfallen	1
Chrisoms	9	Kild accidentally with a Carbine, at St. Michael Woodstreet	1
Collick	1	Overlaid	1
Consumption	65	Rickets	9
Convulsion	41	Rising of the Lights	2
Cough	5	Rupture	2
Dropsie	43	Scalded in a Brewers Mash, at St. Giles Cripplegate	1
Drowned at S Kathar. Tower	1	Scurvy	4
Feaver	47	Spotted Feaver	2
Flox and Small-pox	15	Stilborn	13
Flux	3	Stopping of the Stomach	11
Found dead in the Street at Stepney	1	Suddenly	1
Griping in the Guts	15	Surfeit	7
		Teeth	27
		Tissick	12
		Ulcer	1
		Vomiting	1
		Winde	1
		Wormes	1

Christned	Males 121	Females 111	In all 232		
Buried	Males 195	Females 198	In all 393	Plague	0

Decreased in the Burials this Week — 69

Parishes clear of the Plague — 130 Parishes Infected — 0

The Assize of Bread set forth by Order of the Lord Maior and Court of Aldermen,
A penny Wheaten Loaf to contain Eleven Ounces, and three half-penny White Loaves the like weight.

https://commons.wikimedia.org/wiki/File:Bills_of_Mortality_Feb_21_-_28_1664_Wellcome_L0043358.jpg

ICD-10 examples

- Diagnoses
  - Cold: J06.9 Acute upper respiratory infection, unspecified.
  - Flu: J11.1 Influenza due to unidentified influenza virus with other respiratory manifestations
  - Broken arm: S52.92XA Unspecified fracture of left forearm, initial encounter for closed fracture
- Procedures
  - Appendix removed: 0DBJ4ZZ Excision of appendix, percutaneous endoscopic approach
  - Gallbladder removed: 0FB44ZZ Excision of gallbladder, percutaneous endoscopic approach

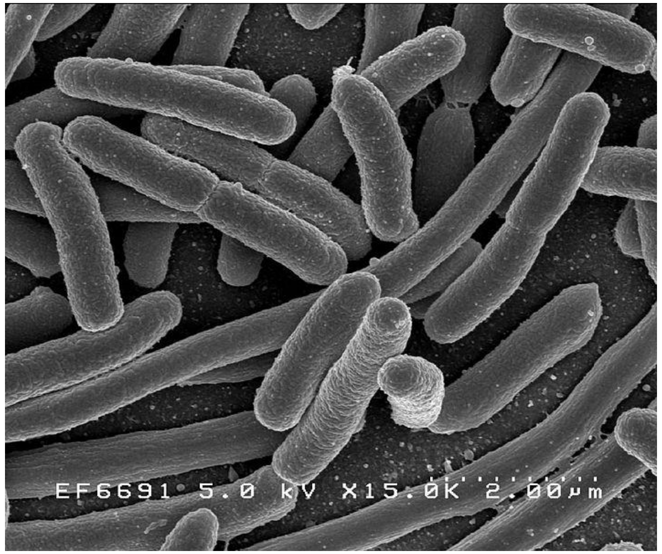
What’s the catch?

- There are over 14,400 different codes in the ICD-10 base classification
- Some expanded ICD editions include over 70,000 codes
- ICD codes are too granular!

https://en.wikipedia.org/wiki/Margaret_Hamilton_(scientist)#/media/File:Margaret_Hamilton_-_restoration.jpg

Food poisoning

0050	Staphylococcal food poisoning
0051	Botulism food poisoning
0052	Food poisoning due to Clostridium perfringens (C. welchii)
0053	Food poisoning due to other Clostridia
0054	Food poisoning due to Vibrio parahaemolyticus
00581	Food poisoning due to Vibrio vulnificus
00589	Other bacterial food poisoning
0059	Food poisoning, unspecified



https://en.wikipedia.org/wiki/File:EscherichiaColi_NIAID.jpg

Diabetes

E08.00	Diabetes mellitus due to underlying condition with hyperosmolarity without nonketotic hyperglycemic-hyperosmolar coma (NKHHC)
E08.01	Diabetes mellitus due to underlying condition with hyperosmolarity with coma
E08.10	Diabetes mellitus due to underlying condition with ketoacidosis without coma
E08.11	Diabetes mellitus due to underlying condition with ketoacidosis with coma
E08.21	Diabetes mellitus due to underlying condition with diabetic nephropathy
E08.22	Diabetes mellitus due to underlying condition with diabetic chronic kidney disease
E08.29	Diabetes mellitus due to underlying condition with other diabetic kidney complication
E08.311	Diabetes mellitus due to underlying condition with unspecified diabetic retinopathy with macular edema
E08.319	Diabetes mellitus due to underlying condition with unspecified diabetic retinopathy without macular edema
E08.321	Diabetes mellitus due to underlying condition with mild nonproliferative diabetic retinopathy with macular edema
E08.329	Diabetes mellitus due to underlying condition with mild nonproliferative diabetic retinopathy without macular edema
E08.331	Diabetes mellitus due to underlying condition with moderate nonproliferative diabetic retinopathy with macular edema
E08.339	Diabetes mellitus due to underlying condition with moderate nonproliferative diabetic retinopathy without macular edema
E08.341	Diabetes mellitus due to underlying condition with severe nonproliferative diabetic retinopathy with macular edema
E08.349	Diabetes mellitus due to underlying condition with severe nonproliferative diabetic retinopathy without macular edema
E08.351	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with macular edema
E08.352	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with traction retinal detachment involving the macula
E08.353	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with traction retinal detachment not involving the macula
E08.354	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment
E08.355	Diabetes mellitus due to underlying condition with stable proliferative diabetic retinopathy
E08.359	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy without macular edema
E08.36	Diabetes mellitus due to underlying condition with diabetic cataract
E08.37	Diabetes mellitus due to underlying condition with diabetic macular edema, resolved following treatment
E08.39	Diabetes mellitus due to underlying condition with other diabetic ophthalmic complication
E08.40	Diabetes mellitus due to underlying condition with diabetic neuropathy, unspecified
E08.41	Diabetes mellitus due to underlying condition with diabetic mononeuropathy
E08.42	Diabetes mellitus due to underlying condition with diabetic polyneuropathy
E08.43	Diabetes mellitus due to underlying condition with diabetic autonomic (poly)neuropathy
E08.44	Diabetes mellitus due to underlying condition with diabetic amyotrophy
E08.49	Diabetes mellitus due to underlying condition with other diabetic neurological complication
E08.51	Diabetes mellitus due to underlying condition with diabetic peripheral angiopathy without gangrene
E08.52	Diabetes mellitus due to underlying condition with diabetic peripheral angiopathy with gangrene
E08.59	Diabetes mellitus due to underlying condition with other circulatory complications
E08.610	Diabetes mellitus due to underlying condition with diabetic arthropathy
E08.618	Diabetes mellitus due to underlying condition with other diabetic arthropathy
E08.620	Diabetes mellitus due to underlying condition with diabetic dermatitis
E08.621	Diabetes mellitus due to underlying condition with foot ulcer
E08.622	Diabetes mellitus due to underlying condition with other skin ulcer
E08.628	Diabetes mellitus due to underlying condition with other skin complications
E08.630	Diabetes mellitus due to underlying condition with periodontal disease
E08.638	Diabetes mellitus due to underlying condition with other oral complications
E08.641	Diabetes mellitus due to underlying condition with hypoglycemia with coma
E08.649	Diabetes mellitus due to underlying condition with hypoglycemia without coma
E08.65	Diabetes mellitus due to underlying condition with hyperglycemia
E08.69	Diabetes mellitus due to underlying condition with other specified complication
E08.8	Diabetes mellitus due to underlying condition with unspecified complication
E08.9	Diabetes mellitus due to underlying condition without complications
E09.00	Drug or chemical induced diabetes mellitus with hyperosmolarity without nonketotic hyperglycemic-hyperosmolar coma (NKHHC)
E09.01	Drug or chemical induced diabetes mellitus with hyperosmolarity with coma
E09.10	Drug or chemical induced diabetes mellitus with ketoacidosis without coma
E09.11	Drug or chemical induced diabetes mellitus with ketoacidosis with coma
E09.21	Drug or chemical induced diabetes mellitus with diabetic nephropathy
E09.22	Drug or chemical induced diabetes mellitus with diabetic chronic kidney disease
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E09.321	Drug or chemical induced diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema
E09.329	Drug or chemical induced diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema
E09.331	Drug or chemical induced diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema
E09.339	Drug or chemical induced diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema
E09.341	Drug or chemical induced diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema
E09.349	Drug or chemical induced diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema
E09.351	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with macular edema

