



Digital Health for better models of care

Richard Hobbs, Director Oxford Institute of Digital Health, Pro-Vice-Chancellor (WP), Mercian Professor of Primary Care, University of Oxford

Question: Do you think that AI and digital health will

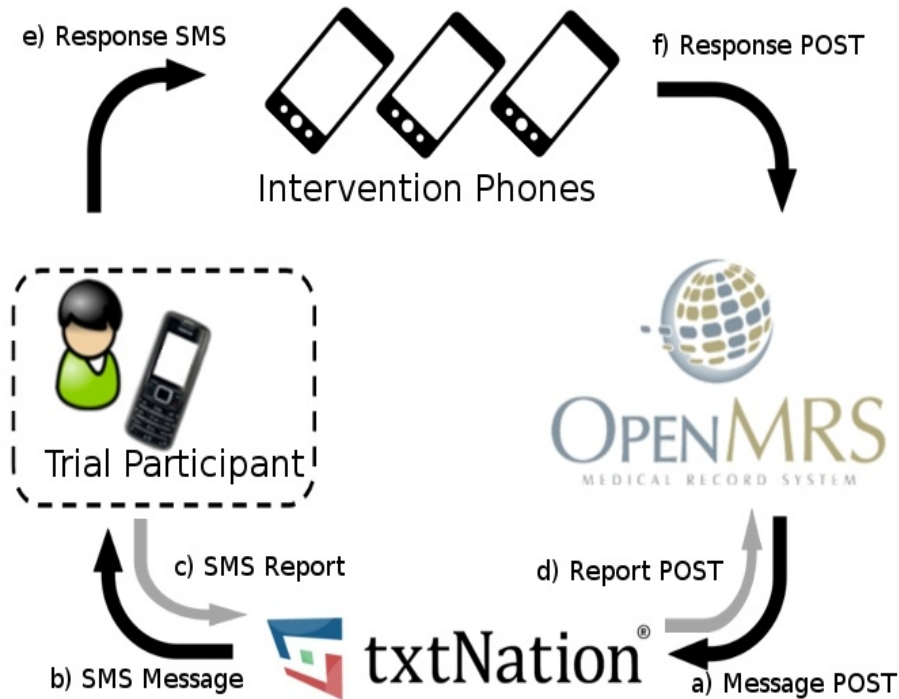
- 1) Substitute and replace some healthcare roles?
- 2) Have no major effect on healthcare?
- 3) Improve the quality of care?
- 4) Increase health-seeking behaviour by patients?

1. Digitally enabled clinical pathways that work:

Integrated health systems

Personalised health solutions

Automated delivery of SMS text-messaging for improved medication uptake in Soweto



* StAR

Patient self-management of hypertension: validated monitors and simple treatment algorithm

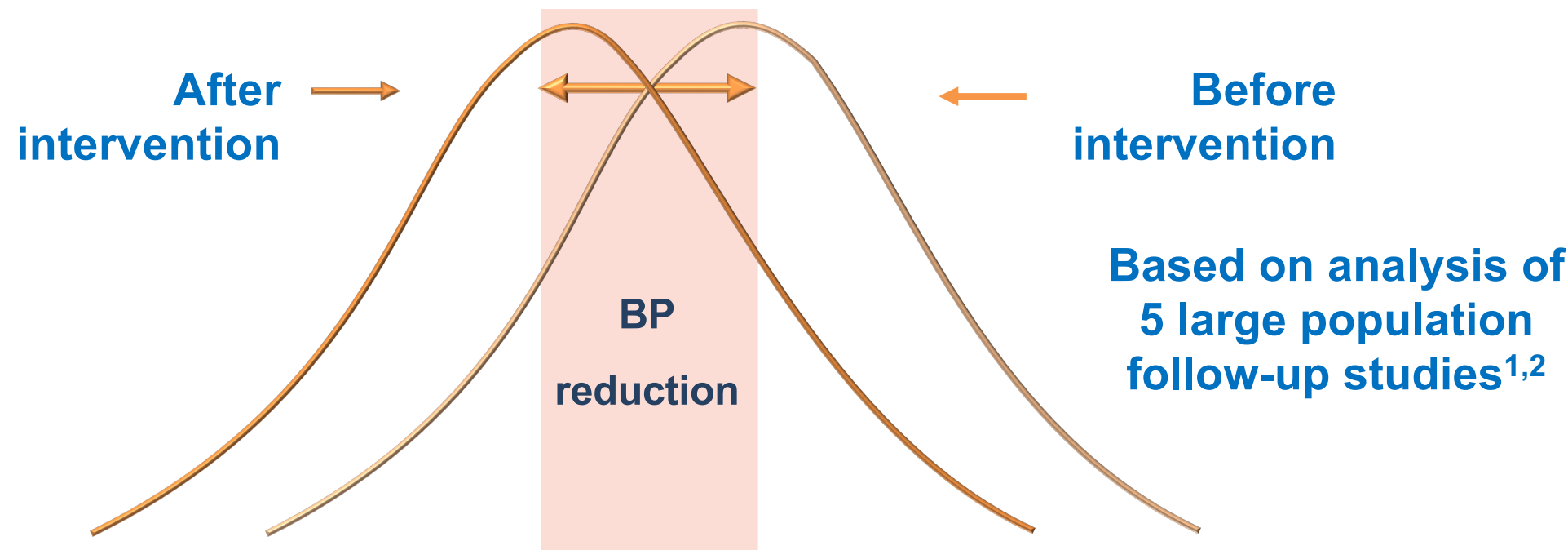
	Mean blood pressure (mm Hg)			Effect size (mm Hg)	
	Baseline	6 months	12 months	Baseline to 6 months	Baseline to 12 months
Systolic blood pressure; unadjusted					
Intervention	152.1 (150.6 to 153.6)	139.0 (137.0 to 141.0)	134.9 (132.6 to 137.1)	3.7 (0.6 to 6.8)	5.5 (2.2 to 8.8)
Control	151.8 (150.3 to 153.3)	142.4 (140.2 to 144.6)	140.1 (138.0 to 142.2)	..	..
Systolic blood pressure; adjusted*					
Intervention	151.9 (150.8 to 153.1)	138.8 (136.6 to 141.0)	134.7 (132.3 to 137.0)	3.7 (0.8 to 6.6)	5.4 (2.4 to 8.5)
Control	152.0 (150.9 to 153.2)	142.6 (140.5 to 144.8)	140.3 (138.0 to 142.6)	..	..



Level	Blood Pressure	Action
HIGH	SYS 201 or more OR DIA 101 or more	Your BP is too high. Make an appointment within 24 hours to see your GP or nurse. Record a RED reading
RAISED may need to alter medication	SYS 131-200 OR DIA 86-100	Your BP is raised. Record an AMBER reading If FOUR or more AMBER readings in one week on 2 consecutive months then look at your medication change instructions.
NORMAL	SYS 101-130 AND DIA 85 or less	Your BP is normal. This is fine provided that you have no side effects. Record a GREEN reading
LOW	SYS 100 or less	Your blood pressure is too low Make appointment to see your GP Record a RED reading

TASMINH2

Small population decreases in blood pressure reduce the risk of cardiovascular mortality



SBP reduction	Reduction in mortality (%)		
	CHD	Stroke	Total
2 mmHg	4	6	3
3 mmHg	5	8	4
5 mmHg	9	14	7

2. Healthcare Big Data analyses:

Based on electronic health records (EHR) for healthcare encounters

1. Use for health service intelligence

- Acute disease surveillance
- Population disease burden data for policy makers
- System, physician, patient behaviour change for care models

2. Potential for AI applications

- Pandemic tracking for Public Health
- Uncoded data – future opportunities

Data collected in primary care



GP Contract Diabetes.

Review Type
Diabetic annual review 15/11/2006

Administration
Last entry: Not found

Examinations/Investigations

Systolic BP	mm Hg	120 mm Hg	30/10/2007
Diastolic BP	mm Hg	56 mm Hg	30/10/2007
Standing Systolic Bp	mm Hg	112 mm Hg	30/05/2007
Standing Diastolic Bp	mm Hg	58 mm Hg	30/05/2007
Height	cm	178 cm	30/10/2007
Weight	Kg	96.4 Kg	30/10/2007
BMI		30.43	30/10/2007
Alcohol intake	units/week	0 units/week	30/10/2007
Haemoglobin A1c level	%	6.3%	10/10/2007
*Serum creatinine	umol/L	104 umol/L	17/10/2007
*Serum cholesterol	mmol/L	3.9 mmol/L	10/10/2007
HDL cholesterol level	mmol/L	0.9 mmol/L	10/10/2007
LDL cholesterol level	mmol/L	2.7 mmol/L	10/10/2007
Serum triglycerides	mmol/L	0.9 mmol/L	10/10/2007
Plasma glucose level	mmol/L	9.4 mmol/L	16/04/2004
Plasma fasting glucose level	mmol/L		Plasma fasting glucose level not found

Medication review
Medication review done 06/03/

History

Diabetic monitoring
Last entry: Diabetic on insulin, 31/10/2006

Self monitoring
Self monitoring of blood glucose, 31/10/2007

Urine protein
Urine protein test negative, 16/02/2007

*Urine microalbumin
Urine albumin creatinine ratio, 31/10/2006

*HbA1C
Hb. A1C - diabetic control, 7.7 %, 02/11/2006

Pulse
O/E - pulse rate, 71 beats/minute, 30/10/2007

Appetite normal 06/03/2007
O/E - oedema of ankles 06/03/2007

Impotence 13/01/2004
Last hypo. attack 13/01/2004

Refer to dietician
Has seen dietician - diabetes 23/0

Health ed - alcohol 30/10/2007
Health ed - diet 30/10/2007
Health ed - exercise 30/10/2007

Follow up
Diabetic Annual Review

Smoking status
*Diabetic foot check
*Diabetic eye check
*Diabetic - recorded diagnostic reviews
Pneumococcal vaccination 10/11/1995
Influenza vaccination 29/10/2007

Injection sites
Albumin / creatinine ratio

Depression screening using questions
Depression Template

OK Cancel Previous Data

Wherever possible values are colour coded. Values in black cant be colour coded or in blue are not date dependent.
Values in GREEN (< 12 months old) Values in RED (> 12 months old) need updating

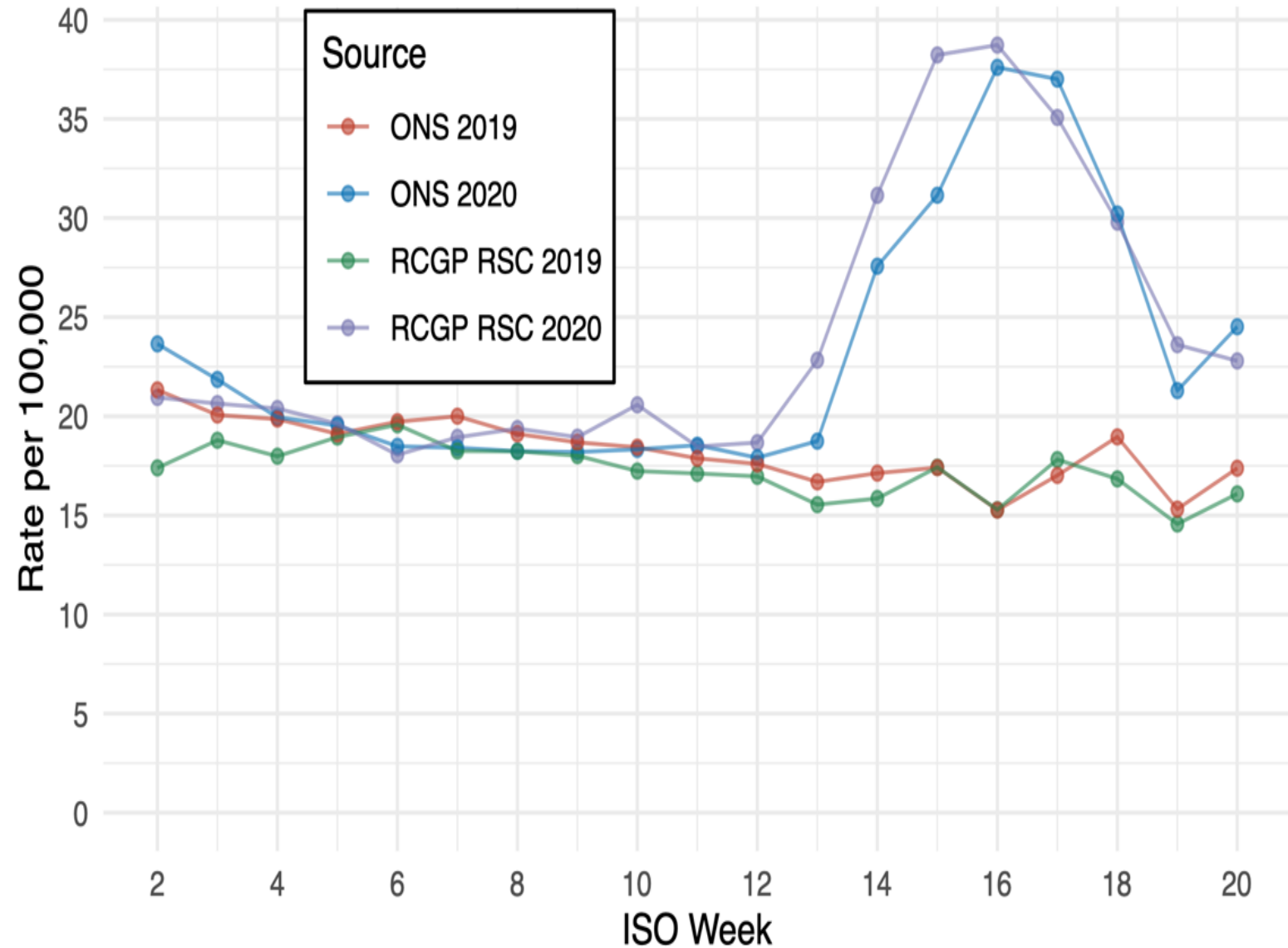
- Demographic, DOB, ethnicity, etc
- Health service activity
- Workload, screening, immunisation, preventative care
- Prescribing
- Laboratory data
- Referrals & admissions
- Waiting times
- NHS spending
- Mortality – cause of death
- Place of death

