Machine Learning in Medicine

Hype and Reality

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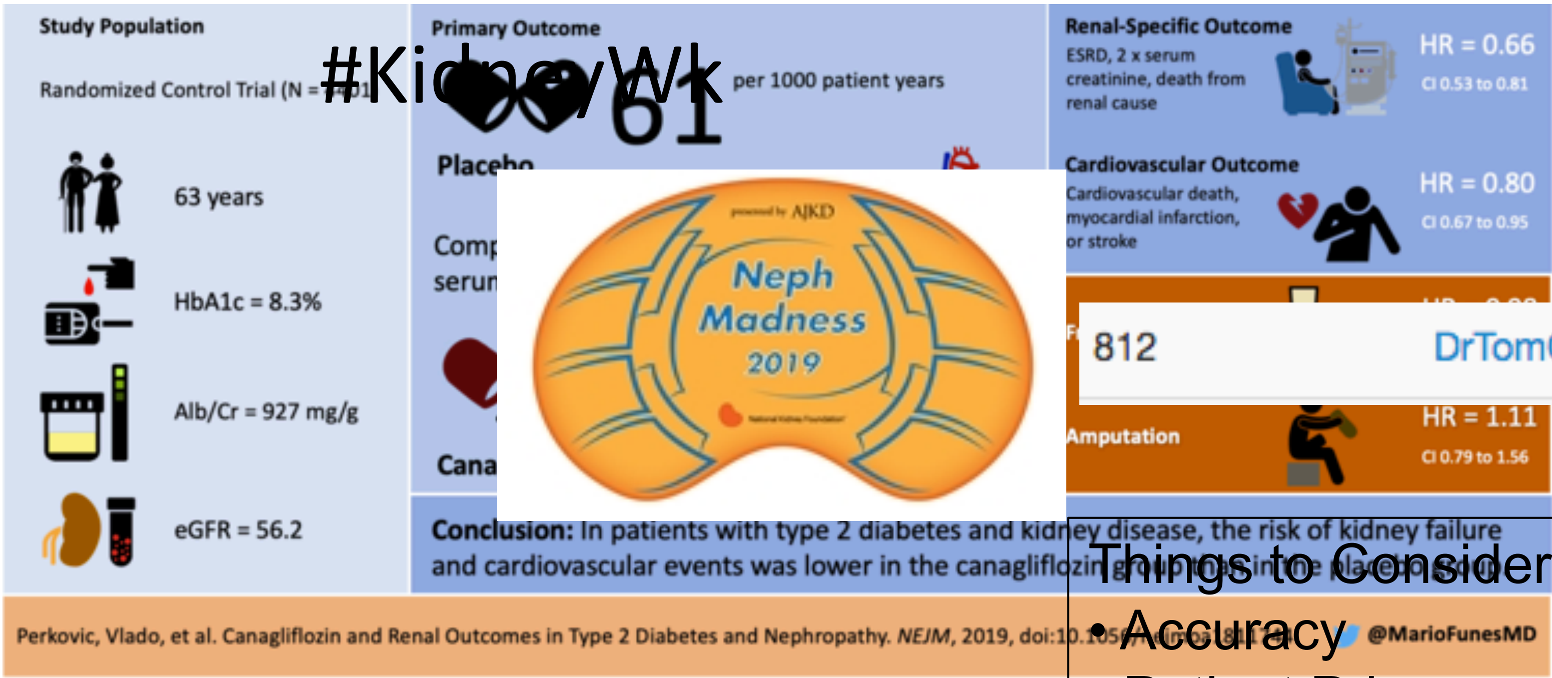
Oxford Kidney Unit 7th May 2019

“If you don’t define yourself online this man will”