E09.352	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula
E09.353	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula
E09.354	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment
E09.355	Drug or chemical induced diabetes mellitus with stable proliferative diabetic retinopathy
E09.359	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy without macular edema
E09.36	Drug or chemical induced diabetes mellitus with diabetic cataract
E09.37	Drug or chemical induced diabetes mellitus with diabetic macular edema, resolved following treatment
E09.39	Drug or chemical induced diabetes mellitus with other diabetic ophthalmic complication
E09.40	Drug or chemical induced diabetes mellitus with neurological complications with diabetic neuropathy, unspecified
E09.41	Drug or chemical induced diabetes mellitus with neurological complications with diabetic mononeuropathy
E09.42	Drug or chemical induced diabetes mellitus with neurological complications with diabetic polyneuropathy
E09.43	Drug or chemical induced diabetes mellitus with neurological complications with diabetic autonomic (poly)neuropathy
E09.44	Drug or chemical induced diabetes mellitus with neurological complications with diabetic amyotrophy
E09.49	Drug or chemical induced diabetes mellitus with neurological complications with other diabetic neurologic complication
E09.51	Drug or chemical induced diabetes mellitus with diabetic peripheral angiopathy without gangrene
E09.52	Drug or chemical induced diabetes mellitus with diabetic peripheral angiopathy with gangrene
E09.59	Drug or chemical induced diabetes mellitus with other circulatory complications
E09.610	Drug or chemical induced diabetes mellitus with diabetic neuropathic arthropathy
E09.618	Drug or chemical induced diabetes mellitus with other diabetic arthropathy
E09.620	Drug or chemical induced diabetes mellitus with diabetic dermatitis
E09.621	Drug or chemical induced diabetes mellitus with foot ulcer
E09.622	Drug or chemical induced diabetes mellitus with other skin ulcer
E09.628	Drug or chemical induced diabetes mellitus with other skin complications
E09.630	Drug or chemical induced diabetes mellitus with periodontal disease
E09.638	Drug or chemical induced diabetes mellitus with other oral complications
E09.641	Drug or chemical induced diabetes mellitus with hypoglycemia with coma
E09.649	Drug or chemical induced diabetes mellitus with hypoglycemia without coma
E09.65	Drug or chemical induced diabetes mellitus with hyperglycemia
E09.69	Drug or chemical induced diabetes mellitus with other specified complication
E09.8	Drug or chemical induced diabetes mellitus with unspecified complications
E09.9	Drug or chemical induced diabetes mellitus without complications
E10.10	Type 1 diabetes mellitus with ketoacidosis without coma
E10.11	Type 1 diabetes mellitus with ketoacidosis with coma
E10.21	Type 1 diabetes mellitus with diabetic nephropathy
E10.22	Type 1 diabetes mellitus with diabetic chronic kidney disease
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E10.331	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema
E10.339	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema
E10.341	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema
E10.349	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema
E10.351	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema
E10.352	**Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula**
E10.353	**Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula**
E10.354	**Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment**
E10.355	**Type 1 diabetes mellitus with stable proliferative diabetic retinopathy**
E10.359	Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema
E10.36	Type 1 diabetes mellitus with diabetic cataract
E10.37	**Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment**
E10.39	Type 1 diabetes mellitus with other diabetic ophthalmic complication

E10.40	Type 1 diabetes mellitus with diabetic neuropathy, unspecified	No change
E10.41	Type 1 diabetes mellitus with diabetic mononeuropathy	No change
E10.42	Type 1 diabetes mellitus with diabetic polyneuropathy	No change
E10.43	Type 1 diabetes mellitus with diabetic autonomic (poly)neuropathy	No change
E10.44	Type 1 diabetes mellitus with diabetic amyotrophy	No change
E10.49	Type 1 diabetes mellitus with other diabetic neurological complication	No change
E10.51	Type 1 diabetes mellitus with diabetic peripheral angiopathy without gangrene	No change
E10.52	Type 1 diabetes mellitus with diabetic peripheral angiopathy with gangrene	No change
E10.59	Type 1 diabetes mellitus with other circulatory complications	No change
E10.610	Type 1 diabetes mellitus with diabetic neuropathic arthropathy	No change
E10.618	Type 1 diabetes mellitus with other diabetic arthropathy	No change
E10.620	Type 1 diabetes mellitus with diabetic dermatitis	No change
E10.621	Type 1 diabetes mellitus with foot ulcer	No change
E10.622	Type 1 diabetes mellitus with other skin ulcer	No change
E10.628	Type 1 diabetes mellitus with other skin complications	No change
E10.630	Type 1 diabetes mellitus with periodontal disease	No change
E10.638	Type 1 diabetes mellitus with other oral complications	No change
E10.641	Type 1 diabetes mellitus with hypoglycemia with coma	No change
E10.649	Type 1 diabetes mellitus with hypoglycemia without coma	No change
E10.65	Type 1 diabetes mellitus with hyperglycemia	No change
E10.69	Type 1 diabetes mellitus with other specified complication	No change
E10.8	Type 1 diabetes mellitus with unspecified complications	No change
E10.9	Type 1 diabetes mellitus without complications	No change
E11.00	Type 2 diabetes mellitus with hyperosmolarity without nonketotic hyperglycemic-hyperosmolar coma (NKHHC)	No change
E11.01	Type 2 diabetes mellitus with hyperosmolarity with coma	No change
E11.10	**Type 2 diabetes mellitus with ketoacidosis without coma**	**Add**
E11.11	**Type 2 diabetes mellitus with ketoacidosis with coma**	**Add**
E11.21	Type 2 diabetes mellitus with diabetic nephropathy	No change
E11.22	Type 2 diabetes mellitus with diabetic chronic kidney disease	No change
E11.29	Type 2 diabetes mellitus with other diabetic kidney complication	No change
E11.311	Type 2 diabetes mellitus with unspecified diabetic retinopathy with macular edema	No change
E11.319	Type 2 diabetes mellitus with unspecified diabetic retinopathy without macular edema	No change
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E11.339	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema	No change
E11.341	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema	No change
E11.349	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema	No change
E11.351	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema	No change
E11.352	**Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula**	**Add**
E11.353	**Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula**	**Add**
E11.354	**Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment**	**Add**
E11.355	**Type 2 diabetes mellitus with stable proliferative diabetic retinopathy**	**Add**
E11.359	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema	No change
E11.36	Type 2 diabetes mellitus with diabetic cataract	No change
E11.37	**Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment**	**Add**
E11.39	Type 2 diabetes mellitus with other diabetic ophthalmic complication	No change
E11.40	Type 2 diabetes mellitus with diabetic neuropathy, unspecified	No change
E11.41	Type 2 diabetes mellitus with diabetic mononeuropathy	No change
E11.42	Type 2 diabetes mellitus with diabetic polyneuropathy	No change
E11.43	Type 2 diabetes mellitus with diabetic autonomic (poly)neuropathy	No change
E11.44	Type 2 diabetes mellitus with diabetic amyotrophy	No change
E11.49	Type 2 diabetes mellitus with other diabetic neurological complication	No change
E11.51	Type 2 diabetes mellitus with diabetic peripheral angiopathy without gangrene	No change
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E11.621	Type 2 diabetes mellitus with foot ulcer	No change
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E11.638	Type 2 diabetes mellitus with other oral complications	No change
E11.641	Type 2 diabetes mellitus with hypoglycemia with coma	No change
E11.649	Type 2 diabetes mellitus with hypoglycemia without coma	No change
E11.65	Type 2 diabetes mellitus with hyperglycemia	No change
E11.69	Type 2 diabetes mellitus with other specified complication	No change
E11.8	Type 2 diabetes mellitus with unspecified complications	No change
E11.9	Type 2 diabetes mellitus without complications	No change
E13.00	Other specified diabetes mellitus with hyperosmolarity without nonketotic hyperglycemic-hyperosmolar coma (NKHHC)	No change
E13.01	Other specified diabetes mellitus with hyperosmolarity with coma	No change
E13.10	Other specified diabetes mellitus with ketoacidosis without coma	No change
E13.11	Other specified diabetes mellitus with ketoacidosis with coma	No change
E13.21	Other specified diabetes mellitus with diabetic nephropathy	No change
E13.22	Other specified diabetes mellitus with diabetic chronic kidney disease	No change
E13.29	Other specified diabetes mellitus with other diabetic kidney complication	No change
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E13.319	Other specified diabetes mellitus with unspecified diabetic retinopathy without macular edema	No change
E13.321	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema	No change
E13.329	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema	No change
E13.331	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema	No change
E13.339	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema	No change
E13.341	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema	No change
E13.349	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema	No change
E13.351	Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema	No change
E13.352	**Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula**	**Add**
E13.353	**Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula**	**Add**
E13.354	**Other specified diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment**	**Add**
E13.355	**Other specified diabetes mellitus with stable proliferative diabetic retinopathy**	**Add**
E13.359	Other specified diabetes mellitus with proliferative diabetic retinopathy without macular edema	No change
E13.36	Other specified diabetes mellitus with diabetic cataract	No change
E13.37	**Other specified diabetes mellitus with diabetic macular edema, resolved following treatment**	**Add**
E13.39	Other specified diabetes mellitus with other diabetic ophthalmic complication	No change
E13.40	Other specified diabetes mellitus with diabetic neuropathy, unspecified	No change
E13.41	Other specified diabetes mellitus with diabetic mononeuropathy	No change
E13.42	Other specified diabetes mellitus with diabetic polyneuropathy	No change
E13.43	Other specified diabetes mellitus with diabetic autonomic (poly)neuropathy	No change
E13.44	Other specified diabetes mellitus with diabetic amyotrophy	No change
E13.49	Other specified diabetes mellitus with other diabetic neurological complication	No change
E13.51	Other specified diabetes mellitus with diabetic peripheral angiopathy without gangrene	No change
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E13.628	Other specified diabetes mellitus with other skin complications	No change
E13.630	Other specified diabetes mellitus with periodontal disease	No change
E13.638	Other specified diabetes mellitus with other oral complications	No change
E13.641	Other specified diabetes mellitus with hypoglycemia with coma	No change
E13.649	Other specified diabetes mellitus with hypoglycemia without coma	No change
E13.65	Other specified diabetes mellitus with hyperglycemia	No change
E13.69	Other specified diabetes mellitus with other specified complication	No change
E13.8	Other specified diabetes mellitus with unspecified complications	No change
E13.9	Other specified diabetes mellitus without complications	No change
O24.414	**Gestational diabetes mellitus in pregnancy, insulin controlled**	**Add**
O24.415	**Gestational diabetes mellitus in pregnancy, controlled by oral hypoglycemic drugs**	**Add**
O24.419	**Gestational diabetes mellitus in pregnancy, unspecified control**	**Add**
O24.424	**Gestational diabetes mellitus in childbirth, insulin controlled**	**Add**
O24.425	**Gestational diabetes mellitus in childbirth, controlled by oral hypoglycemic drugs**	**Add**
O24.429	**Gestational diabetes mellitus in childbirth, unspecified control**	**Add**
O24.434	**Gestational diabetes mellitus in the puerperium, insulin controlled**	**Add**
O24.435	**Gestational diabetes mellitus in the puerperium, controlled by oral hypoglycemic drugs**	**Add**
O24.439	**Gestational diabetes mellitus in the puerperium, unspecified control**	**Add**