Other sources of linkable information

- HES – England only
 - admissions; outpatient appointments; A&E
- ONS Mortality data
 - causes
- Deprivation information from UK Census 2001/2011
 - Townsend score; IMD
- Cancer Registry UK
- MINAP - Myocardial Ischaemia National Audit Project

UK mortality with COVID-19, ORCHID & Oxford-RCGP RSC

- Sentinel PC faster than ONS
- Mortality related to
 - Male gender
 - Increasing age
 - Black ethnicity
 - Deprivation
 - Population density
 - Household size
 - Chronic disease



RWE Pharmacovigilance: Main risks of COVID19 vaccination

thebmj Visual Abstract



Covid-19 and adverse events after vaccination and SARS-CoV-2 infection

Summary



Increased risks of some adverse thrombotic events leading to hospital admission or death were observed in the 28 days after first doses of vaccines. The risks of most of these events were substantially higher and more prolonged after SARS-CoV-2 infection

Study design



Self-controlled case series

Compared **exposed** with **unexposed** periods in the same patient

Population

Data from 1 December 2020 to 24 April 2021



29.1 million people vaccinated with first doses in England

19.6 million ChAdOx1 nCoV-19 *

9.5 million BNT162b2 mRNA †

1.8 million had positive SARS-CoV-2 test



Outcomes 8-28 days after exposure

- with ChAdOx1 nCoV-19 vaccine
- with BNT162b2 mRNA vaccine
- with SARS-CoV-2 infection

Thrombocytopenia

Venous thromboembolism

Arterial thrombosis

Cerebral venous sinus thrombosis

Ischaemic stroke

Myocardial infarction

Other rare arterial thrombotic event



<https://bit.ly/BMJc19ae>

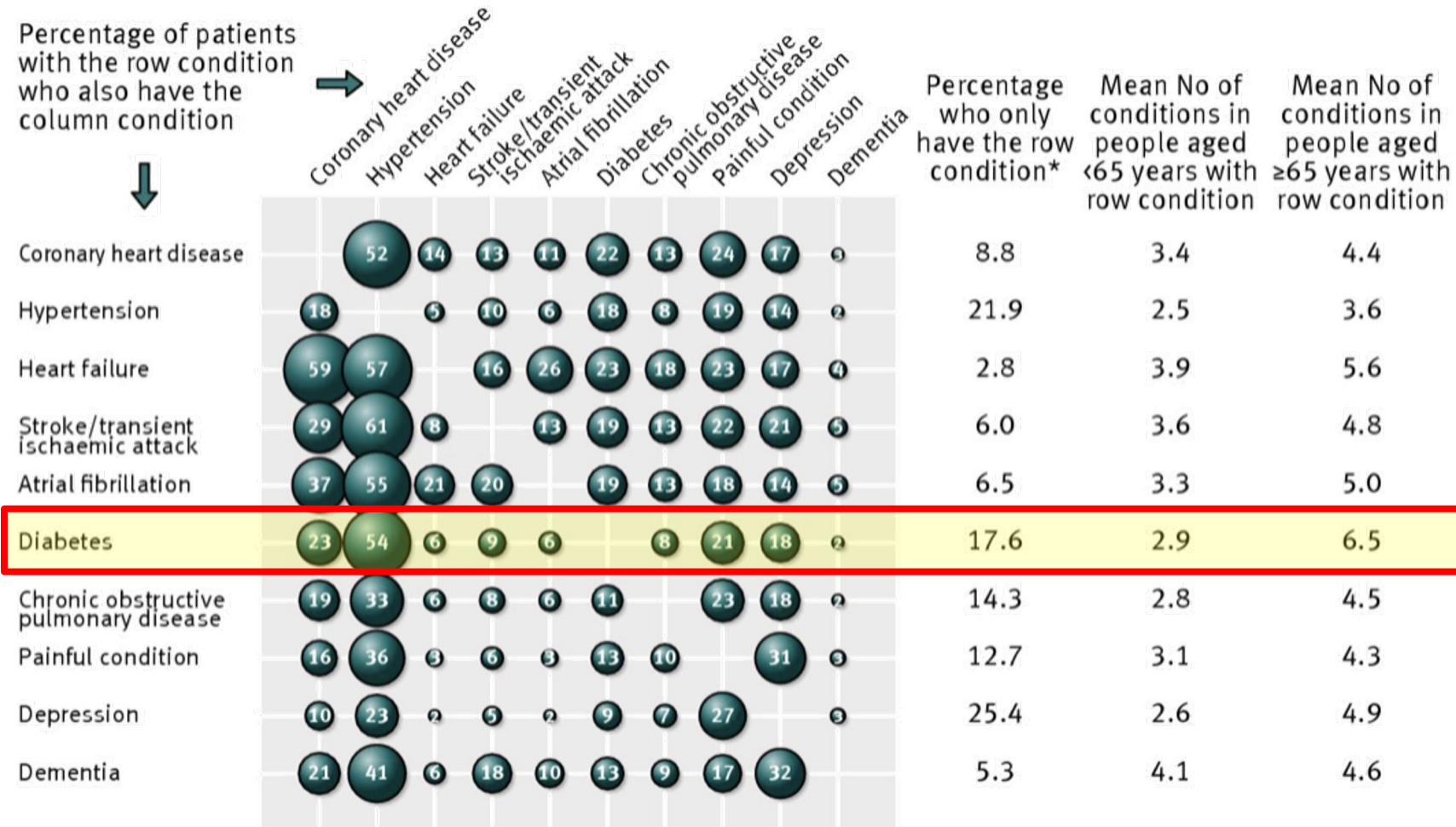
* Oxford-AstraZeneca
† Pfizer-BioNTech

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. Oxford QResearch
Group -, BMJ
2021;374:bmj.n1931

Complexity in routine clinical practice

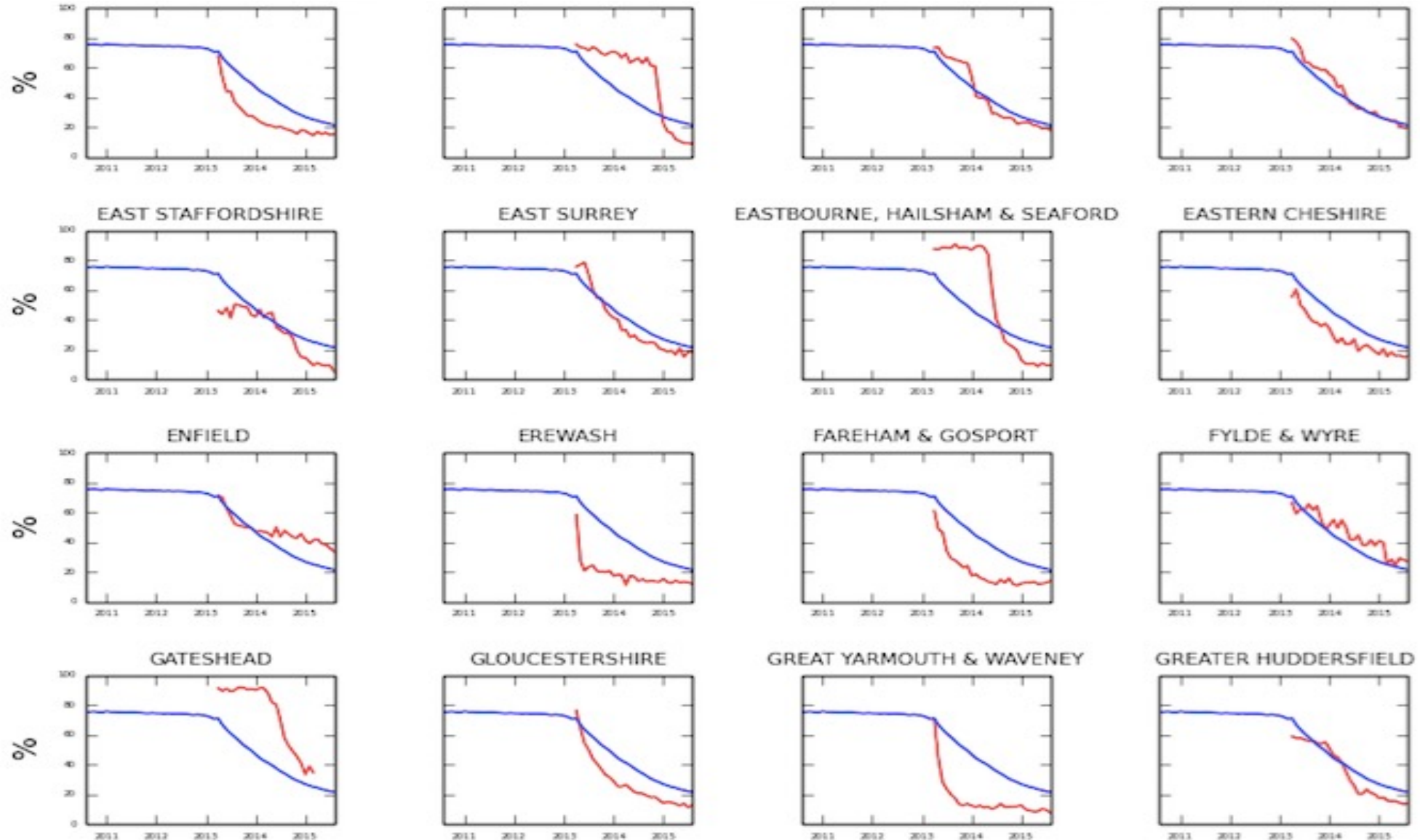
Comorbidity of top 10 common conditions



* Percentage who do not have one of 39 other conditions in the full count

Prescribing big-data analysis/machine learning algorithms

Health district generic switching (red) versus national prescribing (blue)



Oxford-RCGP RSC Dashboard Feedback to GPs

Practices get a dashboard, weekly - most popular for vaccines, some LTC management, data quality

September - October focus: Influenza vaccination performance



Home

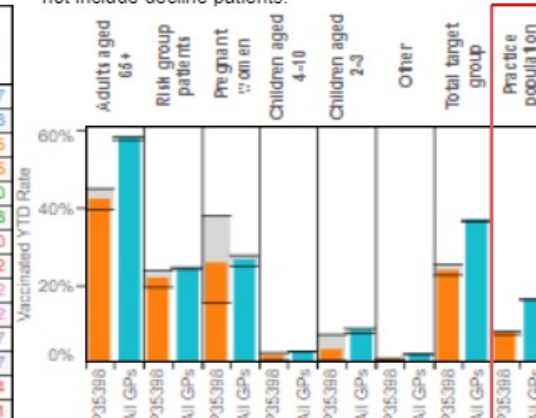
This feedback provides information on how your practice is performing at vaccinating and recording influenza vaccinations compared with the virology practices in the RCGP RSC network participating in the swabbing study. The ideal recording for vaccinations is to record the event and a valid batch number. Please note that 2-10yrs in a risk group are included as risk group patients only.

Please select a week to see historic data : 2019-11-04 - 2019-11-10

Vaccination performance by year, and by past week

		Vaccinated YTD Rate	Vaccinated YTD	Declined YTD	Vaccinated This Week Rate	Vaccinated This Week	Declined This Week
Adults aged 65+	P35398	42.30%	602	86	1.55%	22	27
	All GPs	57.99%	109,496	8,610	1.82%	3,446	546
Risk group patients	P35398	21.92%	318	89	1.86%	27	35
	All GPs	24.46%	25,943	3,488	2.41%	2,551	425
Pregnant women	P35398	25.86%	15	0	1.72%	1	0
	All GPs	26.60%	1,061	76	2.56%	102	6
Children aged 4-10	P35398	1.80%	17	0	0.95%	9	0
	All GPs	3.12%	2,221	68	0.38%	272	12
Children aged 2-3	P35398	3.67%	4	3	1.83%	2	2
	All GPs	8.55%	833	92	4.42%	431	22
Other	P35398	1.04%	99	21	0.15%	14	7
	All GPs	2.43%	13,477	1,117	0.30%	1,652	157
Total target group	P35398	23.98%	956	176	1.53%	61	64
	All GPs	36.75%	139,554	12,332	1.79%	6,802	1,011
Practice population	P35398	7.62%					
	All GPs	16.37%					

Comparison with rest of the virology practices, This does not include decline patients.



Overall Influenza vaccination performance



Your flu vaccine coverage is lower than the RSC. Please code all vaccinations.

If you vaccinated all remaining eligible patients you could earn

£9,368.80

Shingles and Pneumococcal Feedback

Select the data up until : 2019-11-10

Overall shingles vaccination performance

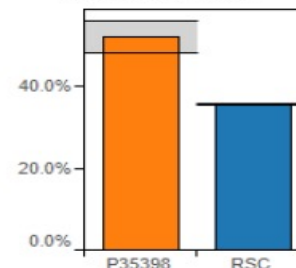


Overall, you are performing really well! Keep up the good work!

If you vaccinated all remaining eligible patients you could earn

£2,967.70

Zoster Vaccination



Herpes Zoster and Post herpetic neuralgia diagnosis 50yrs+

Herpes Zoster Post Herpetic Neuralgia

Select the data up until : 2019-11-10

Overall pneumococcal vaccination performance

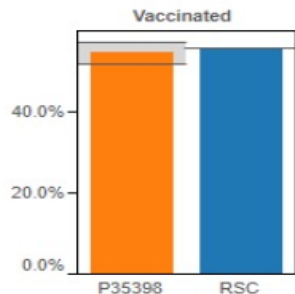


Overall, you are performing at expected levels. Keep working hard to reach your goal!