Social Media in Nephrology

#NephJC



#KidneyWk

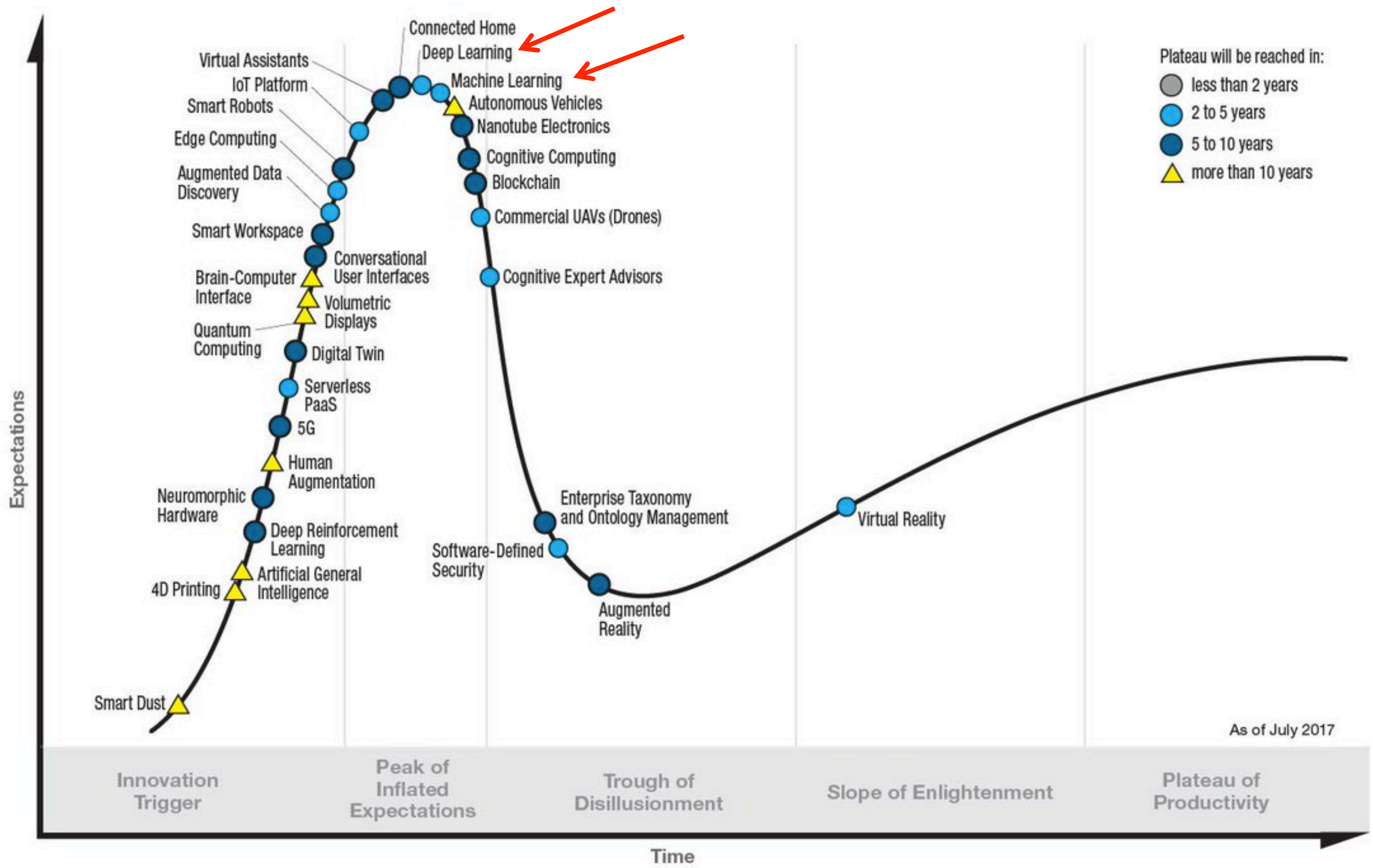
61

812 DrTomCon

Things to Consider
- Accuracy
- Patient Privacy
- Professionalism
- Public Data Trail


NHS
The Topol Review
Preparing the healthcare workforce to deliver the digital future
An independent report on behalf of the Secretary of State for Health and Social Care
February 2019
THE NHS CONSTITUTION
the NHS belongs to us all

The Hype Cycle



Machine Learning

machine learning techniques. Artificial intelligence, which encompasses machine learning, is the scientific discipline that uses computer algorithms to learn from data, to help identify patterns in data, and make predictions. A key feature underpinning the excitement

Collins & Moons, Lancet, 2019

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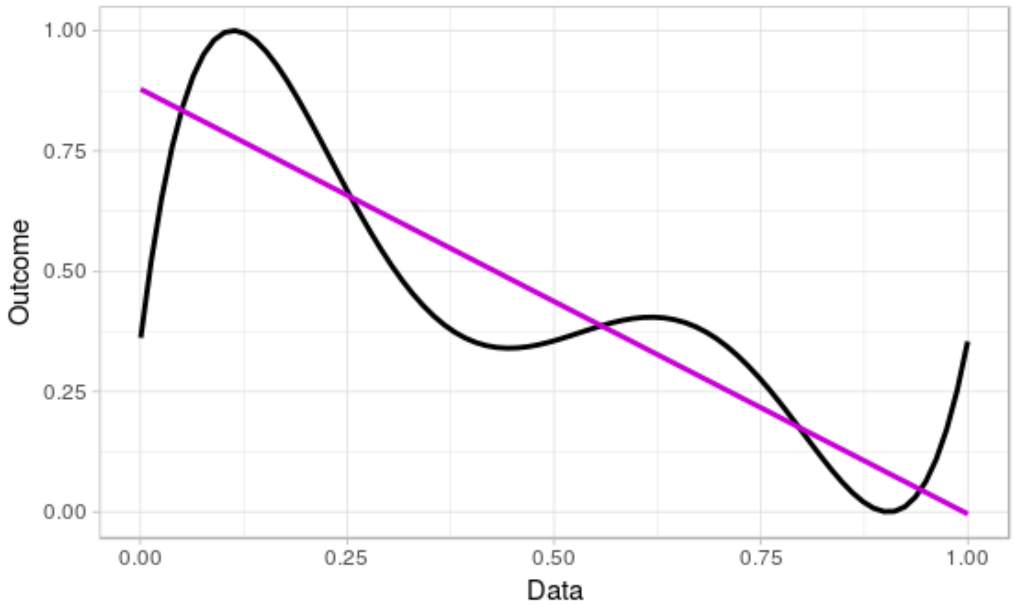
Collins & Moons, Lancet, 2019

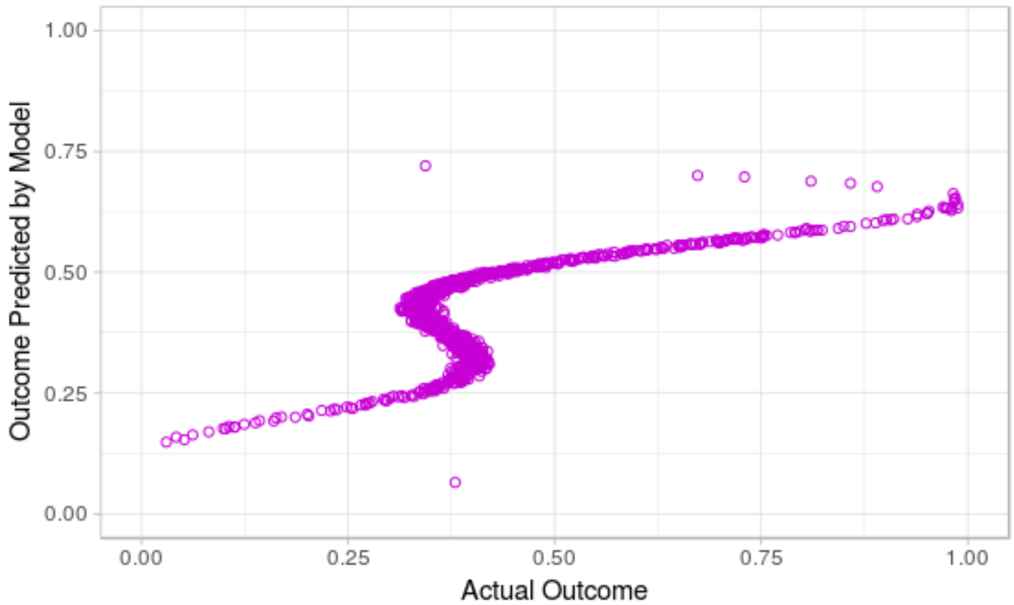
Machine Learning: An *Extremely* Brief Primer