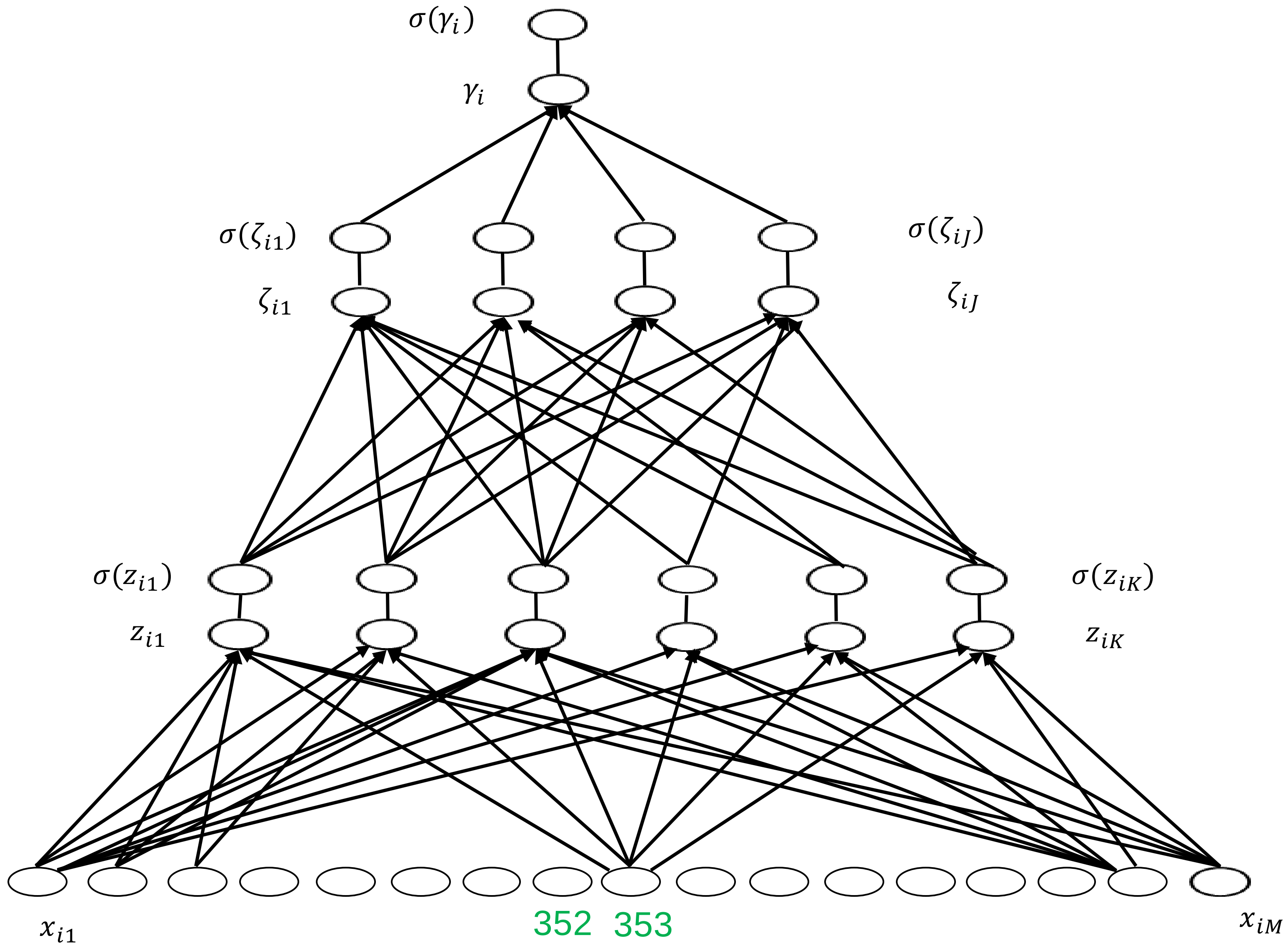
Weird codes…

V97.33XD	Sucked into jet engine, subsequent encounter
W55.41XA	Bitten by pig, initial encounter.
W61.62XD	Struck by duck, subsequent encounter
W220.2XD	Walked into lamppost, subsequent encounter
V91.07XD	Burn due to water-skis on fire, subsequent encounter
V95.43XS	Spacecraft collision injuring occupant, sequela
V00.01XD	Pedestrian on foot injured in collision with roller-skater, subsequent encounter