If you vaccinated all remaining eligible patients you could earn

£6,134.80

Pneumococcal Vaccination (PPV)



Pneumonia diagnosis 50yrs+

Pneumonia

2. Healthcare Big Data analyses:

Based on electronic health records (EHR) for healthcare encounters

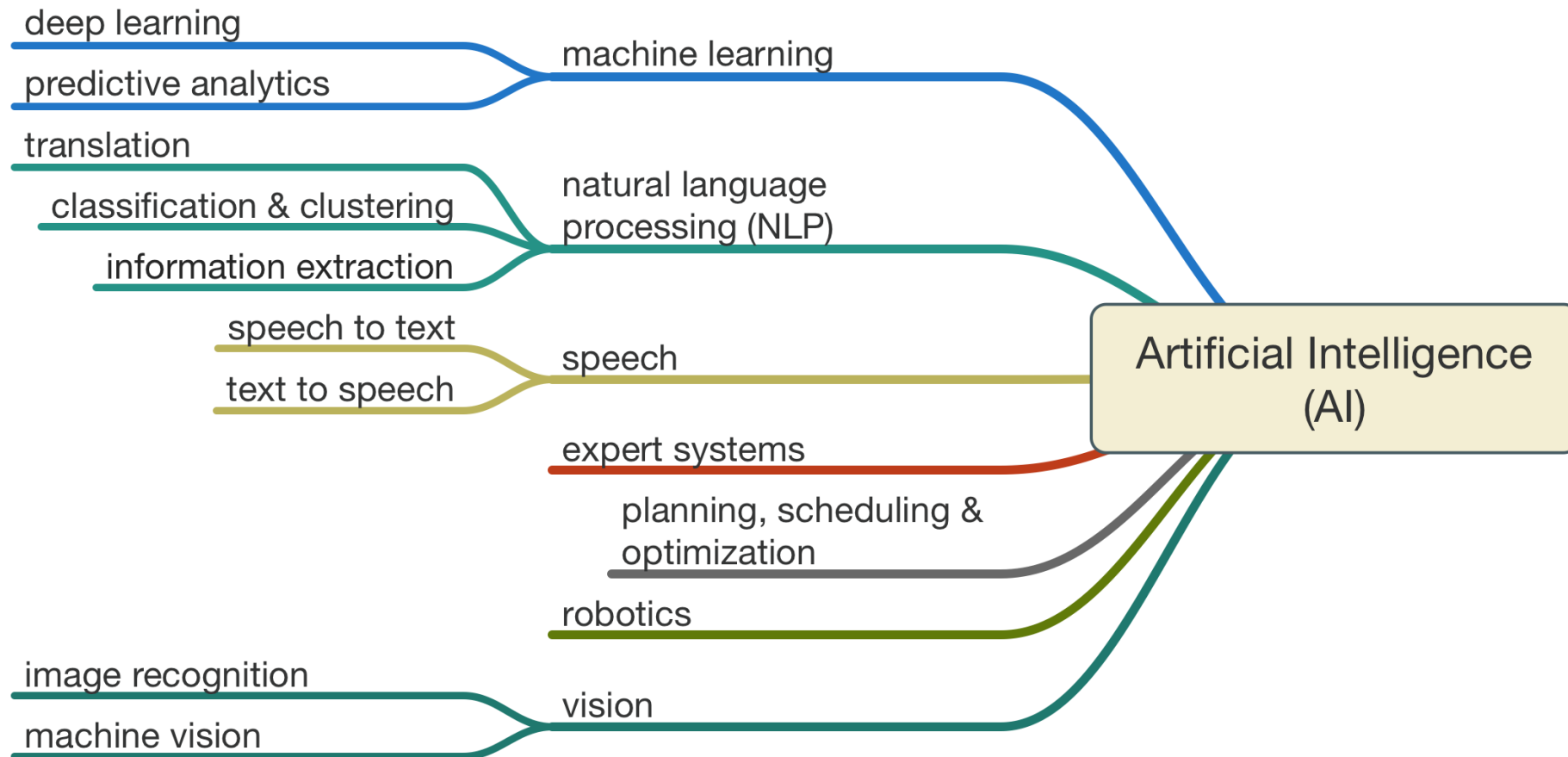
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- System, physician, patient behaviour change for care models

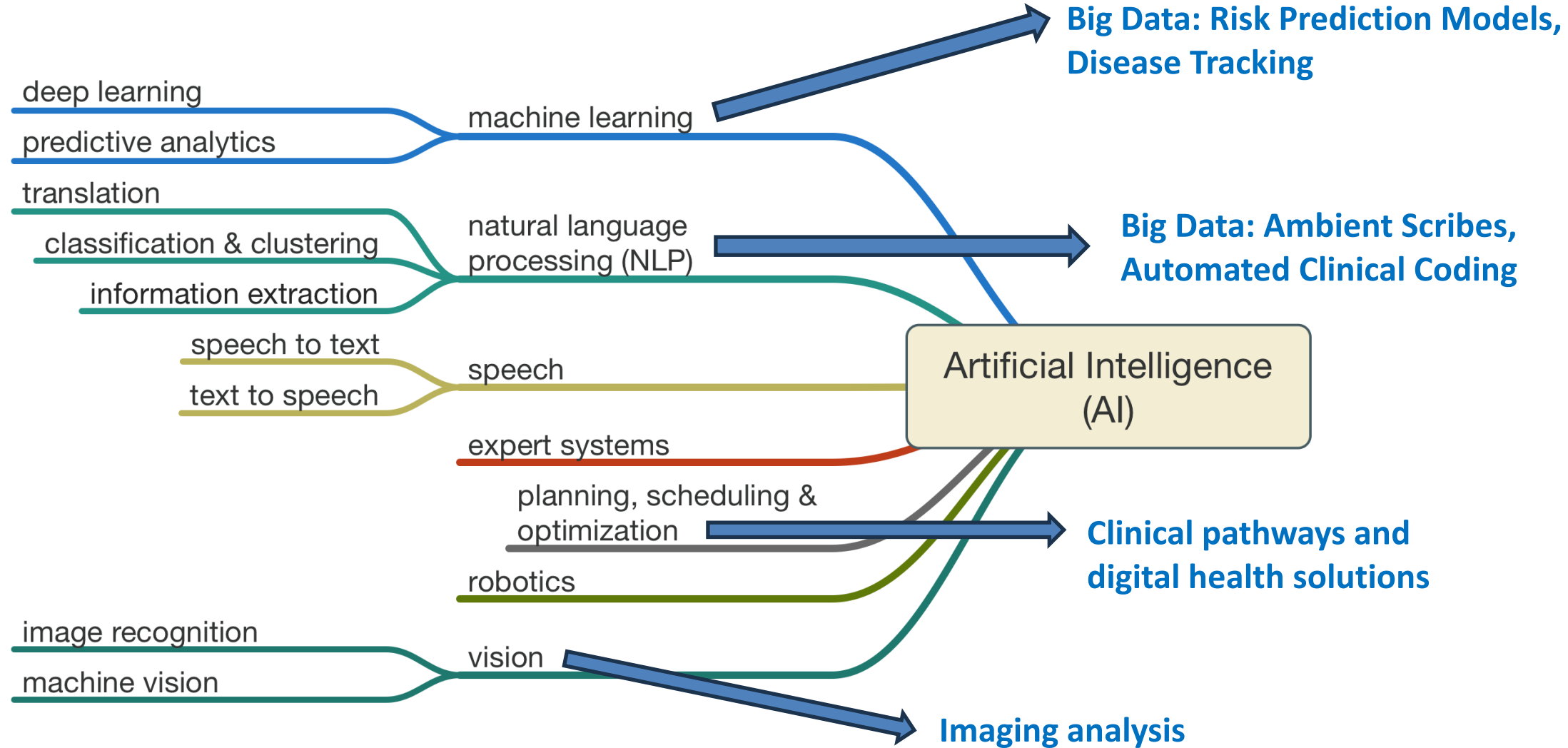
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- Pandemic tracking for Public Health
- Uncoded data – future opportunities

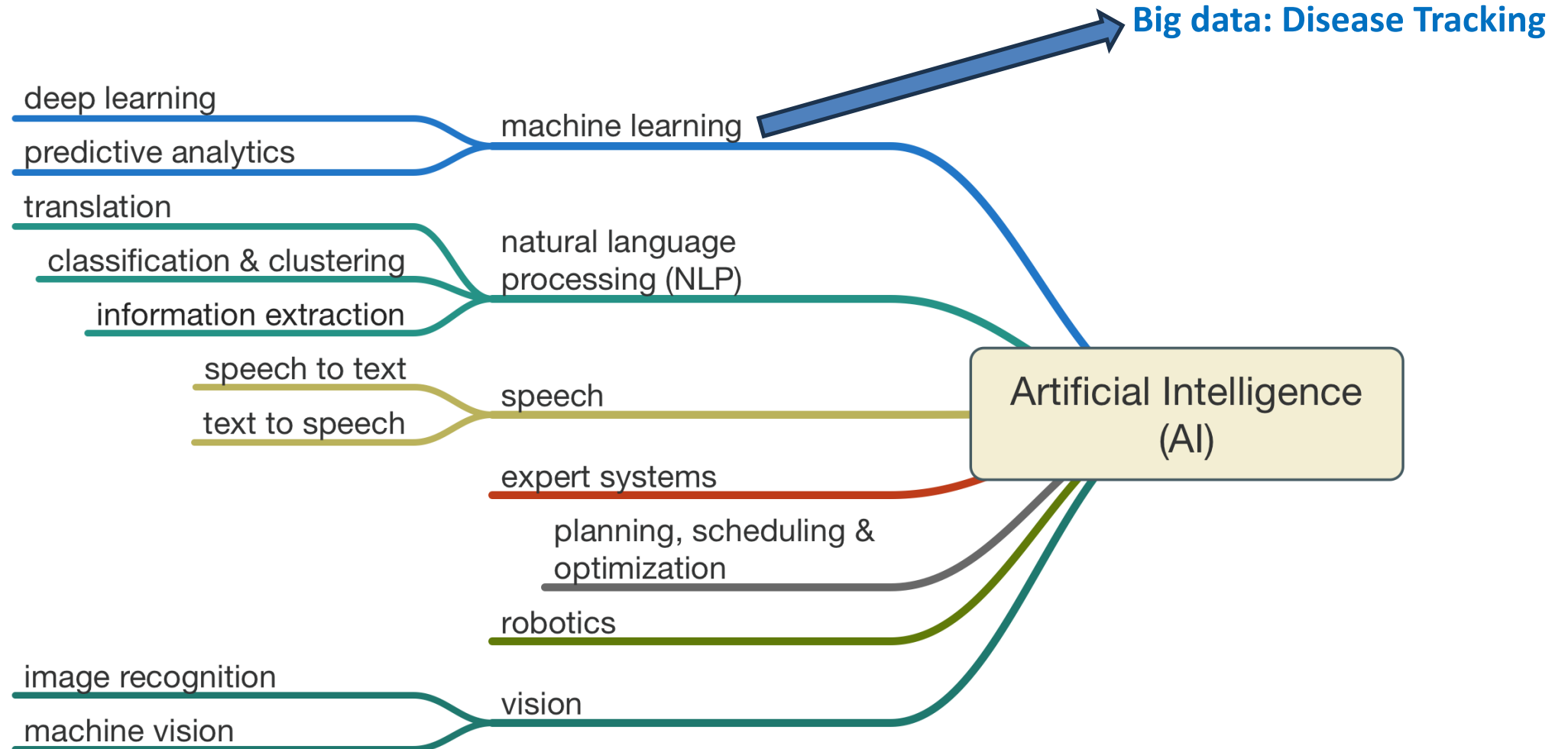
What Do We Mean by AI?



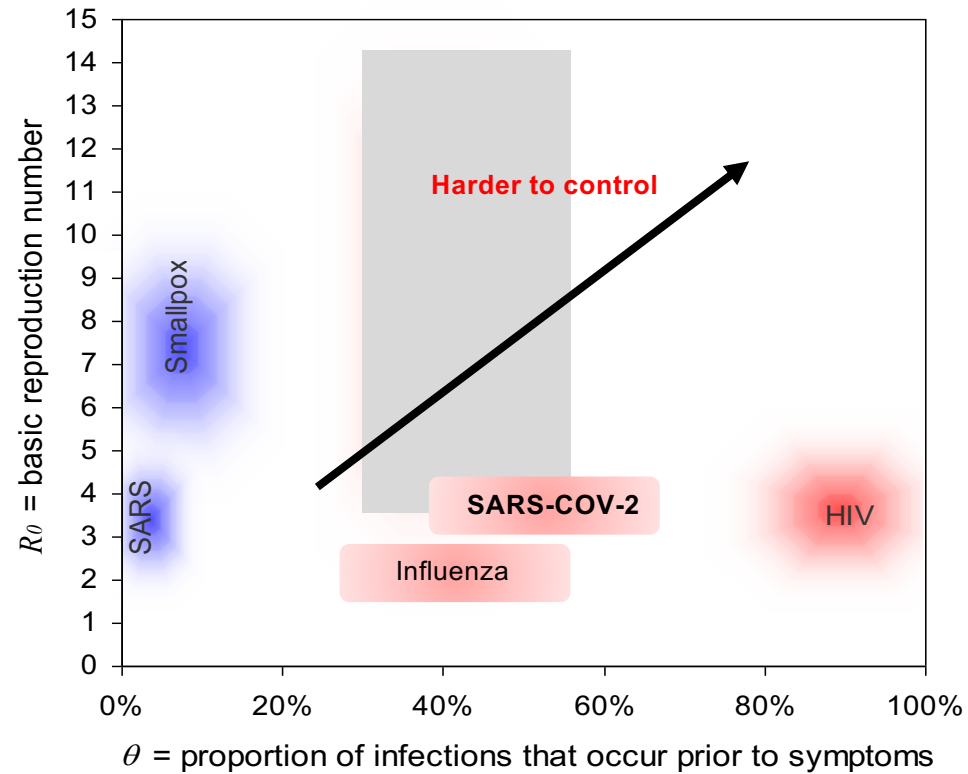
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What Do We Mean by AI?