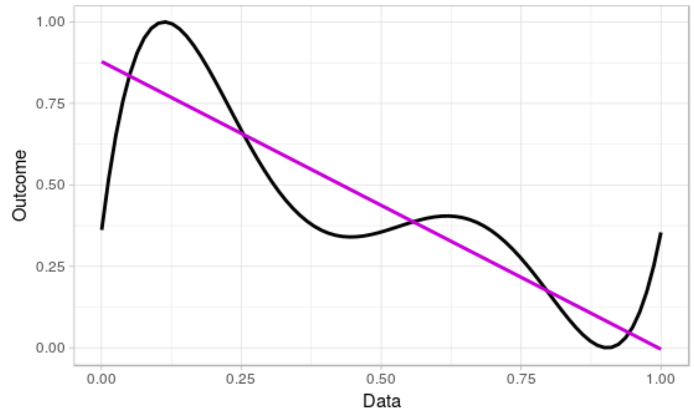


Statistics

- Build a project specific model
- Compute measures of confidence in whether the discovered relationship is true

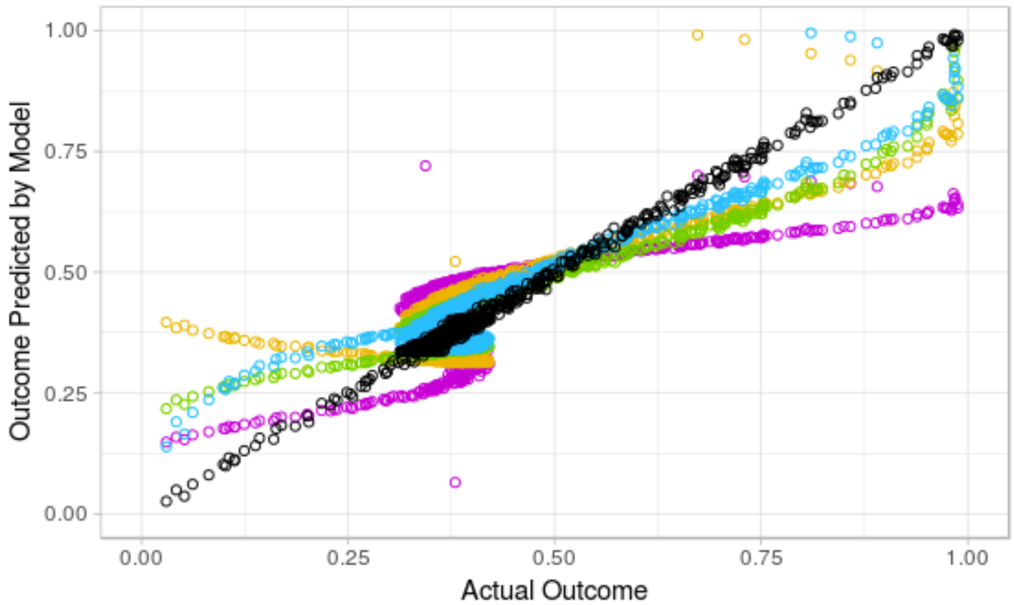
Machine Learning: An *Extremely* Brief Primer

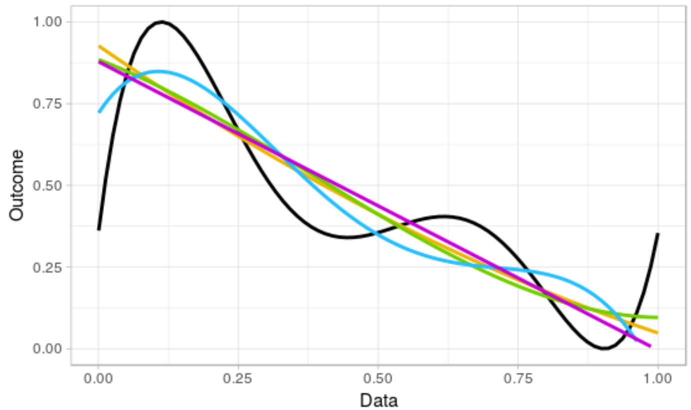




Statistical inference may not be that good at prediction

Machine Learning: An *Extremely* Brief Primer





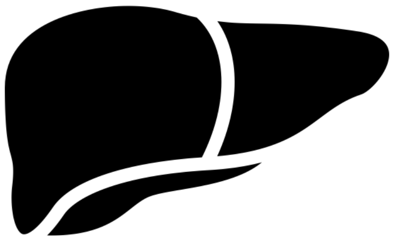
Machine Learning

- Concentrates on prediction
- Lack of explicit models can be useful in routinely collected data but may be hard to interpret

The Promise of Machine Learning

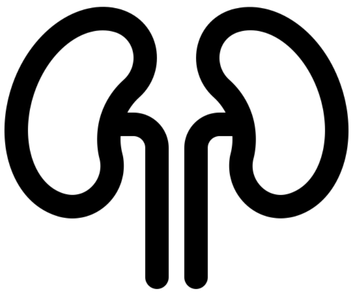
Prediction of Coronary Heart Disease Using Risk Factor Categories

Wilson *et al.*, Circulation, 1998



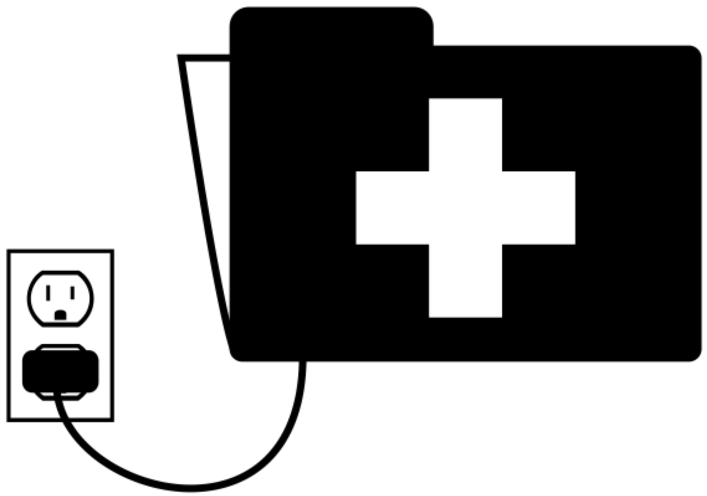
A Model to Predict Poor Survival in Patients Undergoing Transjugular Intrahepatic Portosystemic Shunts