Example

Anne: E08.352 Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with traction retinal detachment *involving the macula*

Bob: E08.353 Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with traction retinal detachment <u>not</u> involving the macula



Anne	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
Bob	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0

The solution

- Clinical Classification Software (CCS)
- A mapping from “detailed ICD code” to “medical concept”
- Free to download
- 14,400 ICD diagnosis codes to 270 CCS codes

Single-level CCS codes

ICD prefixes	CCS Code
24900 25000 25001 7902 79021 79022 79029 7915 7916 V4585 V5391 V6546	49 Diabetes mellitus without complication
24901 24910 24911 24920 24921 24930 24931 24940 24941 24950 24951 24960 24961 24970 24971 24980 24981 24990 24991 25002 25003 25010 25011 25012 25013 25020 25021 25022 25023 25030 25031 25032 25033 25040 25041 25042 25043 25050 25051 25052 25053 25060 25061 25062 25063 25070 25071 25072 25073 25080 25081 25082 25083 25090 25091 25092 25093	50 Diabetes mellitus with complications

Multi-Level CCS codes

ICD prefixes	CCS Code
24900 25000 25001 7902 79021 79022 79029 7915 7916 V4585 V5391 V6546	3.2 Diabetes mellitus without complication

ICD prefixes	CCS Code
24901 24910 24911 25002 25003 25010 25011 25012 25013	3.3.1 Diabetes with ketoacidosis or uncontrolled diabetes
24940 24941 25040 25041 25042 25043	3.3.2 Diabetes with renal manifestations
24950 24951 25050 25051 25052 25053	3.3.3 Diabetes with ophthalmic manifestations
24960 24961 25060 25061 25062 25063	3.3.4 Diabetes with neurological manifestations
24970 24971 25070 25071 25072 25073	3.3.5 Diabetes with circulatory manifestations
24990 24991 25090 25091	3.3.6 Diabetes with unspecified complications
24920 24921 24930 24931 24980 24981 25020 25021 25022 25023 25030 25031 25032 25033 25080 25081 25082 25083 25092 25093	3.3.7 Diabetes with other manifestations

Medications to active ingredients

Brand Names	Ingredients
Advil, Motrin, Proprinal	Ibuprofen
Tylenol	Acetaminophen
Percocet	Acetaminophen, Oxycodone
Excedrin PM Headache	Acetaminophen, Aspirin, Diphenhydramine
Benadryl, Banophen, ZzzQuil	Diphehydramine
Ascriptin, Aspergum, Aspirtab, Bayer, Easprin, Ecotrin, Ecpirin, Entercote, Genacote, Halfprin, Ninoprin, Norwich Aspirin	Aspirin
Bupap, Tencon, Phrenilin, Allzital	Acetaminophen, Butalbital

Medications to active ingredients

Brand Names	Ingredients
Aldocumar, Anasmol, Anticoag, Befarin, Cavamed, Cicoxil, Circuvit, Cofarin, Coumadin, Coumadine, Cumar, Farin, Foley, Haemofarin, Jantoven, Kovar, Lawarin, Maforan, Marevan, Marfarin, Marivanil, Martefarin, Morfarin, Orfarin, Panwarfin, Scheme, Simarc, Varfarin, Varfarins, Varfine, Waran, Warcok, Warf, Warfareks, Warfarin, Warfarina, Warfarine, Warfarinum, Warfen, Warfin, Warik, Warin, Warlin, and Zyfarin	Warfarin

(2) Addressing incompleteness: combine EHR with insurance claims

Using EHR data in combination with insurance claims provides a more complete picture of a patient's medical history

This is especially useful for **ensuring correct admission labels**: we want to label patients admitted to an outside hospital as "admitted"

(3) Addressing irregular timing: discretize time & use counts

- Use all data from the past 12 months to predict future 6-month risk of admission
- Collapse the year of irregular encounters into a single count vector summarizing the year

Patient 123ABZ	Jan-1-18	Mar-5-18	Nov-10-18
Metformin	1	1	1
Insulin	0	1	1
Diabetes	1	1	1
Appendectomy	0	0	1
Lung cancer	0	0	0

Patient 123ABZ	Count
Metformin	3
Insulin	2
Diabetes	3
Appendectomy	1
Lung cancer	0

(4) Addressing noise: use many patients

	Number of patients	Percent of total
Training set	60,016	70
Validation set	12,861	15
Test set	12,860	15
TOTAL	**85,737**	100

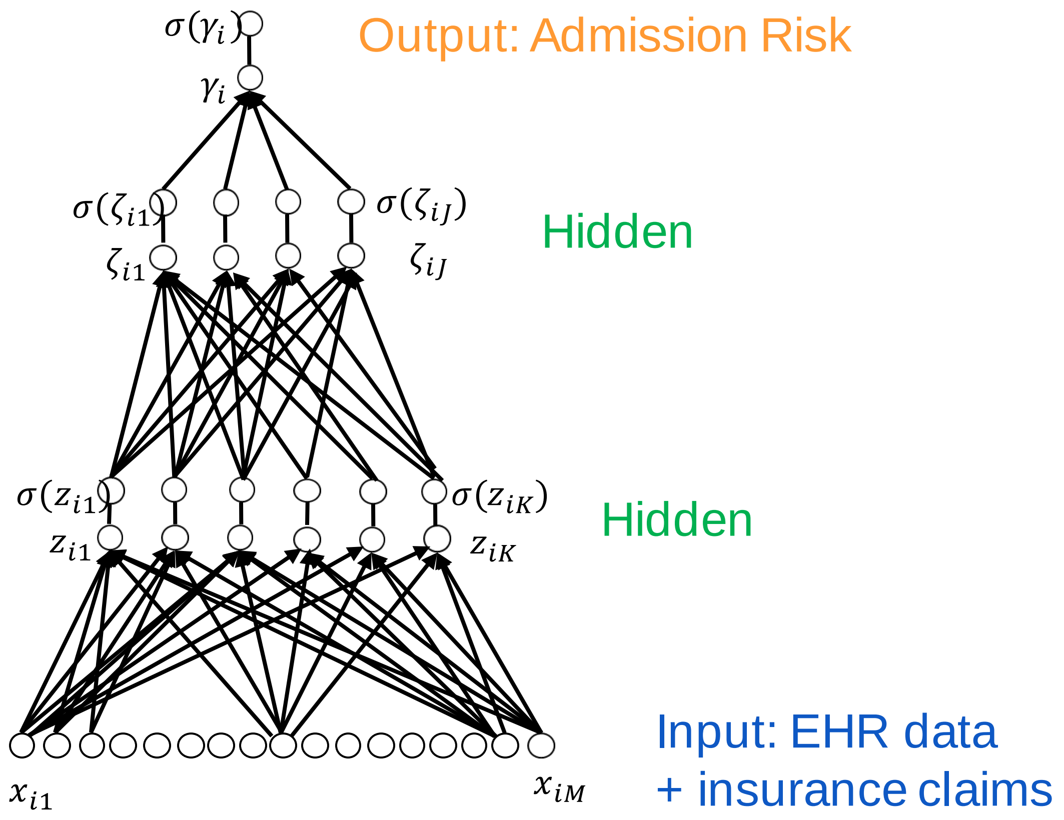
https://en.wikipedia.org/wiki/Pitch_invasion