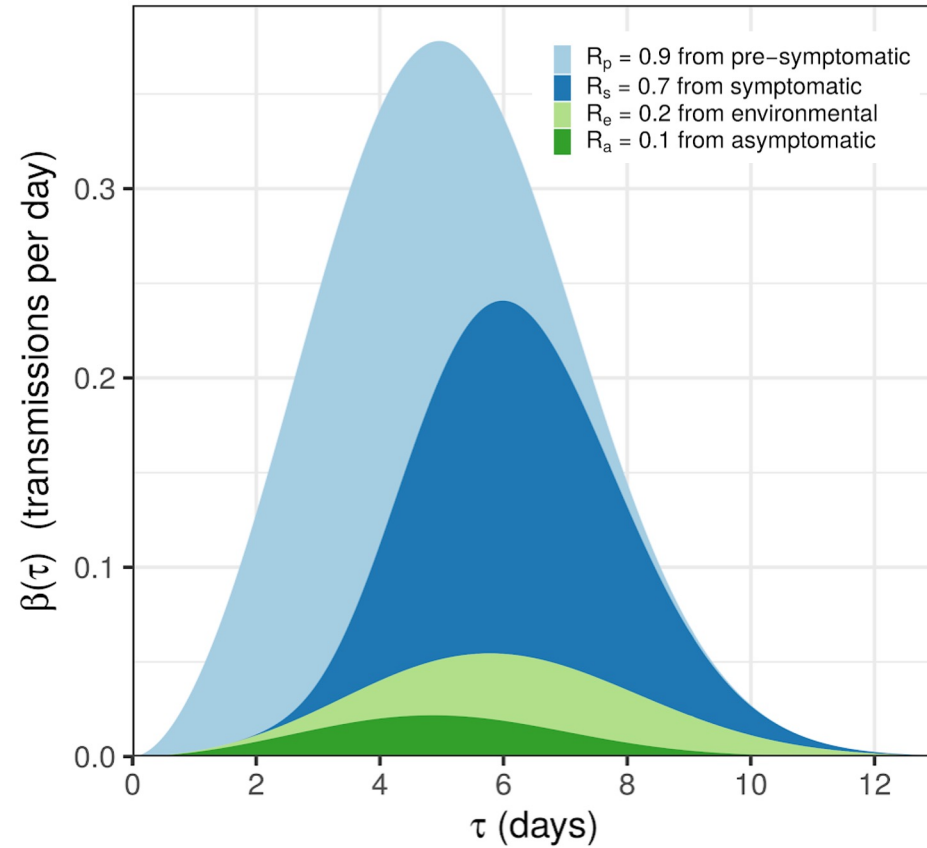


COVID-19/SARS-COV-2 test and trace app

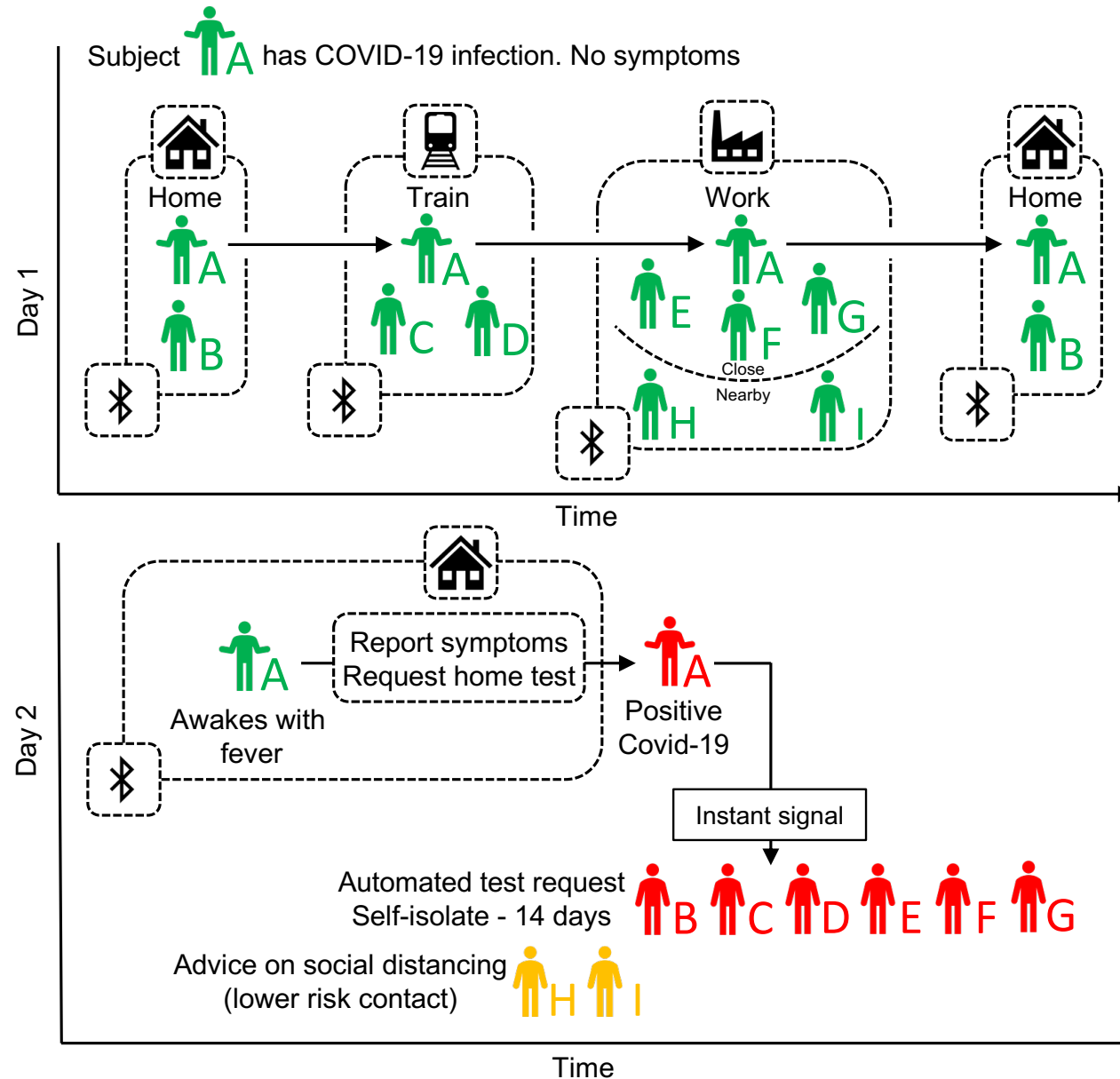


Pre-symptomatic transmission of COVID-19

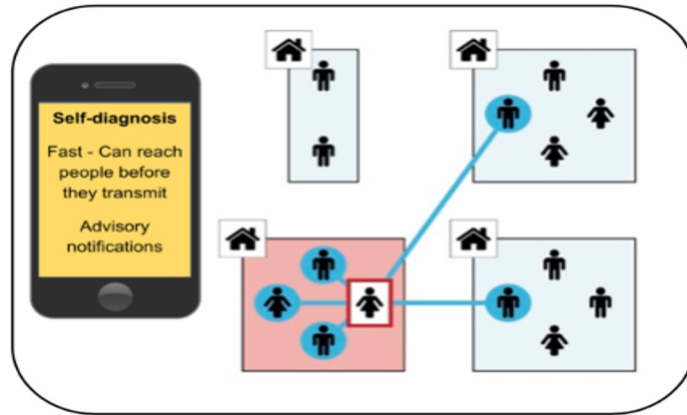
Around half (46%) of transmissions occur before a person shows symptoms of infection



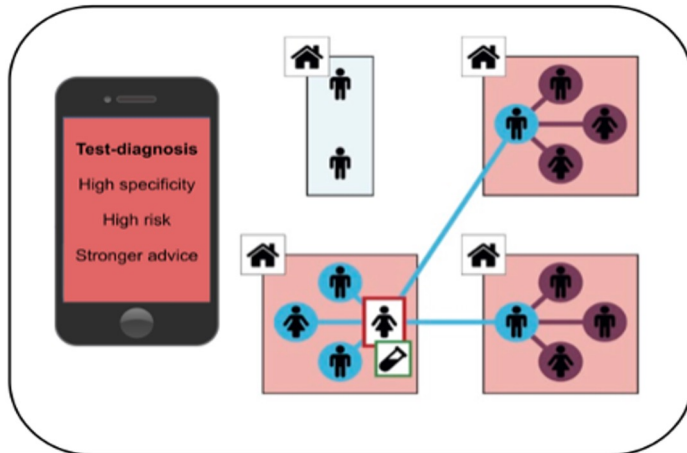
Digital tracing app for COVID



Tracking App notification options



Index tests
positive

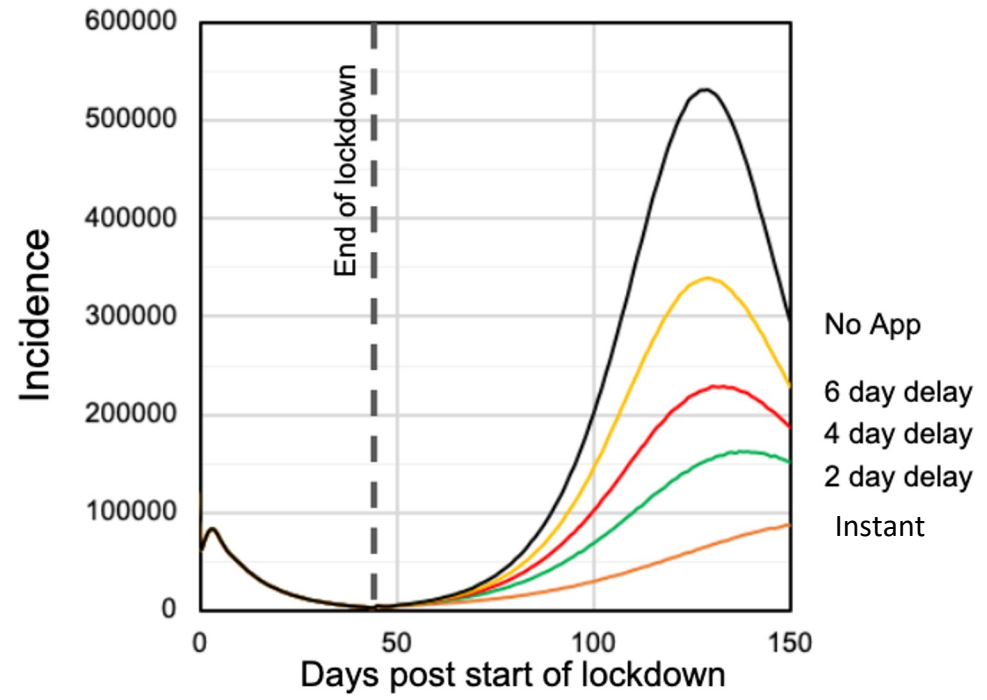
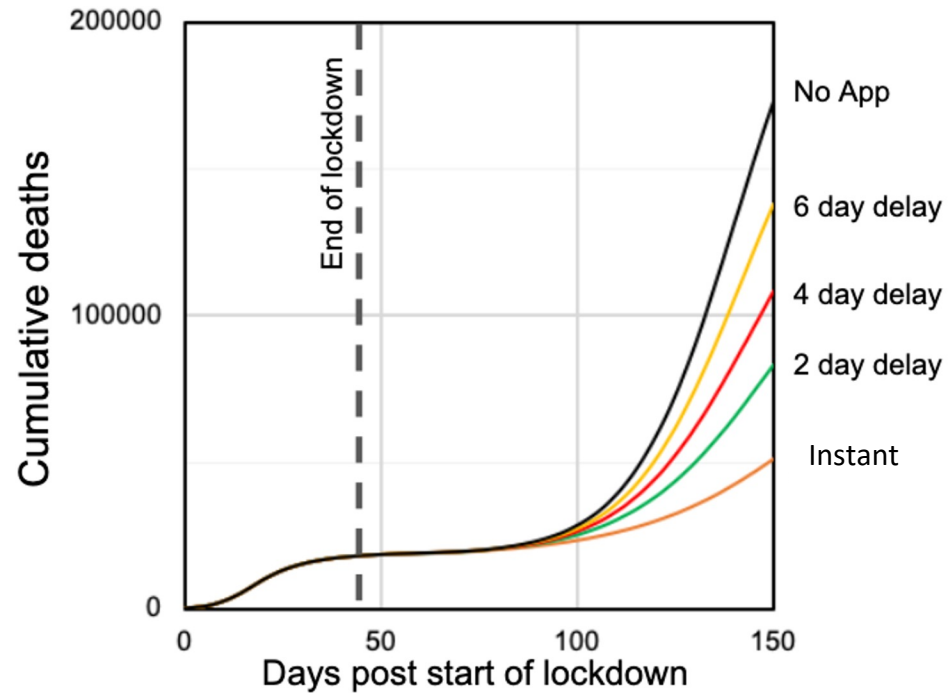


1) **AMBER notifications: an early warning** – trace on self diagnoses symptoms alert “*You’ve come into contact with someone with suspected symptoms of COVID-19, we recommend following NHS guidance on social distancing, hand washing etc.*”

- Time to prepare: e.g. make arrangements at work
- Ensure adherence to social-distancing, consider wearing a mask, increase hand washing etc.
- Don’t visit elderly relative

2) **RED notifications: trace based on a test alert** “*You’ve come into contact with someone with COVID-19 and you need to quarantine and request a test.*”