Malinchoc *et al.*, Hepatology, 2000



A Predictive Model for Progression of Chronic Kidney Disease to Kidney Failure

Tangri *et al.*, JAMA, 2011



A New Era in Healthcare

Many Participants

Many Predictors

New Relationships

A Problem

Table 1.4. Nu

Centre
England
B Heart
B QEH
Basldn
Bradfd
Brightn
Bristol
Camb[c]
Carlis
Carsh
Chelms
Colchr
Covnt
Derby
Donc
Dorset
Dudley
Exeter
Glouc
Hull
Ipswi
Kent
L Barts
L Guys
L Kings
L Rfree
L St.G
L West

UK area	CCG/HB	population (2016)	2011 O/E	2012 O/E	2013 O/E	2014 O/E	2015 O/E	O/E	rate pmp	O/E	LCL	UCL	rate pmp[a]	non-White
London	**NHS Barking & Dagenham**	**206,500**	**1.65**	**2.03**	**1.60**	**1.94**	**1.91**	**1.69**	**140**	**1.80**	**1.56**	**2.09**	**141**	**41.7**
	NHS Barnet	**386,100**	**1.41**	**1.46**	**1.23**	**1.29**	**1.41**	**1.27**	**130**	**1.34**	**1.20**	**1.50**	**129**	**35.9**
	NHS Camden	246,200	1.11	1.06	1.32	1.16	1.28	0.99	93	1.15	0.98	1.35	103	33.7
	NHS City and Hackney	**282,900**	**1.68**	**2.02**	**1.83**	**2.11**	**1.13**	**1.84**	**148**	**1.76**	**1.55**	**2.01**	**134**	**44.6**
	NHS Enfield	**331,400**	**1.98**	**1.59**	**1.58**	**1.53**	**1.55**	**1.59**	**157**	**1.63**	**1.46**	**1.83**	**151**	**39.0**
	NHS Haringey	**278,500**	**1.69**	**2.27**	**2.21**	**1.64**	**1.56**	**1.94**	**172**	**1.88**	**1.66**	**2.12**	**157**	**39.5**
	NHS Havering	252,800	1.20	1.04	0.83	0.92	1.08	0.78	91	0.97	0.83	1.13	106	12.3
	NHS Islington	**232,900**	**1.53**	**2.05**	**1.44**	**1.11**	**1.60**	**1.06**	**90**	**1.46**	**1.25**	**1.70**	**117**	**31.8**
	NHS Newham	**341,000**	**2.12**	**1.86**	**2.14**	**2.24**	**2.31**	**2.44**	**191**	**2.19**	**1.97**	**2.44**	**161**	**71.0**
	NHS Redbridge	**299,200**	**1.38**	**2.15**	**1.98**	**1.45**	**1.45**	**1.73**	**167**	**1.68**	**1.50**	**1.90**	**153**	**57.5**
	NHS Tower Hamlets	**304,900**	**1.61**	**1.82**	**2.02**	**2.26**	**2.33**	**1.84**	**134**	**1.99**	**1.76**	**2.25**	**137**	**54.8**
	NHS Waltham Forest	**275,800**	**1.81**	**1.26**	**1.62**	**2.08**	**1.70**	**1.51**	**138**	**1.66**	**1.47**	**1.89**	**143**	**47.8**
	NHS Brent	**328,300**	**2.08**	**2.43**	**1.95**	**2.51**	**2.23**	**2.02**	**195**	**2.20**	**1.99**	**2.43**	**200**	**63.7**
	NHS Central London (Westminster)	178,400	1.29	1.17	1.37	1.08	0.97	1.09	112	1.16	0.97	1.38	112	36.2
	NHS Ealing	**343,200**	**1.91**	**2.26**	**1.68**	**1.78**	**2.25**	**1.77**	**175**	**1.94**	**1.76**	**2.15**	**181**	**51.0**
	NHS Hammersmith and Fulham	**179,700**	**1.43**	**1.49**	**0.99**	**1.44**	**1.13**	**1.80**	**167**	**1.38**	**1.16**	**1.64**	**121**	**31.9**
	NHS Harrow	**248,800**	**2.23**	**1.59**	**1.06**	**1.54**	**1.43**	**1.70**	**185**	**1.59**	**1.40**	**1.80**	**162**	**57.8**
	NHS Hillingdon	**302,500**	**1.46**	**1.50**	**1.42**	**1.00**	**1.08**	**1.16**	**116**	**1.26**	**1.10**	**1.44**	**118**	**39.4**
	NHS Hounslow	**271,100**	**1.83**	**1.73**	**2.02**	**1.28**	**1.29**	**1.65**	**159**	**1.62**	**1.43**	**1.84**	**147**	**48.6**
	NHS West London (Kensington and Chelsea, Queen's Park and Paddington)	226,000	1.20	0.91	0.98	1.50	0.67	1.23	128	1.08	0.92	1.27	106	33.4
	NHS Bexley	**244,800**	**1.17**	**0.87**	**1.01**	**1.11**	**1.24**	**1.65**	**184**	**1.19**	**1.03**	**1.37**	**124**	**18.1**
	NHS Bromley	326,900	0.69	0.72	0.85	0.99	1.50	0.82	95	0.94	0.82	1.08	102	15.7
	NHS Croydon	**382,300**	**1.26**	**2.00**	**1.95**	**1.79**	**1.93**	**1.64**	**167**	**1.76**	**1.60**	**1.95**	**169**	**44.9**
	NHS Greenwich	**279,800**	**1.03**	**1.15**	**2.38**	**1.23**	**1.68**	**1.62**	**147**	**1.52**	**1.33**	**1.74**	**130**	**37.5**
	NHS Kingston	176,100	0.96	1.08	1.11	1.11	0.78	0.96	97	1.00	0.82	1.21	95	25.5
	NHS Lambeth	**327,900**	**1.76**	**1.68**	**1.39**	**1.87**	**1.95**	**1.38**	**116**	**1.67**	**1.48**	**1.89**	**132**	**42.9**
	NHS Lewisham	**301,900**	**1.78**	**1.85**	**1.47**	**1.52**	**1.48**	**1.31**	**116**	**1.56**	**1.37**	**1.77**	**130**	**46.5**
	NHS Merton	**205,000**	**1.57**	**1.78**	**1.30**	**1.44**	**1.61**	**1.73**	**171**	**1.57**	**1.36**	**1.82**	**146**	**35.1**
	NHS Richmond	*195,800*	*0.69*	*0.79*	*0.98*	*0.78*	*0.60*	*0.65*	*71*	*0.74*	*0.61*	*0.92*	*77*	*14.0*