Percent admitted: 11.5%

MODEL:
MULTILAYER PERCEPTRON

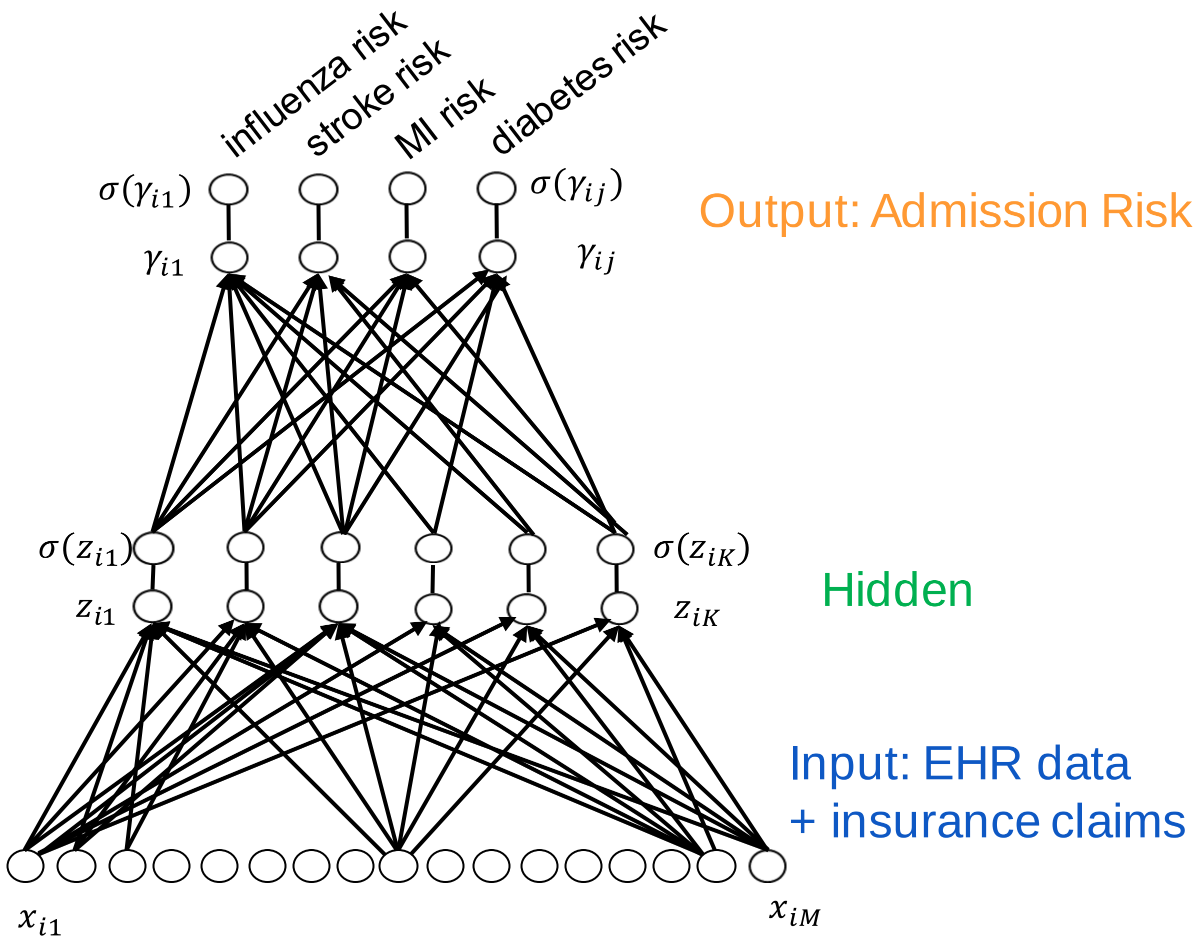
Multilayer perceptron for admission prediction

- The model in this diagram only outputs a single value
  - e.g., risk of any admission
- What if we want to predict the risk of admission for specific conditions?



Predicting more than one output

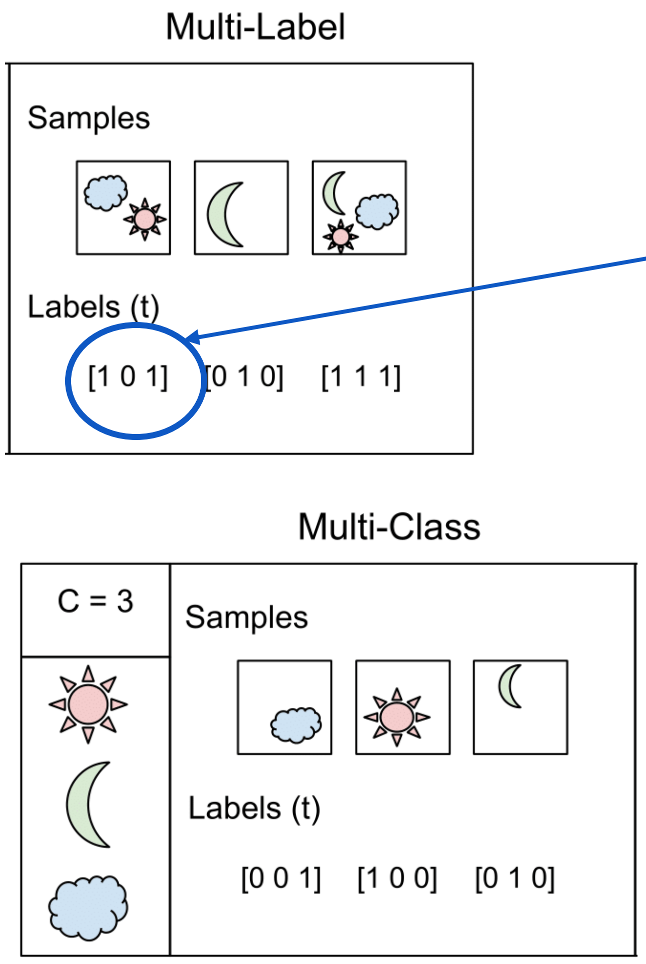
- When building a neural network, you can specify the size of each layer – including the size of the output layer
- We design the model to output **30 risk probabilities,** corresponding to the top 30 most common admission reasons



Multi-label vs. multi-class

- Admission prediction is a **multi-label** problem:
  - More than one right answer
  - i.e., a patient can be admitted for more than one disease in the next six months
- Other machine learning problems are **multi-class**:
  - Only one right answer
  - e.g., MNIST digit classification

e.g., in the 6-month window the patient was admitted for stroke and MI but not influenza



https://gombru.github.io/2018/05/23/cross_entropy_loss/

Multi-label vs. multi-class

- **Multi-label** (admission prediction): apply **sigmoid** function $\sigma(z_i)$ to each element of the output independently
  - Classes are **NOT mutually exclusive**: each example can belong to more than one class
  - Each element of the output vector is between 0 and 1
  - Entire output vector does NOT have to sum to 1

$$\sigma(z_j) = \frac{e^{z_j}}{1+e^{z_j}}$$

- **Multi-class** (digit classification): apply **softmax** to the whole output
  - Classes **ARE mutually exclusive**: each example can belong to exactly one class
  - Each element of the output vector is between 0 and 1
  - Increasing the output value of one class requires the output values for the other classes to decrease
  - Entire output vector sums to 1