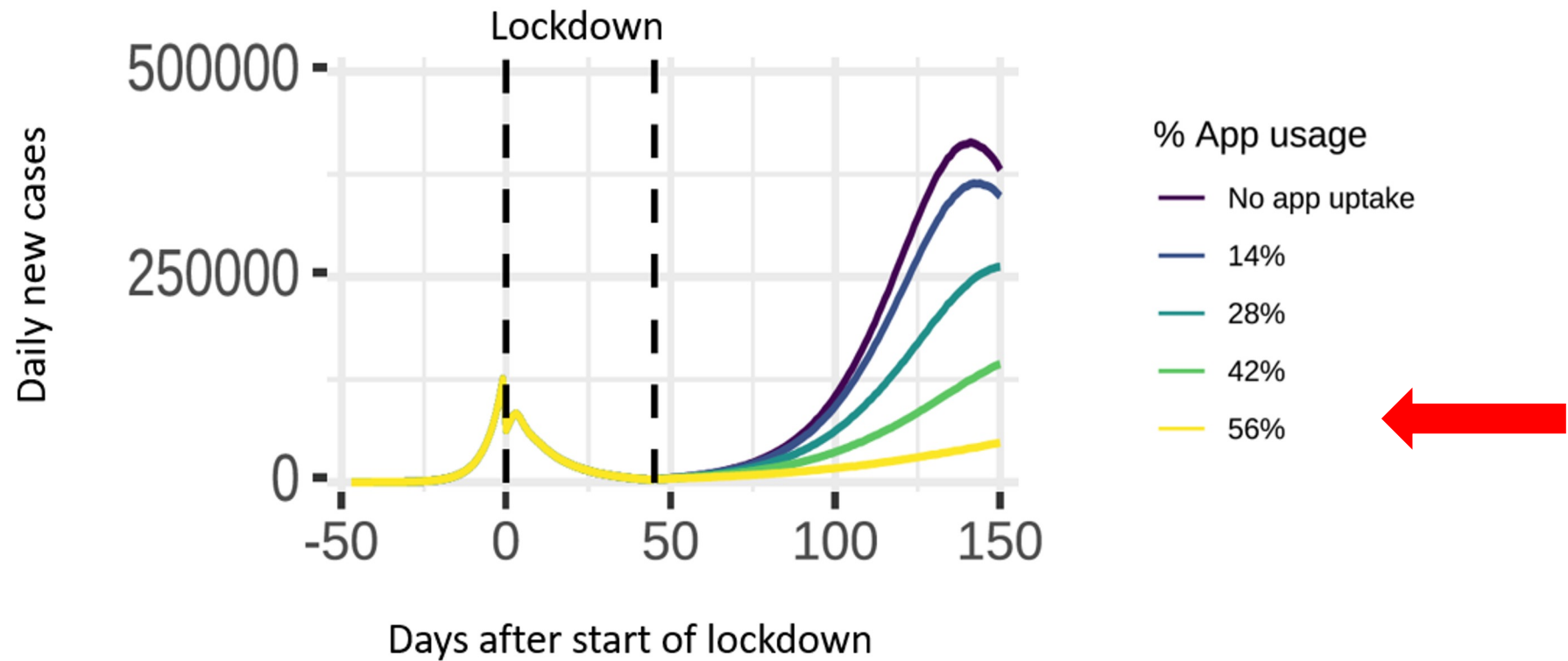
Speed matters: test & trace ideally within 24 hours



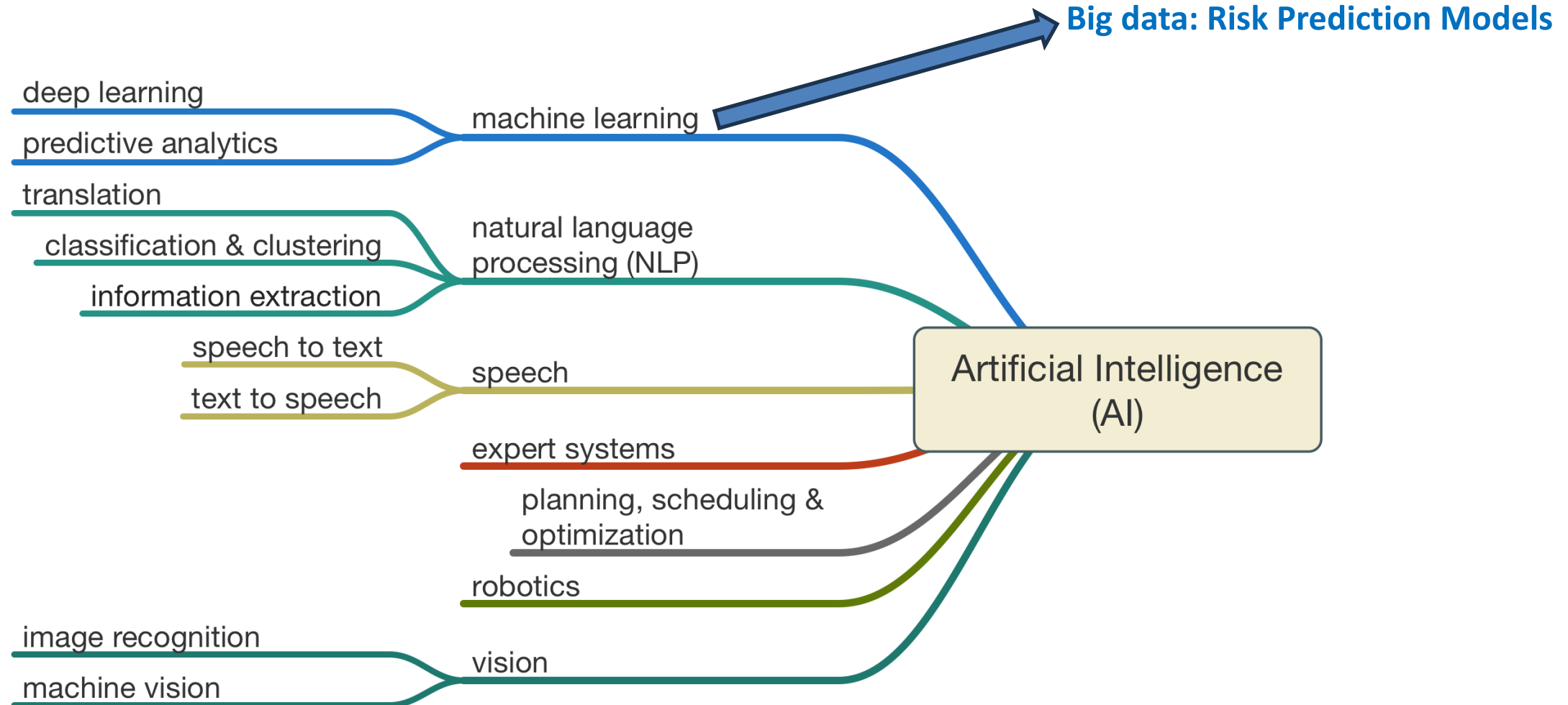
Benefit of contact-tracing is lost if tracing is delayed e.g. higher risks of transmission if testing is delayed 2, 4 or 6 days

Uptake : the more app users the greater impact

If we reduce potentially infectious contacts by 20%, and **56%** of the population use the app, we can considerably slow the epidemic. The app has an effect at all levels of uptake.



What Do We Mean by AI?



Article

Factors associated with COVID-19-related death using OpenSAFELY

<https://doi.org/10.1038/s41586-020-2521-4>

Received: 15 May 2020

Accepted: 1 July 2020

Published online: 8 July 2020

 Check for updates

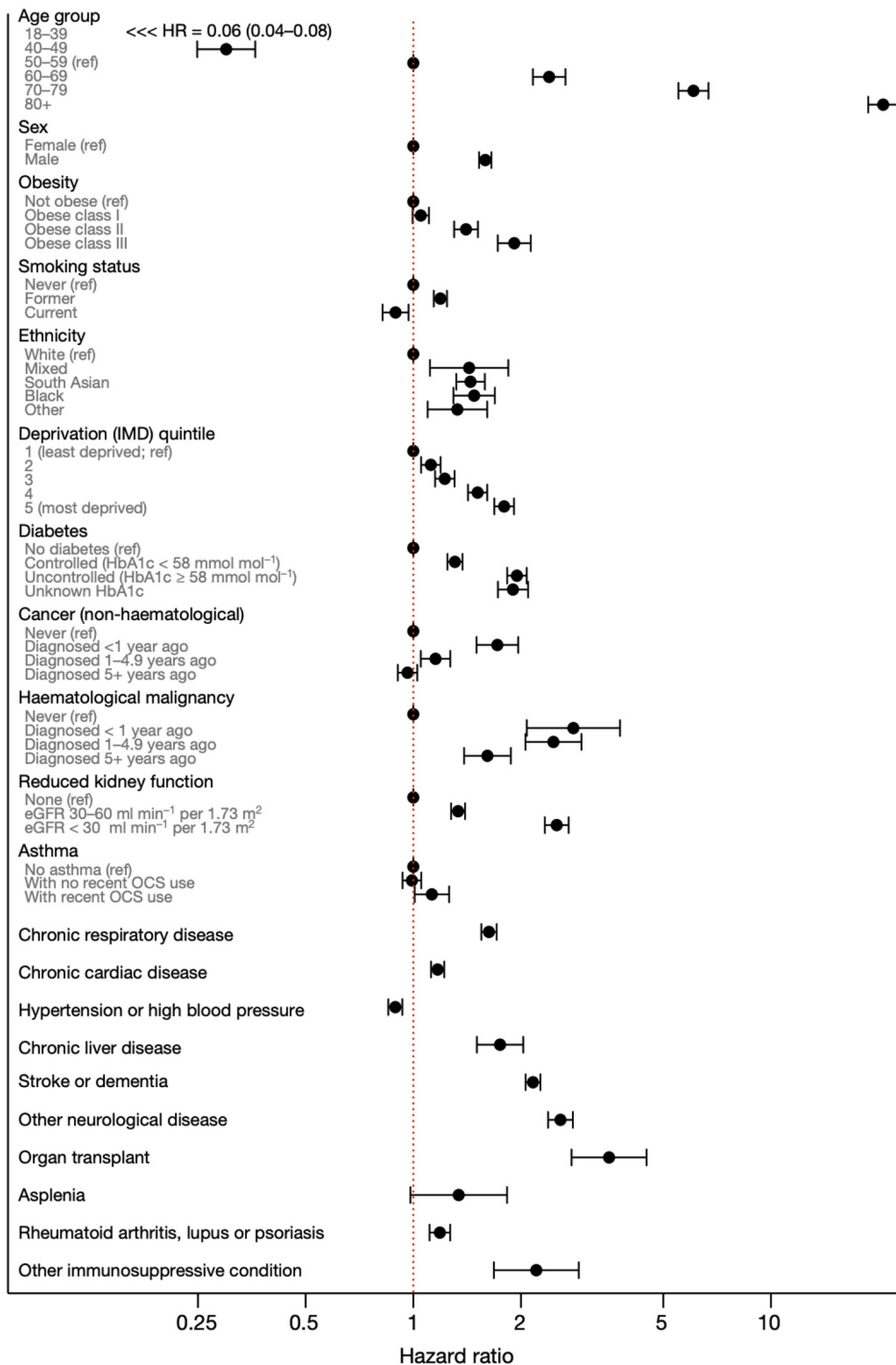
Elizabeth J. Williamson^{1,6}, Alex J. Walker^{2,6}, Krishnan Bhaskaran^{1,6}, Seb B. Carroll^{1,6}, Caroline E. Morton², Helen J. Curtis², Amir Mehrkar², David Evans², Peter Jonathan Cockburn², Helen I. McDonald^{1,4}, Brian MacKenna², Laurie Tonin², Ian J. Douglas¹, Christopher T. Rentsch¹, Rohini Mathur¹, Angel Y. S. Wong¹, David Harrison⁵, Harriet Forbes¹, Anna Schultze¹, Richard Croker², John Sam Harper², Rafael Perera², Stephen J. W. Evans¹, Liam Smeeth^{1,4,7} & Ben

Coronavirus disease 2019 (COVID-19) has rapidly affected mortal and is unprecedented urgency to understand who is most at risk of severe disease. This requires new approaches for the timely analysis of large data sets. In the context of NHS England, we created OpenSAFELY—a secure health data centre that covers 40% of all patients in England and holds patient data from a major vendor of primary care electronic health records. We used OpenSAFELY to examine factors associated with COVID-19-related deaths. COVID-19-related death was associated with: older age (HR 1.59 (95% confidence interval 1.53–1.65)); greater age (both with a strong gradient); diabetes; severe asthma; and various other conditions. Compared with people of white ethnicity, Black and Asian people were at higher risk, even after adjustment for other factors (HR 1.45 (1.32–1.58), respectively). We have quantified a range of clinical factors associated with COVID-19-related death in one of the largest cohort studies to date. More patient records are rapidly being added to OpenSAFELY, and we will extend our results regularly.