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of

Approaching East London's CKD Problem

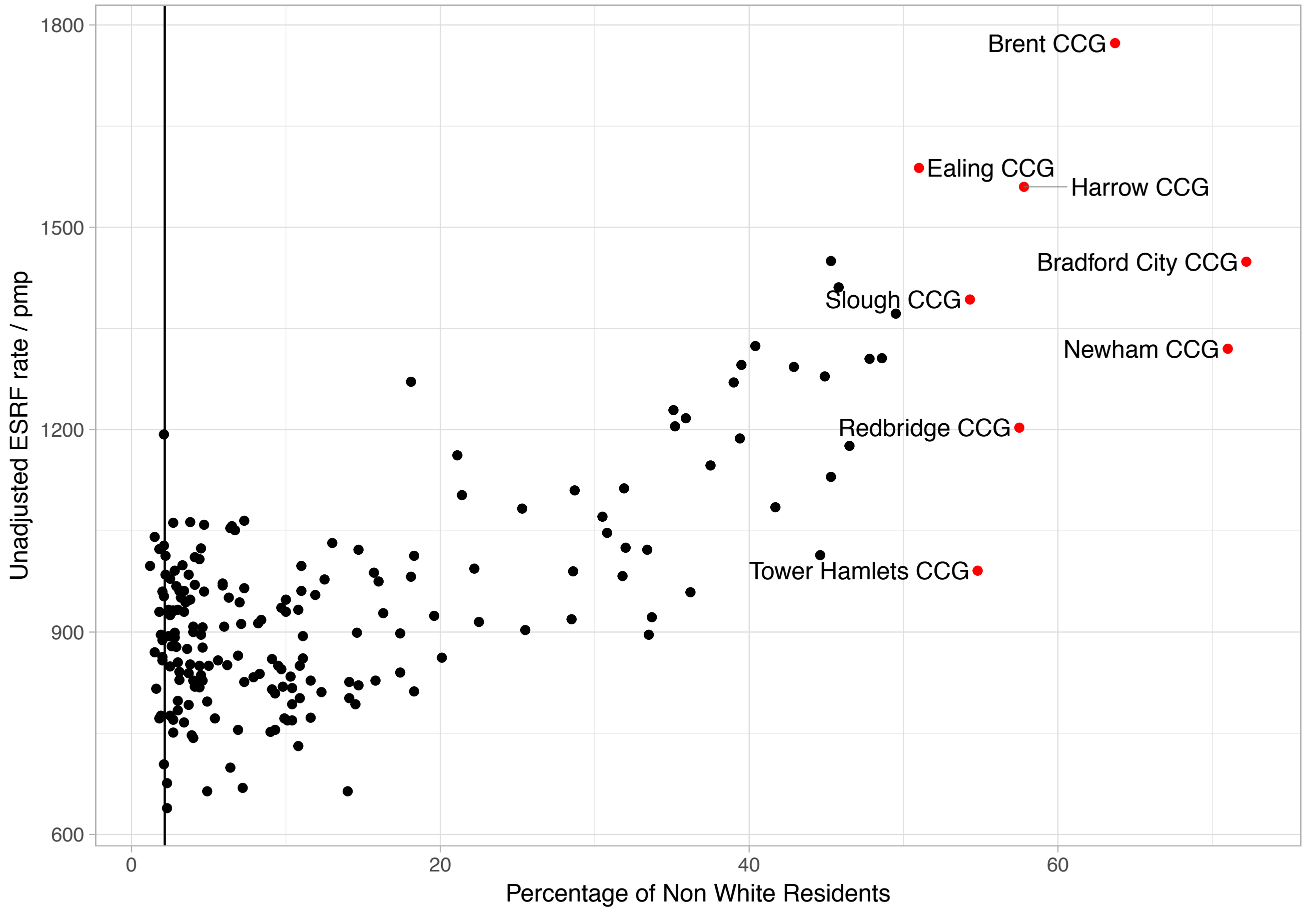
Predicting the risk of Chronic Kidney Disease in Men and Women in England and Wales: prospective derivation and external validation of the QKidney® Scores

Hippisley-Cox & Coupland, BMC Family Practice, 2010

Predicting the risk of chronic kidney disease in the UK:

an evaluation of QKidney® scores using a primary care database

Collins & Altman, BJGP, 2012



Approaching East London's CKD Problem

Will ML Improve on Standard Statistical Methods?

Modern modelling techniques are data hungry: a simulation study for predicting dichotomous endpoints

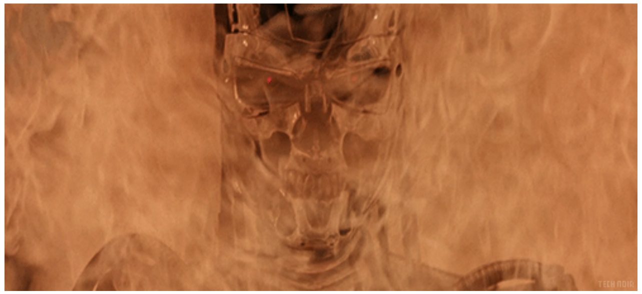
Van der Ploeg *et al.*, BMC MRM, 2014

	Cohort		
	HNSCC	**TBI**	**CHIP**
Outcome	5 year survival	6 months mortality	Intracranial findings
Type	dichotomous	dichotomous	dichotomous
Event/total	601/1282 (46.9%)	386/1731 (22.3%)	243/3181 (7.6%)
Predictors	2 dichotomous	4 dichotomous	9 dichotomous
	4 categorial	1 categorial	1 categorial
	1 continuous	4 continuous	2 continuous

$$p(x) = \frac{1}{1 + e^{-(\beta_0 + \beta_{1x})}}$$

Logistic Regression

Machine Learning



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Predictors	2 dichotomous	4 dichotomous	9 dichotomous
	4 categorial	1 categorial	1 categorial
	1 continuous	4 continuous	2 continuous