Softmax function $\sigma(\mathbf{z})_j$

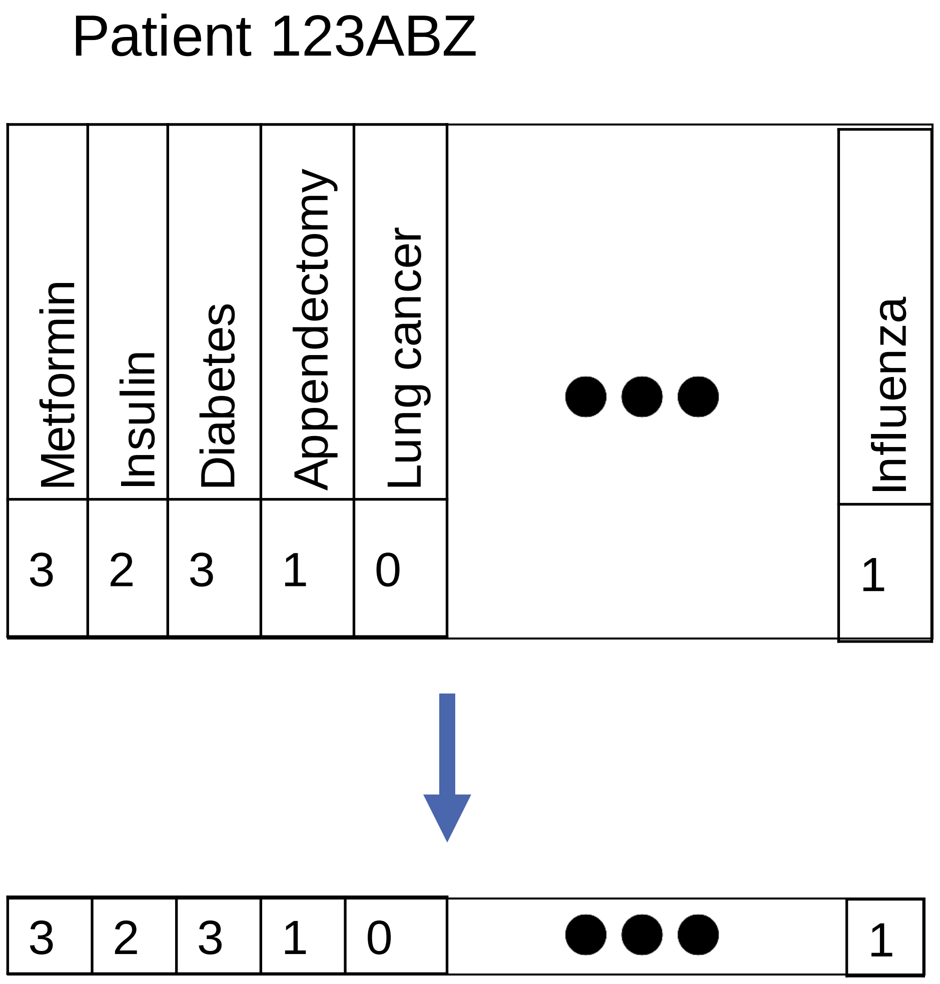
$$\sigma(\mathbf{z})_j = \frac{e^{z_j}}{\sum_{k=1}^{K} e^{z_k}} \quad \text{for } j = 1, \cdots, K.$$

Multi-label vs. multi-class

Example raw output values	[3.2, -5.7, 0.6]
Result of applying **sigmoid** (multi-label, admission prediction) to raw outputs	[0.96, 0.003, 0.65] $\sigma(3.2) = \frac{e^{3.2}}{1+e^{3.2}} = 0.96$ Sum: 0.96 + 0.0033 + 0.65 = 1.61 $\neq$ 1
Result of applying **softmax** (multi-class, digit classification) to raw outputs	[0.93, 0.0001, 0.07] *Softmax function* $\sigma(\mathbf{z})_j$ $\sigma(\mathbf{z})_j = \frac{e^{z_j}}{\sum_{k=1}^{K} e^{z_k}}$ for $j = 1, \cdots, K$. $= \frac{e^{3.2}}{e^{3.2}+e^{-5.7}+e^{0.6}} = 0.93$ Sum: 0.93 + 0.069 + 0.00013 = 1

Input for one patient

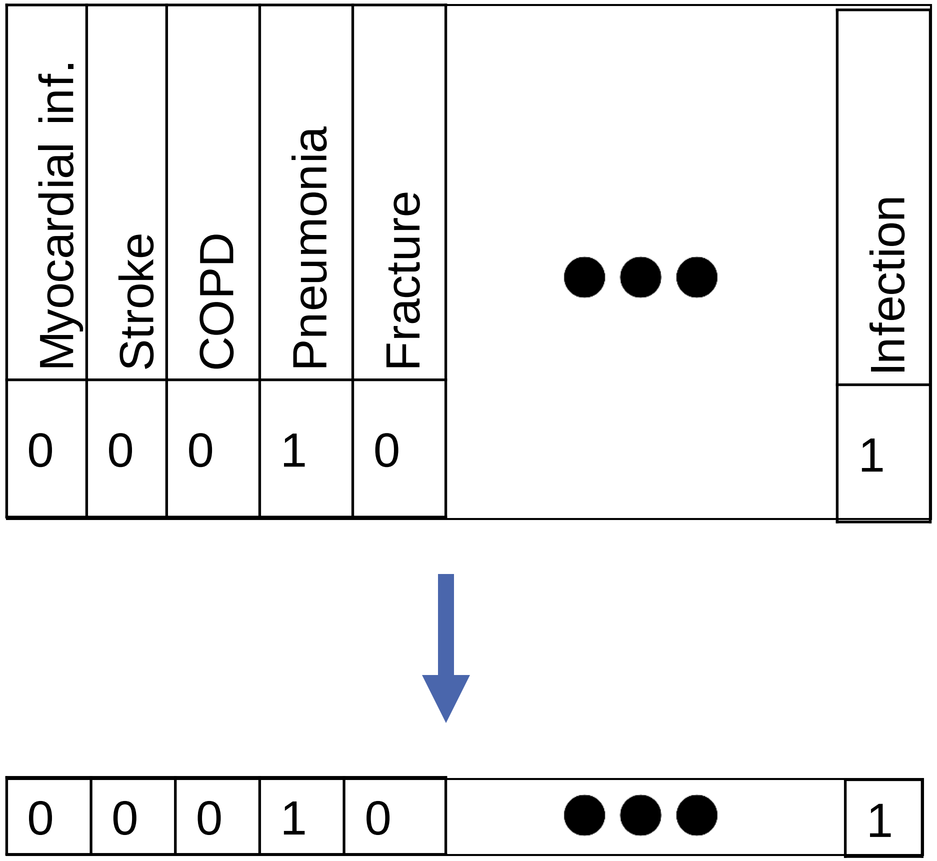
- Counts over the past year for 1,395 clinical variables
  - Diagnoses (as CCS codes)
  - Procedures (as CCS codes)
  - Medications (as active ingredients)
- The EHR data and the insurance claims data both contribute to the total counts
- Sparse



Output for one patient

- Binary vector of length 30, corresponding to the top 30 most common admission diagnoses
  - 1 if patient was admitted for that diagnosis in the 6-month window
  - 0 otherwise
- Sparse