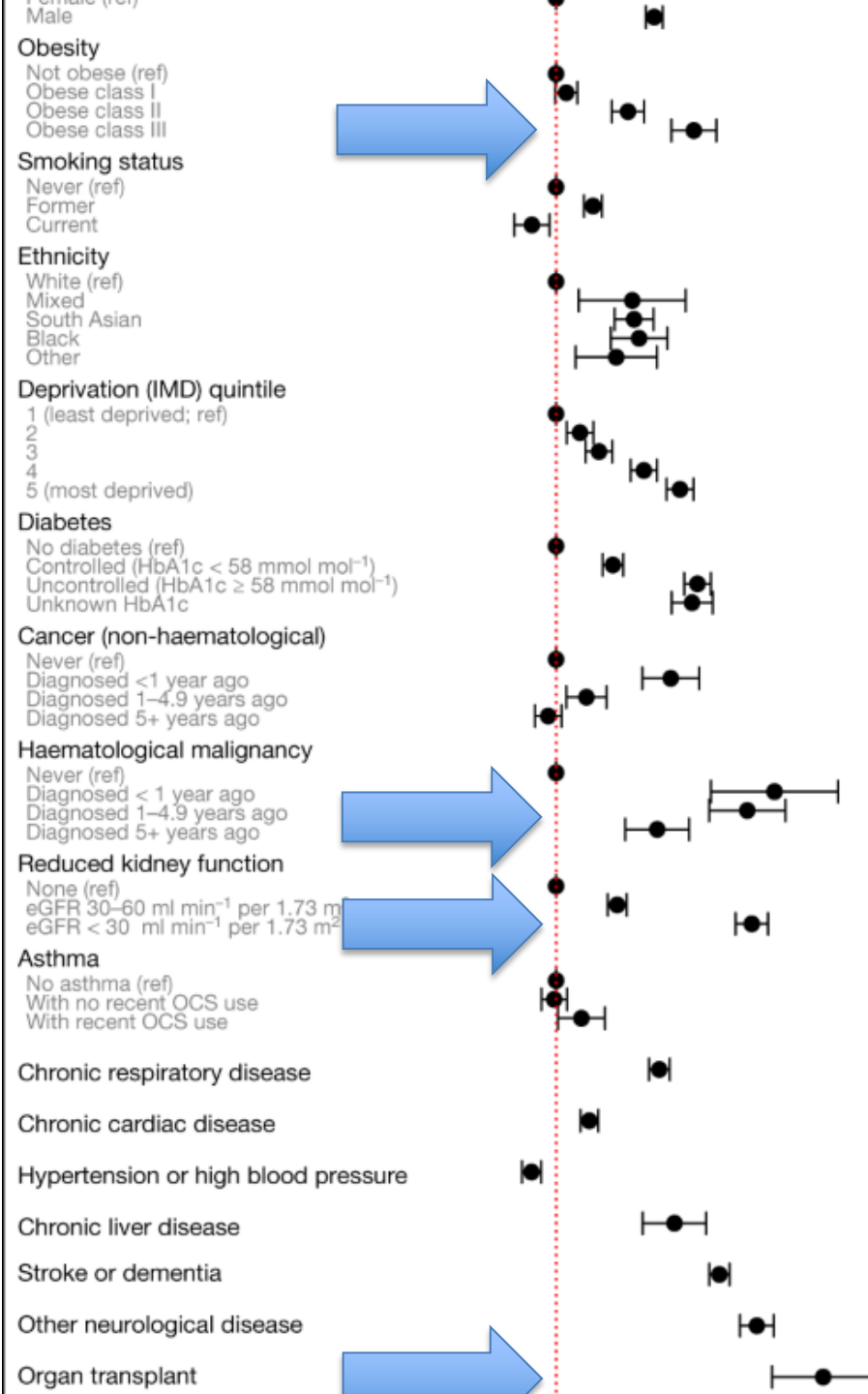
On 11 March 2020, the World Health Organization (WHO) characterized COVID-19—which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)—as a pandemic, after 118,000 cases and 4,291 deaths were reported in 114 countries¹. As of 6 May 2020 (the date of latest data availability for this study), cases had reached over 3.5 million globally, with more than 240,000 deaths attributed to the virus¹. On the same day in the UK, there had been 206,715 confirmed cases of COVID-19, and 30,615 COVID-19-related deaths². COVID-19 is a well-established risk factor for severe COVID-19-related death in the UK have

in a French intensive care cohort³ ($n = 12$), presentation cohort⁴ ($n = 3,615$). The risk of death is unclear^{9–11}. People from Black and Asian ethnicities are at increased risk of poor outcomes from COVID-19^{12,13}.

Patient care is typically managed through primary care, which are commonly used in research. However, the analysis of electronic health records from small samples of historic data. Evaluation of cause of death requires a new approach. A



Williamson EJ, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature* **584**, 430–436 (2020).
<https://doi.org/10.1038/s41586-020-2521-4>



Q-COVID score

Used by UK to determine

- Need to shield
- Ordering of first wave COVID vaccination

Estimated 10 year risk of cardiovascular disease

QRISK3 Web calculator <https://qrisk.org/three/>

How does your 10-year score compare?

Your score

Your 10-year QRISK [®] 3 score	21.4%
The score of a healthy person with the same age, sex, and ethnicity [*]	5.8%
Relative risk ^{**}	3.7
Your QRISK [®] 3 Healthy Heart Age ^{***}	74

^{*} This is the score of a healthy person of your age, sex and ethnic group, i.e. with no adverse clinical indicators and a cholesterol ratio of 4.0, a stable systolic blood pressure of 125, and BMI of 25.

^{**} Your relative risk is your risk divided by the healthy person's risk.

^{***} Your QRISK[®]3 Healthy Heart Age is the age at which a healthy person of your sex and ethnicity has your 10-year QRISK[®]3 score.

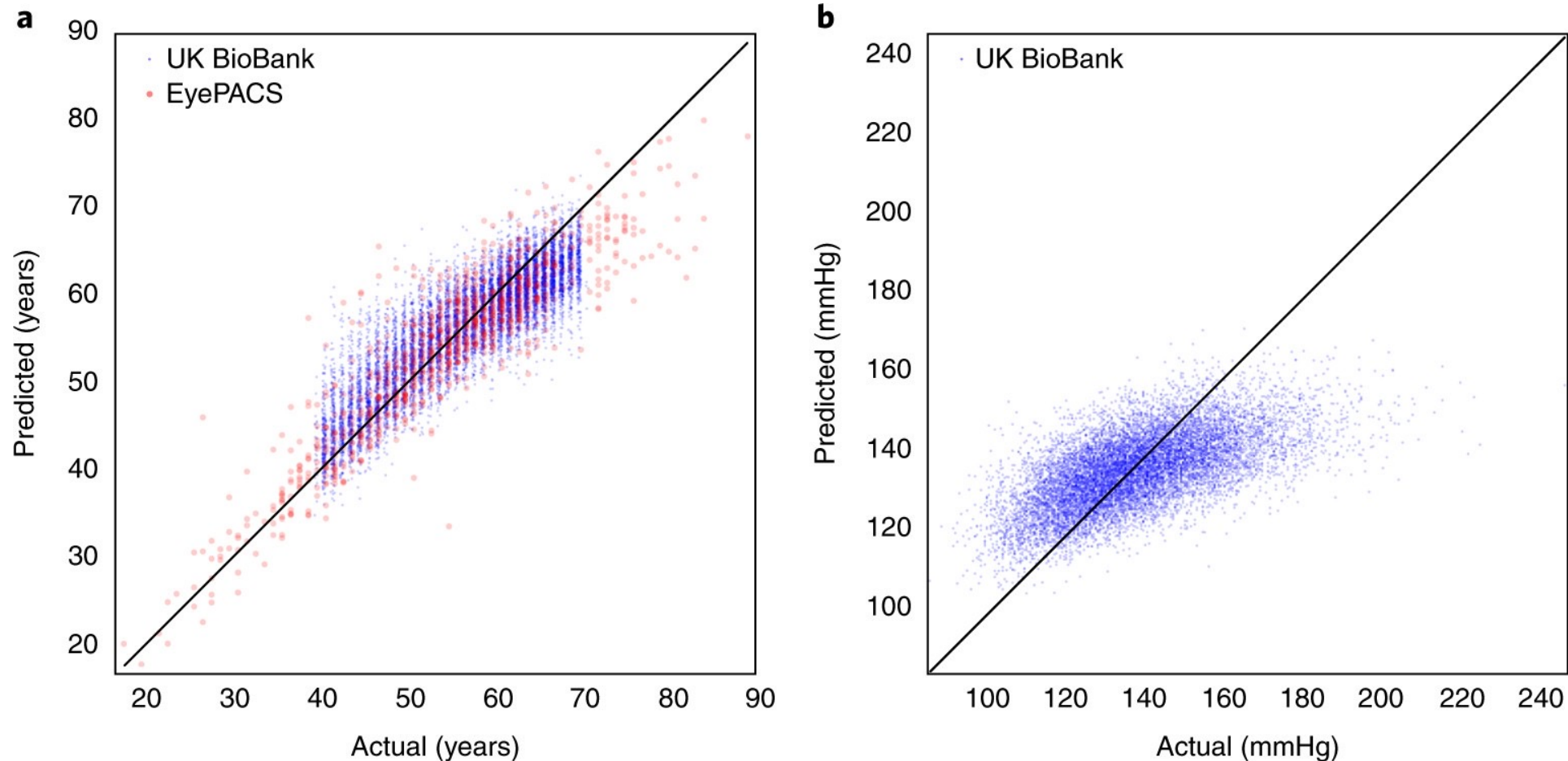
- 55yr old heavy smoker
- FH CHD
- SMI
- Atypical antipsychotics
- QRISK2 score = 13.6%
- QRISK3 score = 21.4%

Current disease risk calculators limitations

- Standard big data risk factor driven algorithms are fairly accurate (AUC of around 80%)
- But clinical records on average hold data on only 30% of all risk factors
- Can machine learning algorithms help?

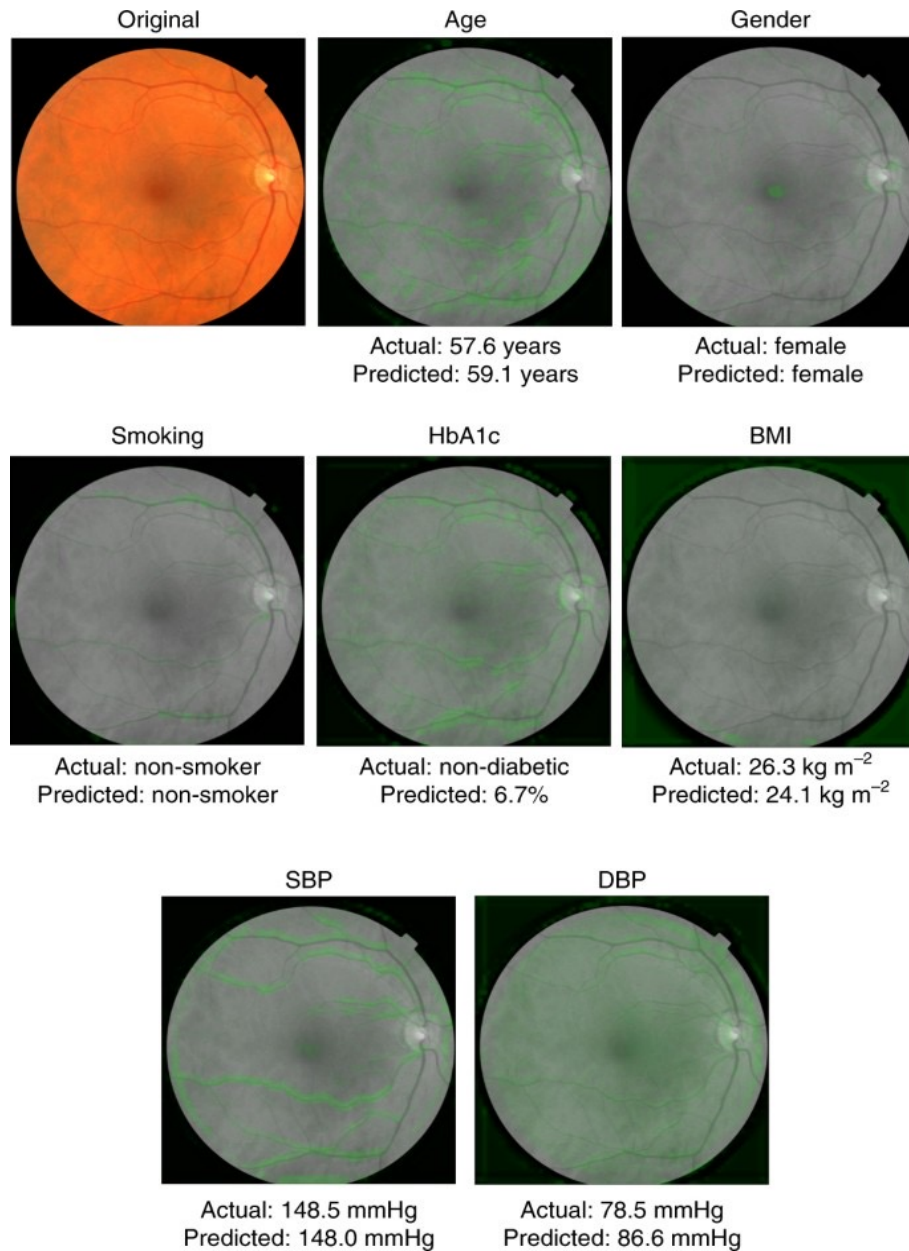
Predicting CV risk factors from retinal images

Convolutional neural network trained on data & retinal fundus images from 284,335 patients (48,101 UK Biobank (<http://www.ukbiobank.ac.uk/about-biobank-uk>) and 236,234 patients from EyePACS (<http://www.eyepacs.org>) and validated these models using images from 12,026 patients from the UK Biobank and 999 patients from EyePACS