DATA HUNGER
Machine Learning techniques **require >10x as many outcome events per input variable** to match or improve upon logistic regression

Predicting the risk of chronic kidney disease in the UK:

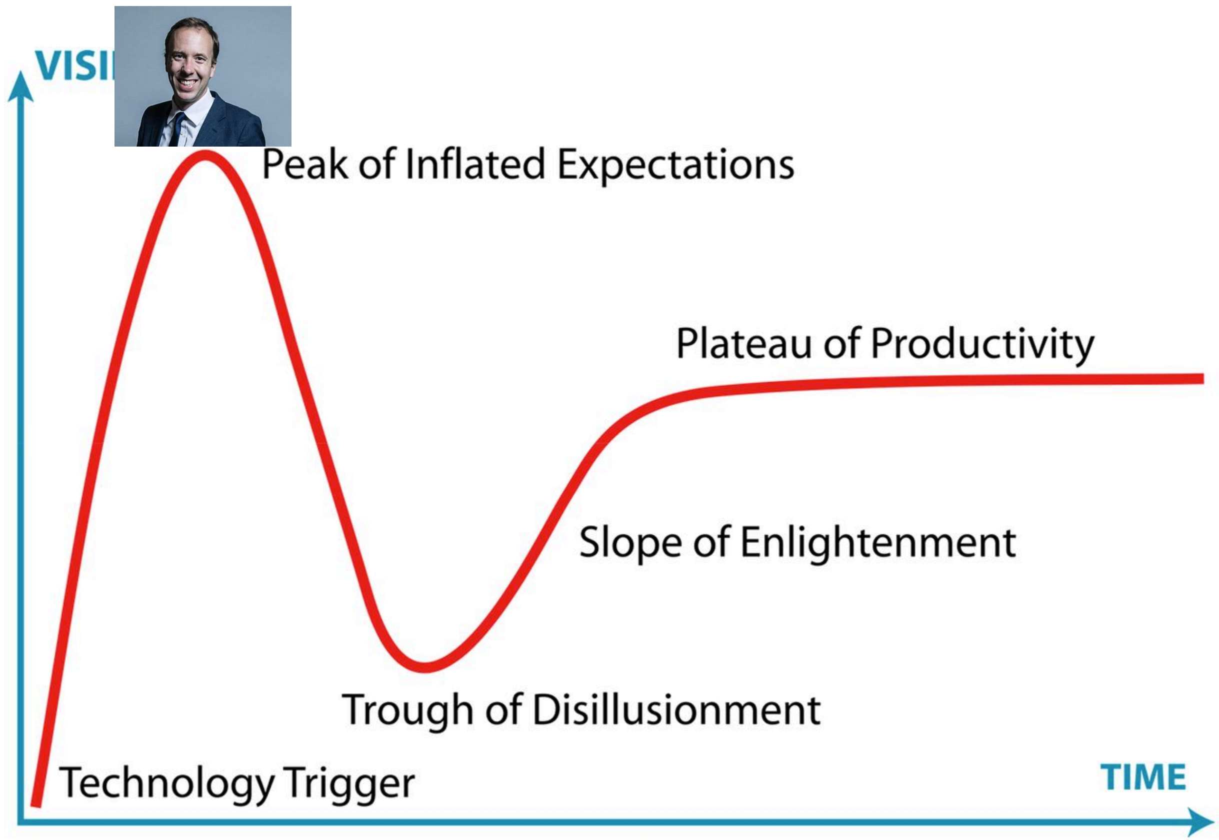
an evaluation of QKidney® scores using a primary care database

Collins & Altman, BJGP, 2012

Mod to Severe CKD	2.7%
ESRF	0.17%

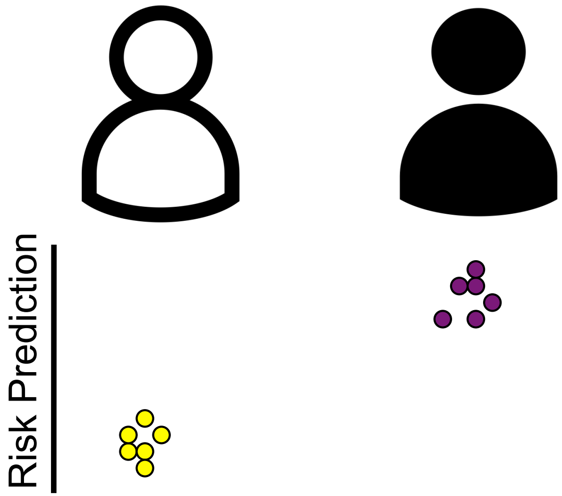
What Is Sustaining The Hype?

“A rusty nail placed near a faithful compass, will sway it from the truth, and wreck the Argosy.”



What Is Sustaining The Hype?

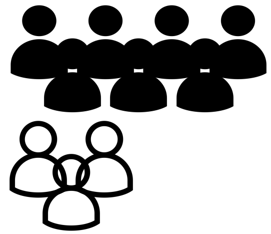
Discrimination



Ability to differentiate between "outcomes" & "non-outcomes"

Calibration

70% Risk Prediction



How closely prediction of outcomes matches actual outcomes

A systematic review shows no performance benefit of machine learning over logistic regression for clinical prediction models

Christodoulou *et al.*, J Clin Epi, 2019

Discrimination	Biased assessment
Calibration	Not assessed 79%

What Is Sustaining The Hype?