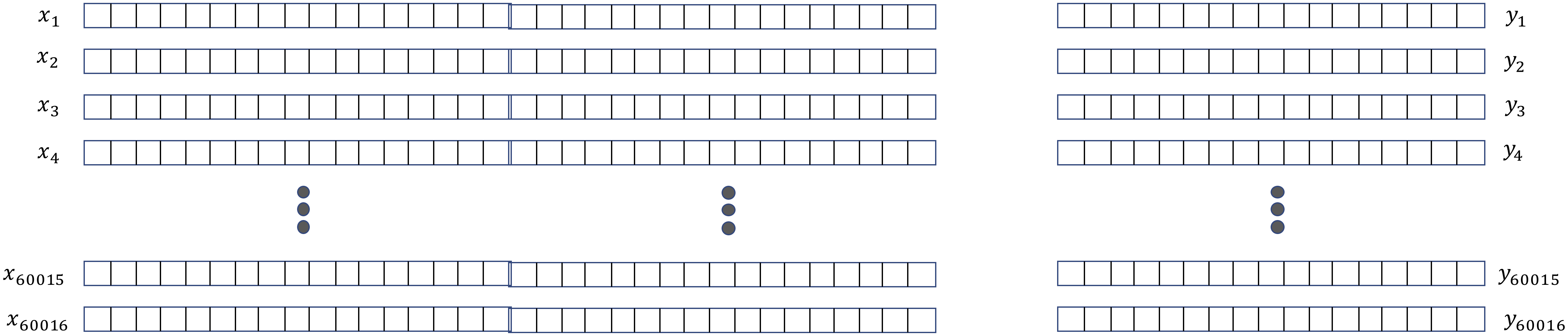
Patient 123ABZ



Training data: 60,016 patients

Input x

Output y

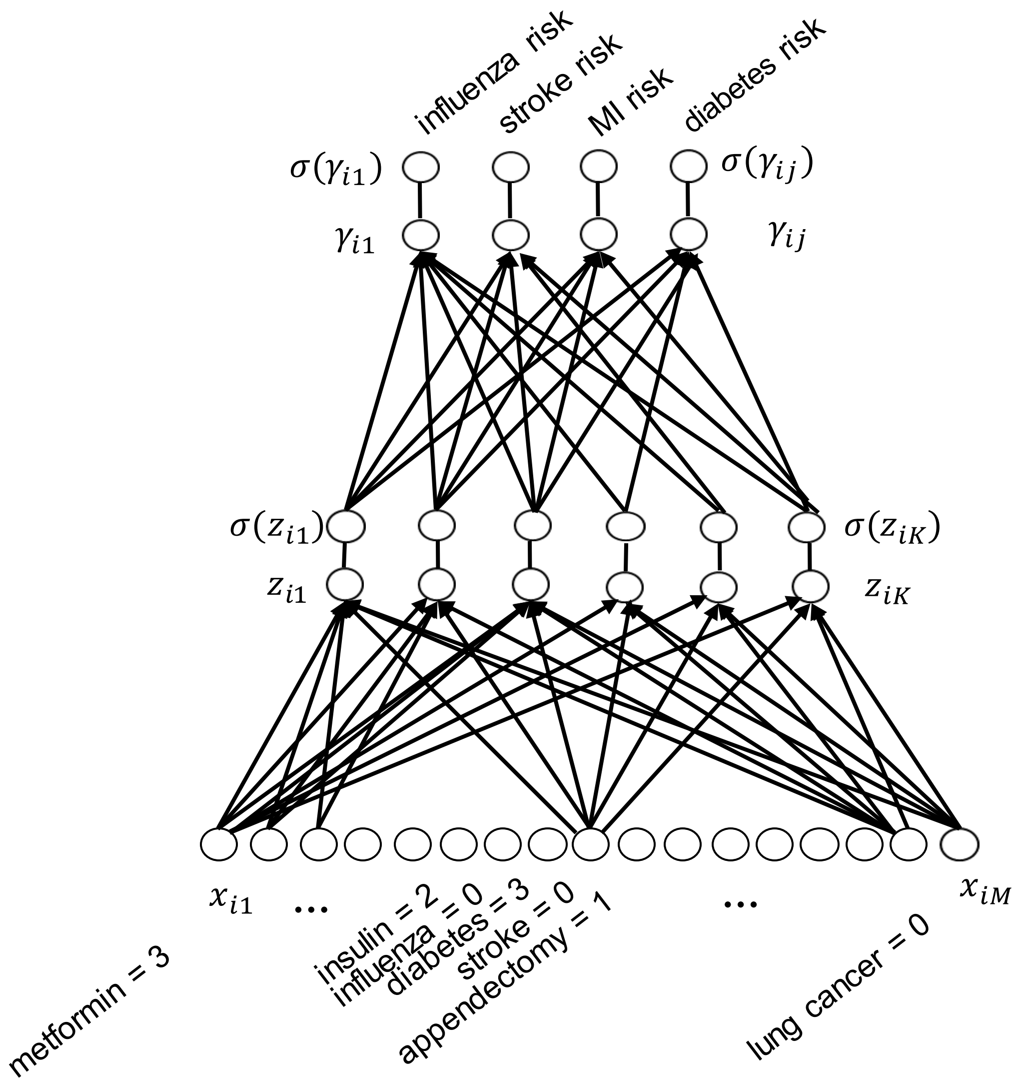


60,016 positive integer vectors (each of length 1,395): counts for each diagnosis, procedure, and medication
Over the past year

60,016 binary vectors (each of length 30): admitted or not for the top 30 most common admission reasons
Over the next 6 months

Modified from figure by David Carlson

Multilayer perceptron model



Output: 30 nodes (risk for top 30 admission reasons)

Hidden layer: 600 nodes

Input: 1,395 nodes (diagnoses, procedures, and medications)

Gradient descent

- **Stochastic gradient descent:** calculates error and updates the model one (randomly-chosen) example at a time
- **Batch gradient descent:** calculates error for all examples, then updates the model after all training examples have been evaluated (one epoch)
- **Mini-batch gradient descent:** splits training dataset into small batches that are used to calculate error and update the model

Advantages of stochastic gradient descent (one example per update)

- Usually **much faster** than batch learning
  - especially on large redundant datasets
  - e.g., 10 examples the same, batch will wastefully calculate gradient on all before updating
- Often results in better solutions
  - Batch discovers the minimum of whatever basin the weights are initially placed
  - Noise in stochastic learning can result in weights jumping into the basin of another possibly better local minimum
- Can be used for tracking changes over time
  - Batch learning: changes over time are undetected, can get bad results by averaging over several rules
  - Learning one example at a time can allow model to track changes in the data

https://en.wikipedia.org/wiki/Hill#/media/File:Rolling_Hills_Paranal.jpg

Efficient BackProp

Yann LeCun[1], Leon Bottou[1], Genevieve B. Orr[2], and Klaus-Robert Müller[3]

Advantages of batch gradient descent (all examples per update)

- Conditions of convergence are well understood
  - In stochastic learning, the noise prevents convergence to the exam minimum
  - Decreasing the learning rate over time can reduce fluctuations around the minimum
- Many acceleration techniques are only applicable to batch learning
  - e.g., second order methods which estimate not only the gradient but also the curvature of the cost surface

https://en.wikipedia.org/wiki/Hill#/media/File:Rolling_Hills_Paranal.jpg

Efficient BackProp

Yann LeCun[1], Leon Bottou[1], Genevieve B. Orr[2], and Klaus-Robert Müller[3]

Advantages of mini-batch gradient descent (~32 examples per update)

- Compromise between batch gradient descent and stochastic gradient descent
- More frequent updates (than batch) can help with convergence
- Injects enough noise to possibly find better solution
- Still relatively fast
- Don’t need to have all training data in memory

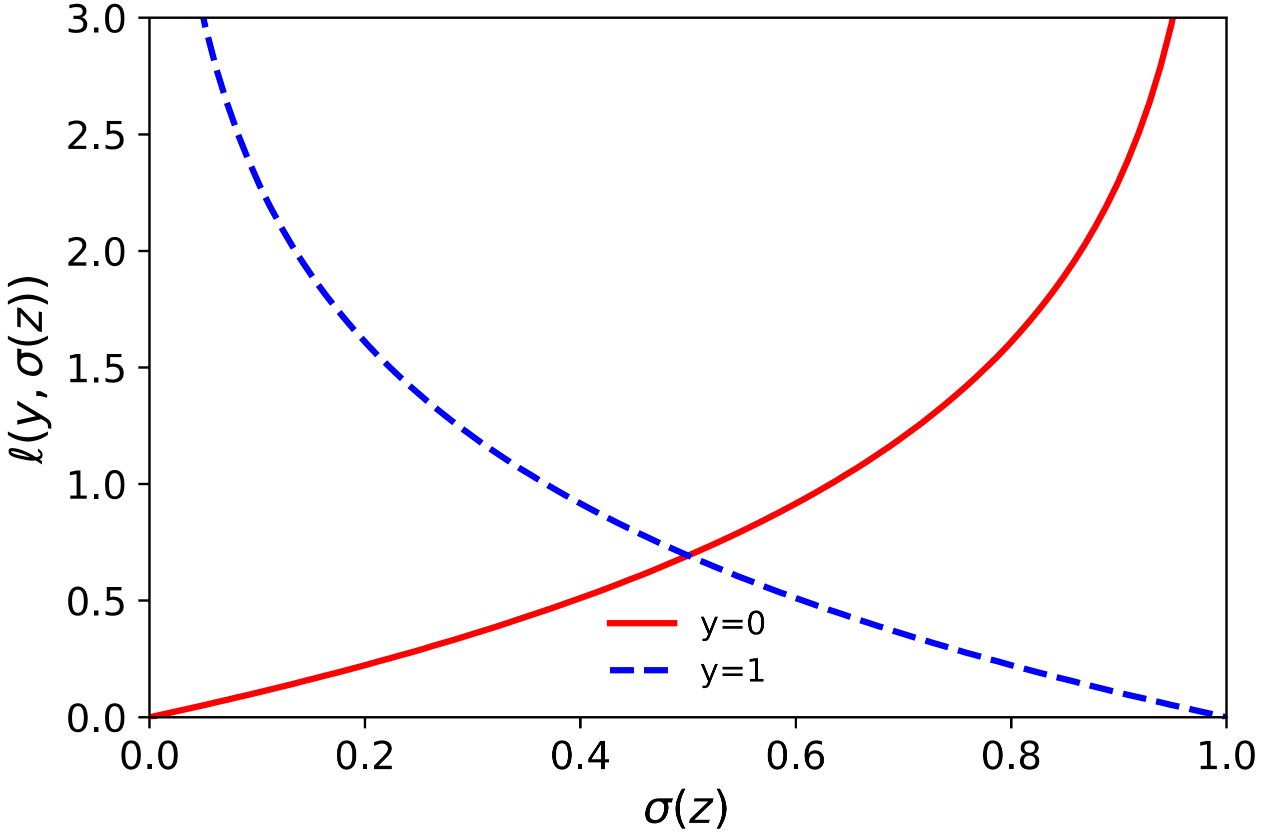
https://en.wikipedia.org/wiki/Hill#/media/File:Rolling_Hills_Paranal.jpg