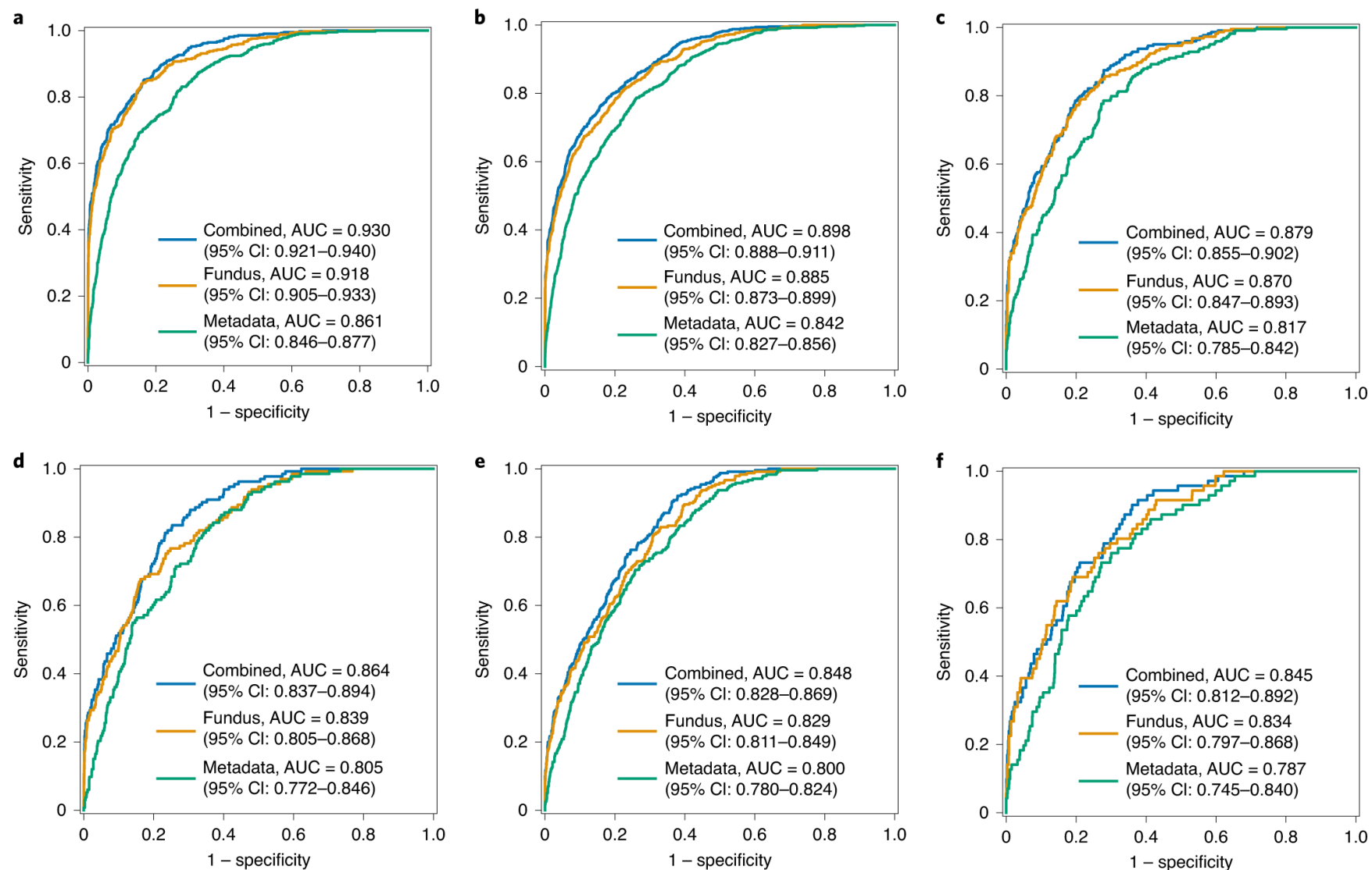
Poplin, R., Varadarajan, A.V., Blumer, K. *et al.* Prediction of cardiovascular risk factors from retinal fundus photographs via deep learning. *Nat Biomed Eng* **2**, 158–164 (2018). <https://doi.org/10.1038/s41551-018-0195-0>

Predicting CV risk factors from retinal images



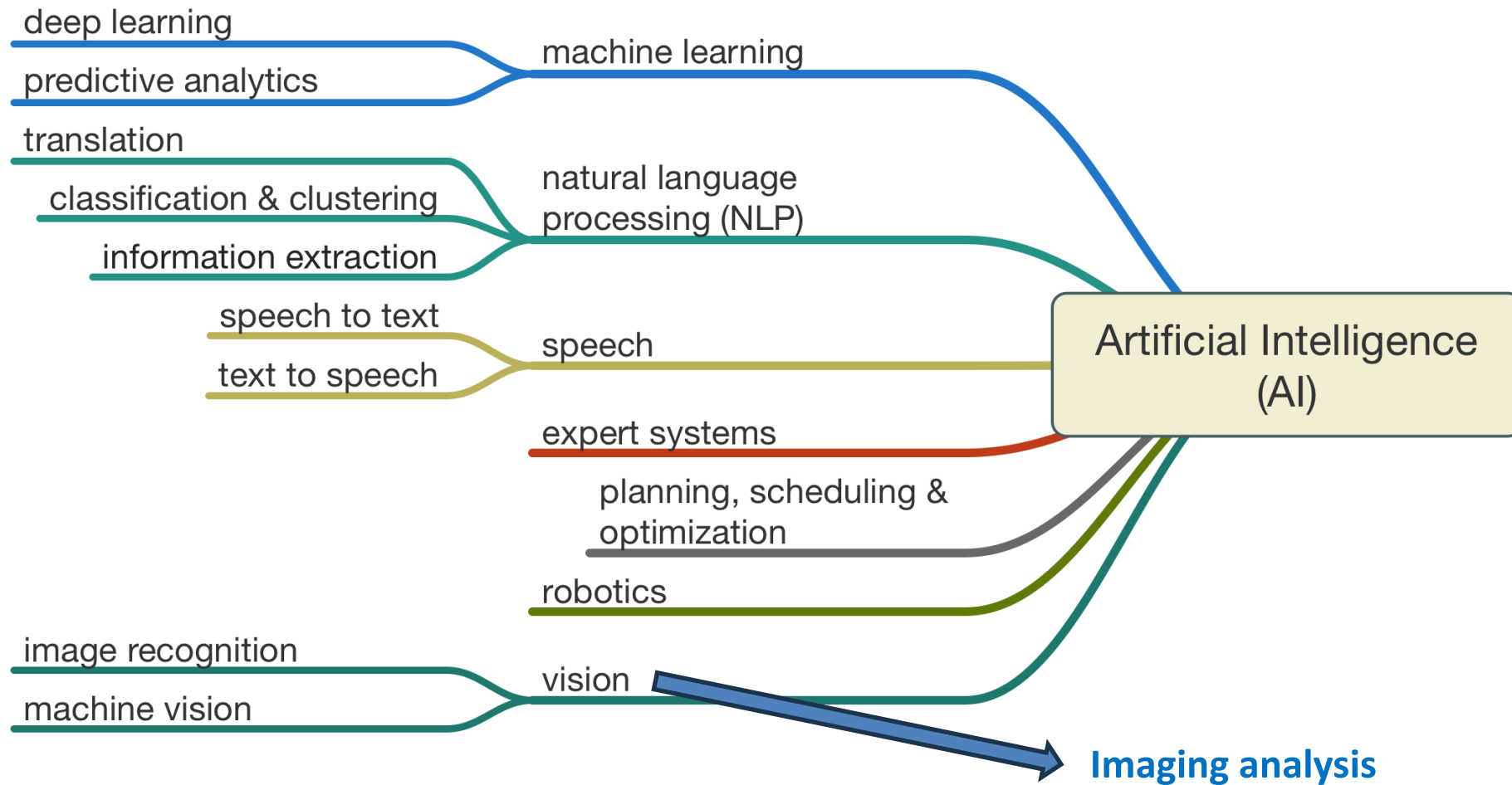
Poplin R, Varadarajan AV, Blumer K. *et al.* Prediction of cardiovascular risk factors from retinal fundus photographs via deep learning. *Nat Biomed Eng* **2**, 158–164 (2018). <https://doi.org/10.1038/s41551-018-0195-0>

AI system to detect CKD from smartphone retinal images



Zhang, K., Liu, X., Xu, J. *et al.* Deep-learning models for the detection and incidence prediction of chronic kidney disease and type 2 diabetes from retinal fundus images. *Nat Biomed Eng* 5, 533–545 (2021). <https://doi.org/10.1038/s41551-021-00745-6>

What Do We Mean by AI?

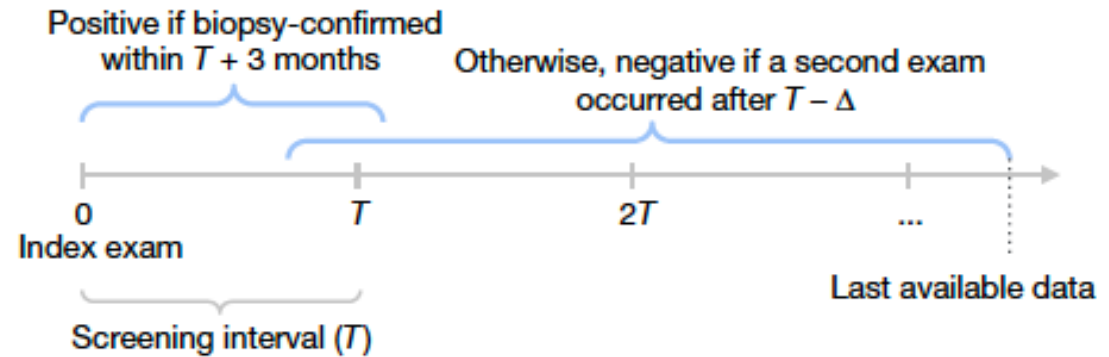


International evaluation of an AI system for breast cancer screening

Test datasets

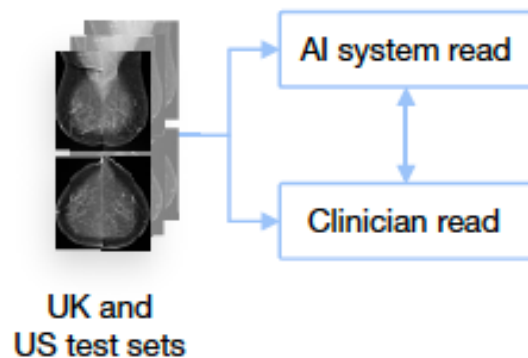
		
Number of women	25,856	3,097
Interpretation	Double reading	Single reading
Screening interval	3 years	1 or 2 years
Cancer follow-up	39 months	27 months
Number of cancers	414 (1.6%)	686 (22.2%)

Ground-truth determination

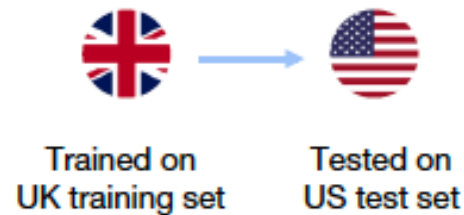


Evaluation

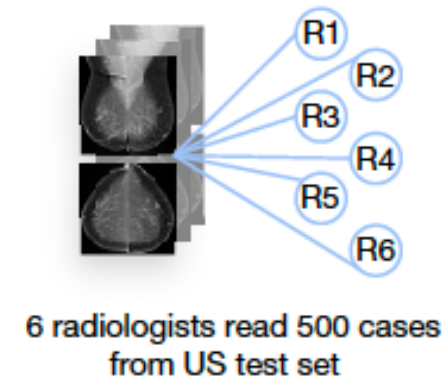
Comparison with retrospective clinical performance



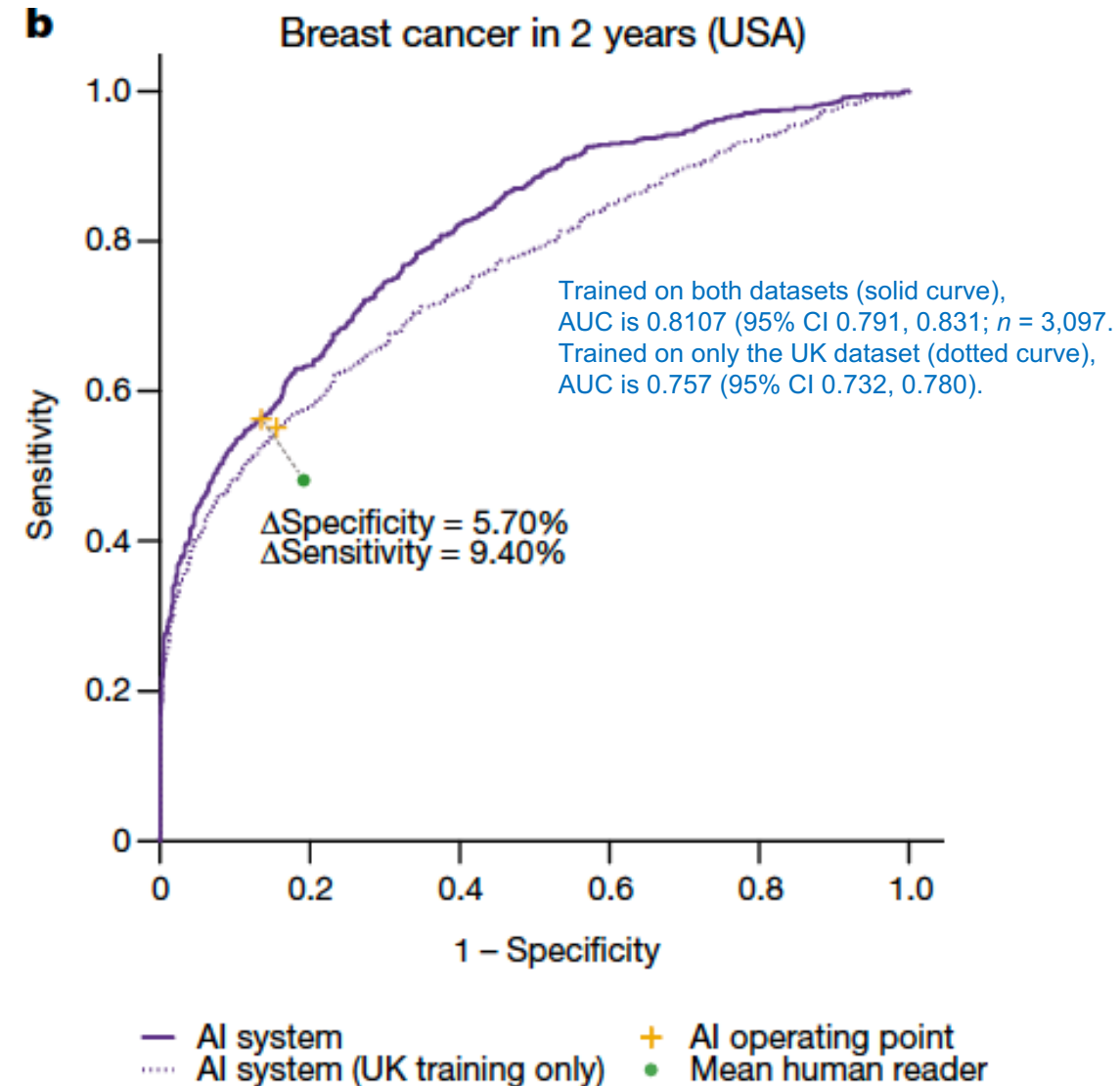
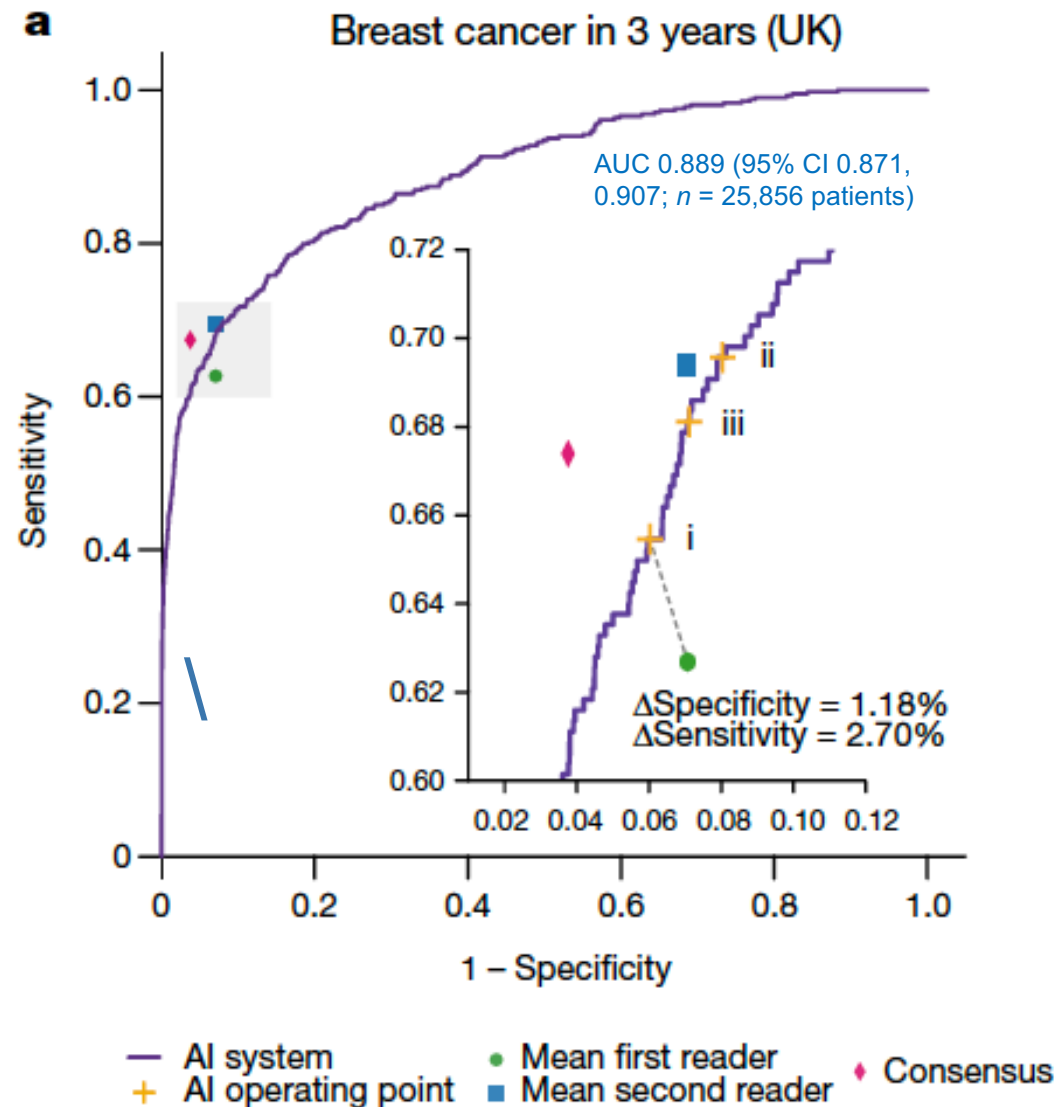
Generalization across datasets