Specialty	Images	Publication
Radiology/Neurology	CT head, acute neuro events	Titano, Nature Medicine, 2018
	CT head for brain hemorrhage	Arbabshirani, NPJ (Nature) Digital Medicine, 2018
Pathology	Breast cancer	Bejnordi, JAMA, 2017
	Brain tumors (+ methylation)	Capper, Nature, 2018
Dermatology	Skin cancers	Esteva, Nature, 2017
	Melanoma	Haenssle, Annals of Oncology, 2018
	Skin lesions	Han, Journal of Investigative Dermatology
Ophthalmology	Diabetic retinopathy	Gulshan, JAMA, 2016
	Diabetic retinopathy	Abramoff, NPJ (Nature) Digital Medicine, 2018
	Congenital cataracts	Long, Nature Biomedical Engineering, 2017
	Retinal diseases (OCT)	De Fauw, Nature Medicine, 2018
	Macular degeneration	Burlina, JAMA Ophthalmology, 2018
	Retinopathy of Prematurity	Brown, JAMA Ophthalmology, 2018
	AMD and diabetic retinopathy	Kermany, Cell, 2018
Gastroenterology	Polyps at colonoscopy	Mori et al, Annals Internal Medicine, 2018
Cardiology	Echocardiography	Madani, NPJ (Nature) Digital Medicine, 2018

An Eric Topol tweet

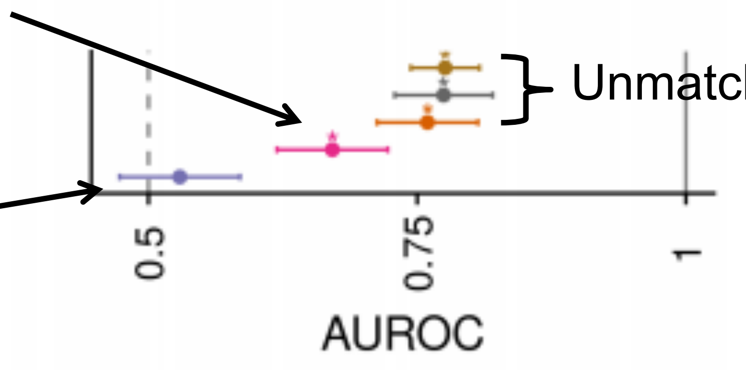
What Is Sustaining The Hype?

Deep Learning Predicts Hip Fracture using Confounding Patient and Healthcare Variables

Badgeley *et al.*, arxiv, 2018

Matched on pt features

Matched on pt features & process measures

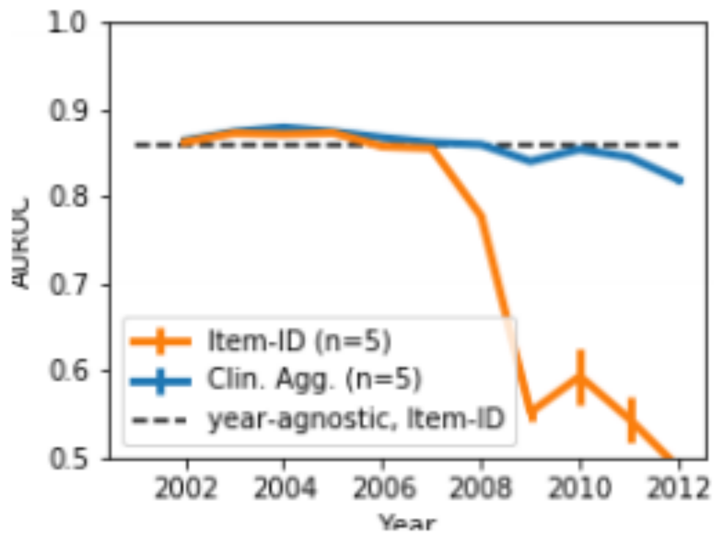


Unmatched

Rethinking clinical prediction: Why machine learning must consider year of care and feature aggregation

Nestor *et al.*, arxiv, 2018

EHR upgrade in 2007…



Summary

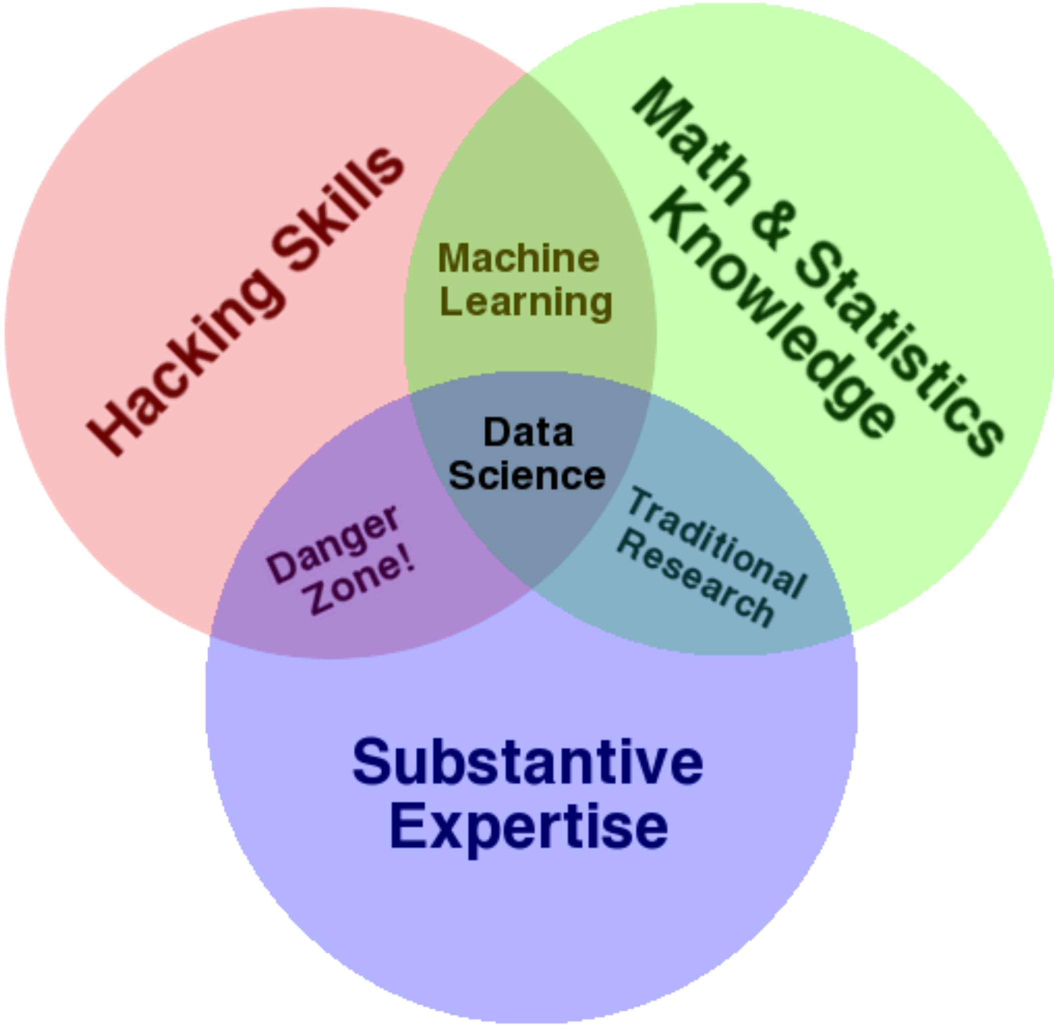
AI/ML approaches probably will change how we do highly replicable things