Mini-batch gradient descent

- Introduces mini-batch size hyperparameter ("batch size")
  - Common choice is 32
  - For admission prediction, 64
- Choice of mini-batch size ("batch size"):
  - 1: stochastic gradient descent
  - Small: faster convergence, noisier training
  - Large: slower convergence, less noisy training
  - n (full training set size): batch gradient descent

Cross-entropy loss function

- The cross-entropy loss is:
  $$\ell(y, \sigma(z)) = -y \log \sigma(z) - (1-y)\log(1-\sigma(z))$$
- 1 = admitted, 0 = not admitted
- If we guess 0.05 and the true answer is 1, we pay a large penalty
- If we guess 0.99 and the true answer is 1, we pay almost no penalty



Predicted Probability of a “one” (admitted)

RESULTS

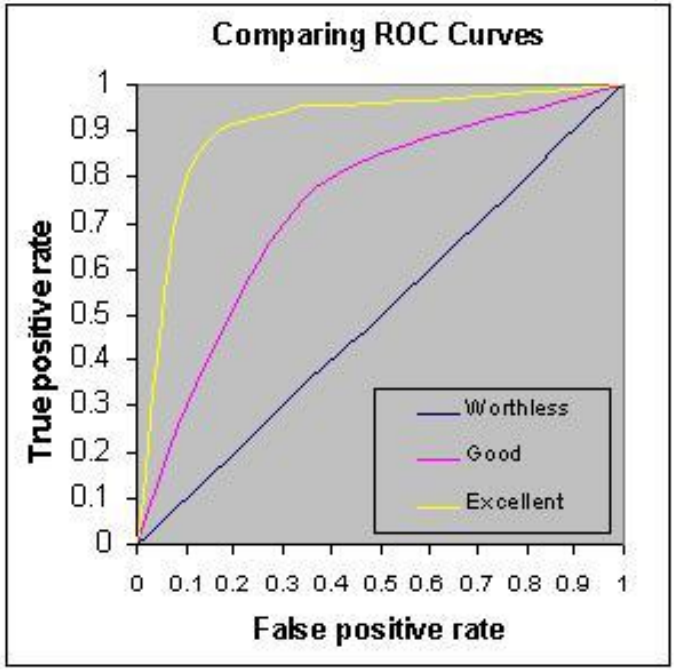
Evaluating performance

- Evaluate on held-out, unseen test set
- Imbalanced data: only 11.5% of patients were admitted
- That means a naïve model that always guesses “no” will get 88.5% accuracy
- What performance metric can we use instead of accuracy?

https://pixabay.com/en/target-dart-aim-success-goal-1414775/

Area under the receiver operating characteristic (AUROC)

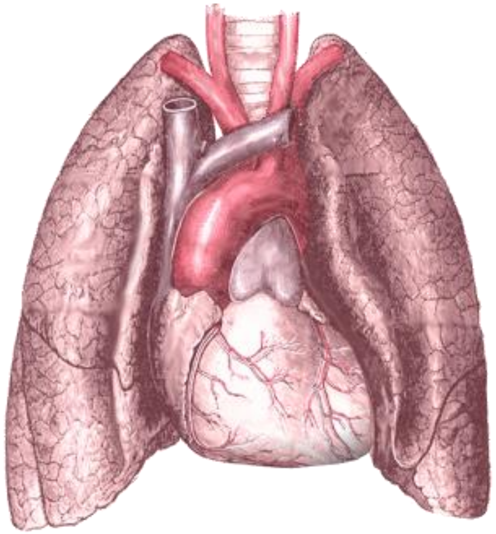
- AUROC is also known as the “c-statistic”
  - Sometimes “AUC” (vague; area under what curve?)



- Random guessing: AUROC = 0.5
- Perfect model: AUROC = 1
- The AUROC is the probability that a randomly chosen positive example will have a higher score than a randomly chosen negative example

http://gim.unmc.edu/dxtests/roc3.htm

AUROC: blood, lungs, heart



Blood

Sickle cell anemia	1.00
Deficiency and other anemia	0.70

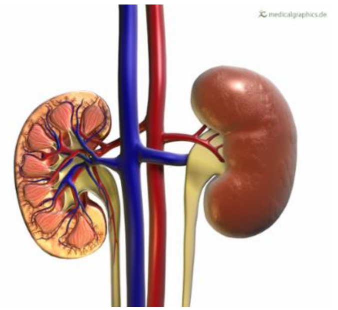
Lungs

Chronic obstructive pulmonary disease and bronchiectasis	0.92
Respiratory failure; insufficiency; arrest (adult)	0.83
Pneumonia (except that caused by tuberculosis or sexually transmitted disease)	0.77
Aspiration pneumonitis; food/vomitus	0.67

Heart

Hypertension with complications and secondary hypertension	0.93
Congestive heart failure; nonhypertensive	0.88
Coronary atherosclerosis and other heart disease	0.80
Cardiac dysrhythmias	0.77
Acute myocardial infarction	0.71
Pulmonary heart disease	0.68

AUROC: GI/GU, ID, & Complications



Gastrointestinal & Genitourinary

Acute and unspecified renal failure	0.81
Gastrointestinal hemorrhage	0.80
Intestinal obstruction without hernia	0.70
Biliary tract disease	0.64
Diverticulosis and diverticulitis	0.60

Infectious Disease & Complications

Complication of device; implant or graft	0.81
Skin and subcutaneous tissue infections	0.81
Urinary tract infections	0.80
Complications of surgical procedures or medical care	0.78
Septicemia (except in labor)	0.72

AUROC: miscellaneous

Diabetes mellitus with complications	0.91
Mood disorders	0.89
Fluid and electrolyte disorders	0.81
Secondary malignancies	0.76
Other nervous system disorders	0.73
Acute cerebrovascular disease	0.67
Fracture of neck of femur (hip)	0.65
Other fractures	0.59

https://pixnio.com/science/medical-science/blood-sugar-meter-device-technology-digital-insulin-syringe-needle

https://en.wikipedia.org/wiki/Hip_fracture

CONCLUSION

Summary

- Careful preparation of health data is critical
- A multilayer perceptron model achieves high performance for predicting admission risk of numerous medical conditions
- Highly predictable: diabetes, mood disorders, COPD, hypertension
- Harder to predict: hip fractures, other fractures, diverticulosis/itis
- Further work on this data set:
  - Convolutional neural networks
  - Generative adversarial networks/DATE (Ash Chapfuwa)
  - Recurrent neural networks (Yan Zhao)

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