Advantages of ML over classical statistics probably won't be realised until we address data accessibility and sharing

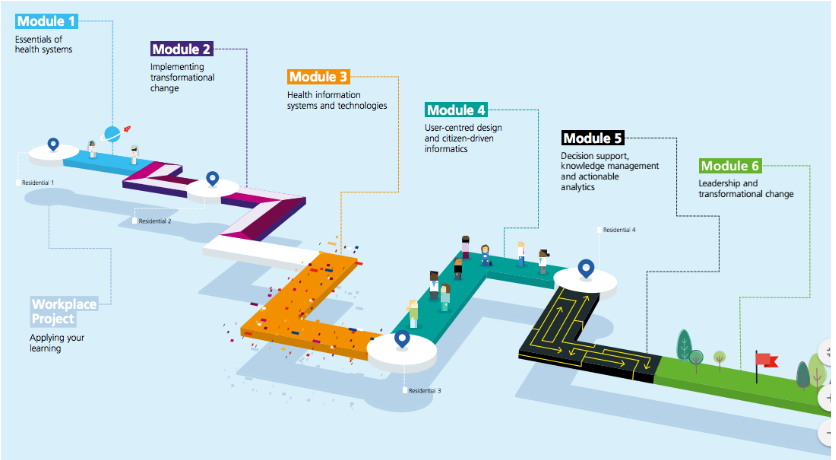
Big data usage in healthcare requires statistical rigour & methodological honesty

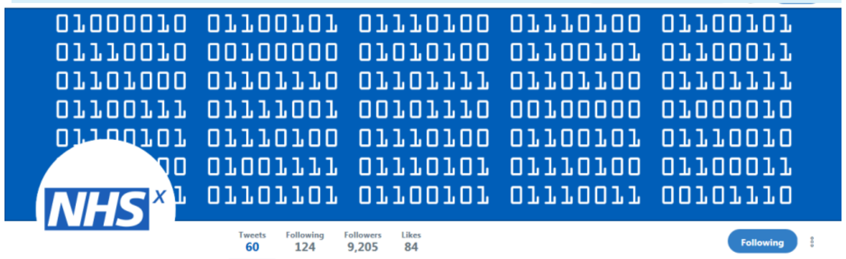
"A medical device with a plausible sales pitch is a very hard thing to counter with mere evidence"
Richard Lehman June 2018

What Should the NHS do?



What is the NHS doing?





DHSC Media Centre
@DHSCmedia
Following

The #Healthtech Advisory Board met for the first time today to guide Health Secretary @MattHancock on how to harness the potential of technology to revolutionise health and social care
gov.uk/government/new ...

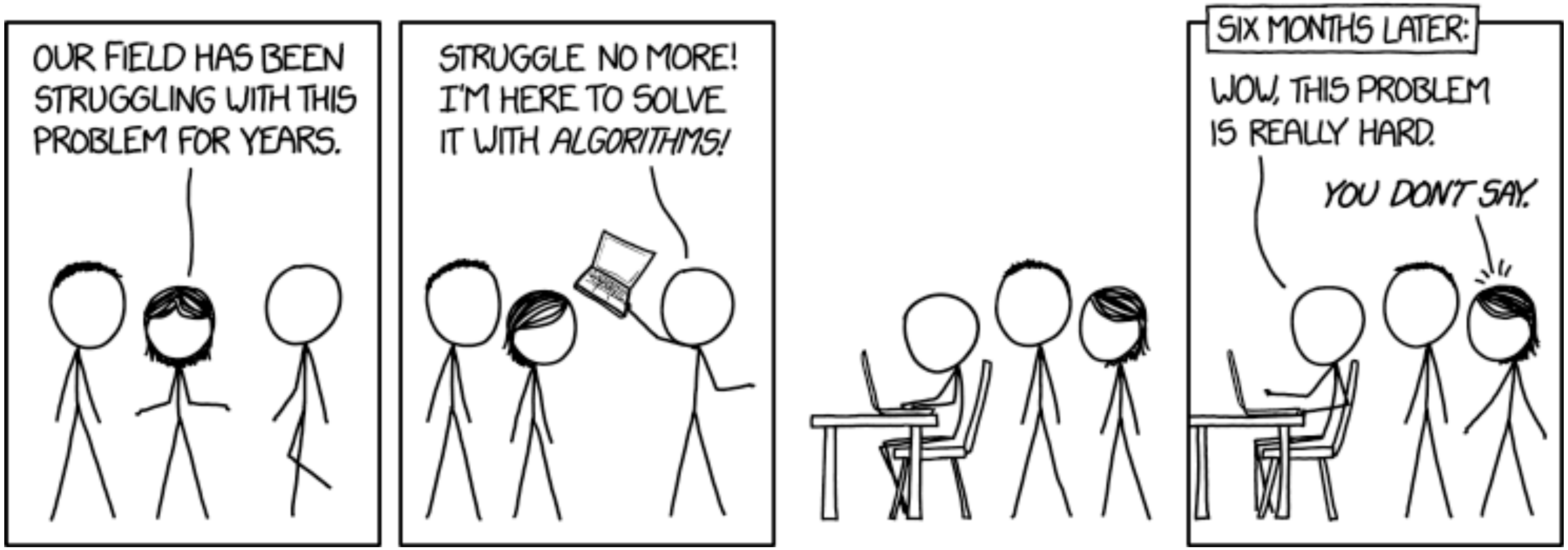
Acknowledgments

- These slides can be found on my github page:
  - toates19/ML-in-Medicine

- The idea for the plots illustrating what machine learning does are from Bzdok *et al.*, Nat Methods, 2017. The R code for these plots is on my github page

- The examples of non-ML predictive models are from Collins & Moons, Lancet, 2019

- The examples showing potential issues with ML were taken from a talk by Samuel Finlayson which is on his github page (sgfin)



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