Independently conducted reader study



International evaluation of an AI system for breast cancer screening



International evaluation of AI system for breast cancer screening

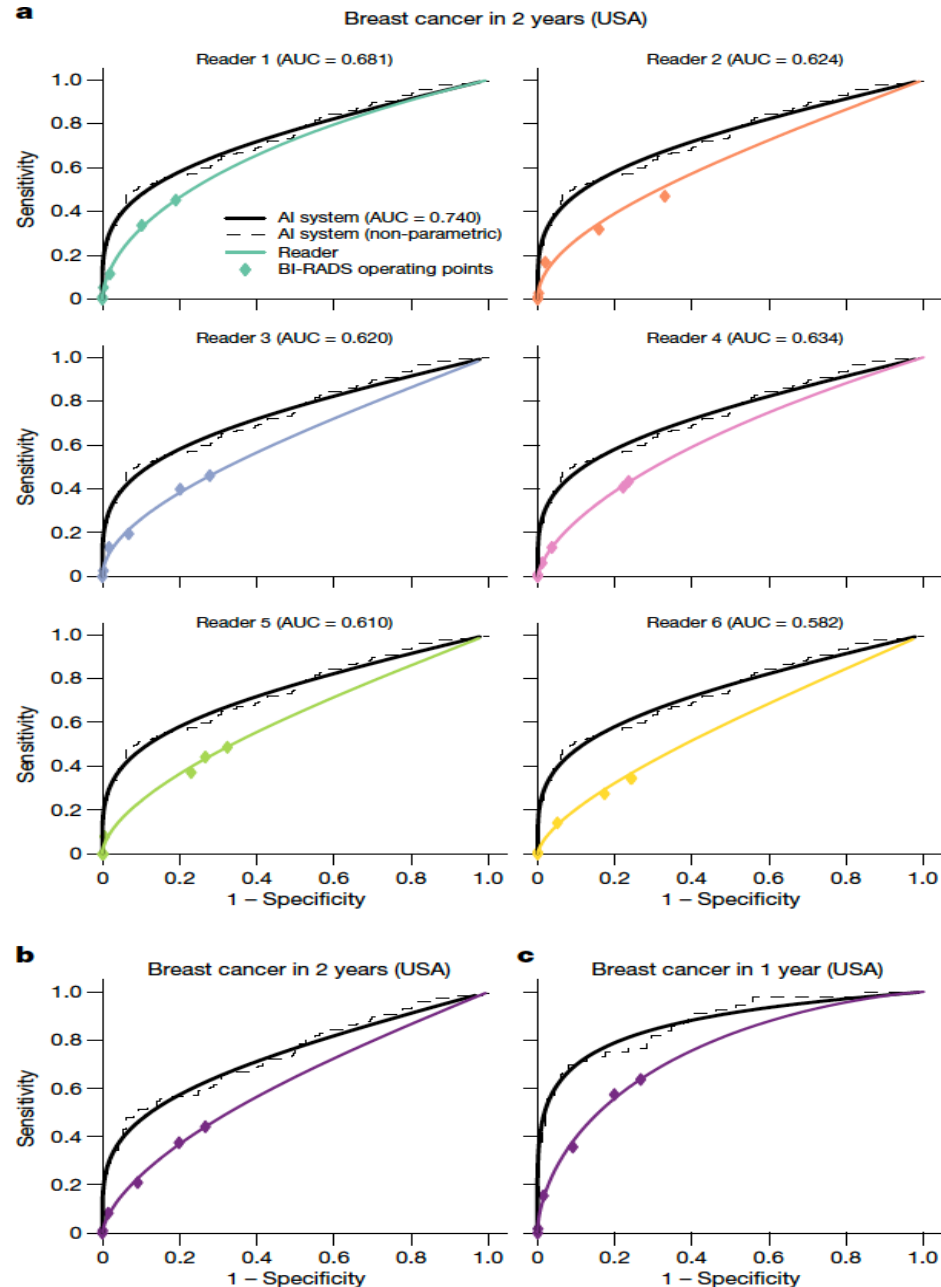
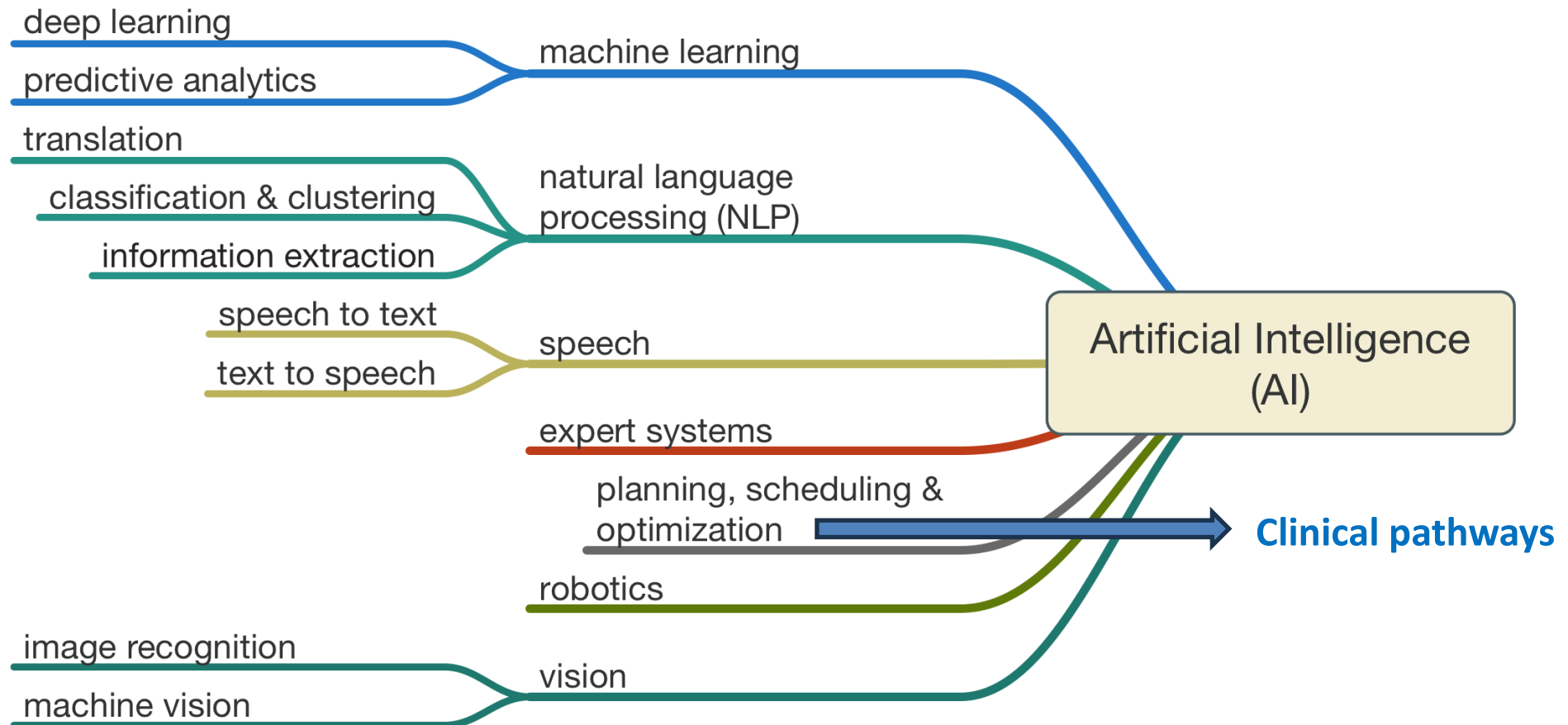


Fig. 3 | Performance of the AI system in breast cancer prediction compared to six independent readers. a, Six readers rated each case ($n = 465$) using the six-point BI-RADS scale. A fitted ROC curve for each of the readers is compared to the ROC curve of the AI system (see Methods section ‘Statistical analysis’). For reference, a non-parametric ROC curve is presented in tandem. Cases were considered positive ($n = 113$) if they received a pathology-confirmed diagnosis of cancer within 27 months of the time of screening. Note that this sample of cases was enriched for patients who received a negative biopsy result ($n = 119$), making this a more-challenging population for screening. The mean reader AUC was 0.625 (s.d. 0.032), whereas the AUC for the AI system was 0.740 (95% CI 0.696, 0.794). The AI system exceeded human performance by a significant margin ($\Delta\text{AUC} = +0.115$, 95% CI 0.055, 0.175; $P = 0.0002$ by two-sided ORH method (see Methods section ‘Statistical analysis’)). For results using a 12-month interval, see Extended Data Fig. 2. **b**, Pooled results from all six readers from **a**. **c**, Pooled results ($n = 408$) from all 6 readers using a 12-month interval for cancer definition. Cases were considered positive ($n = 56$) if they received a pathology-confirmed cancer diagnosis within one year (Extended Data Table 3).

What Do We Mean by AI?



Patient self-management of hypertension: validated monitors and simple treatment algorithm

	Mean blood pressure (mm Hg)			Effect size (mm Hg)	
	Baseline	6 months	12 months	Baseline to 6 months	Baseline to 12 months
Systolic blood pressure; unadjusted					
Intervention	152.1 (150.6 to 153.6)	139.0 (137.0 to 141.0)	134.9 (132.6 to 137.1)	3.7 (0.6 to 6.8)	5.5 (2.2 to 8.8)
Control	151.8 (150.3 to 153.3)	142.4 (140.2 to 144.6)	140.1 (138.0 to 142.2)	..	..
Systolic blood pressure; adjusted*					
Intervention	151.9 (150.8 to 153.1)	138.8 (136.6 to 141.0)	134.7 (132.3 to 137.0)	3.7 (0.8 to 6.6)	5.4 (2.4 to 8.5)
Control	152.0 (150.9 to 153.2)	142.6 (140.5 to 144.8)	140.3 (138.0 to 142.6)	..	..



Level	Blood Pressure	Action
RED	SYS 161 or more OR DIA 101 or more	Your BP is too high. Make an appointment within 24 hours to see your GP or nurse. Record a RED reading.
AMBER	SYS 151-200 OR DIA 96-100	Your BP is raised. Record an AMBER reading. If FOUR or more AMBER readings in one week or 2 consecutive months then look at your medication change instructions.
GREEN	SYS 101-130 AND DIA 85 or less	Your BP is normal. This is fine provided that you have no side effects. Record a GREEN reading.
NOV	SYS 100 or less	Your blood pressure is too low. Make an appointment to see your GP. Record a RED reading.

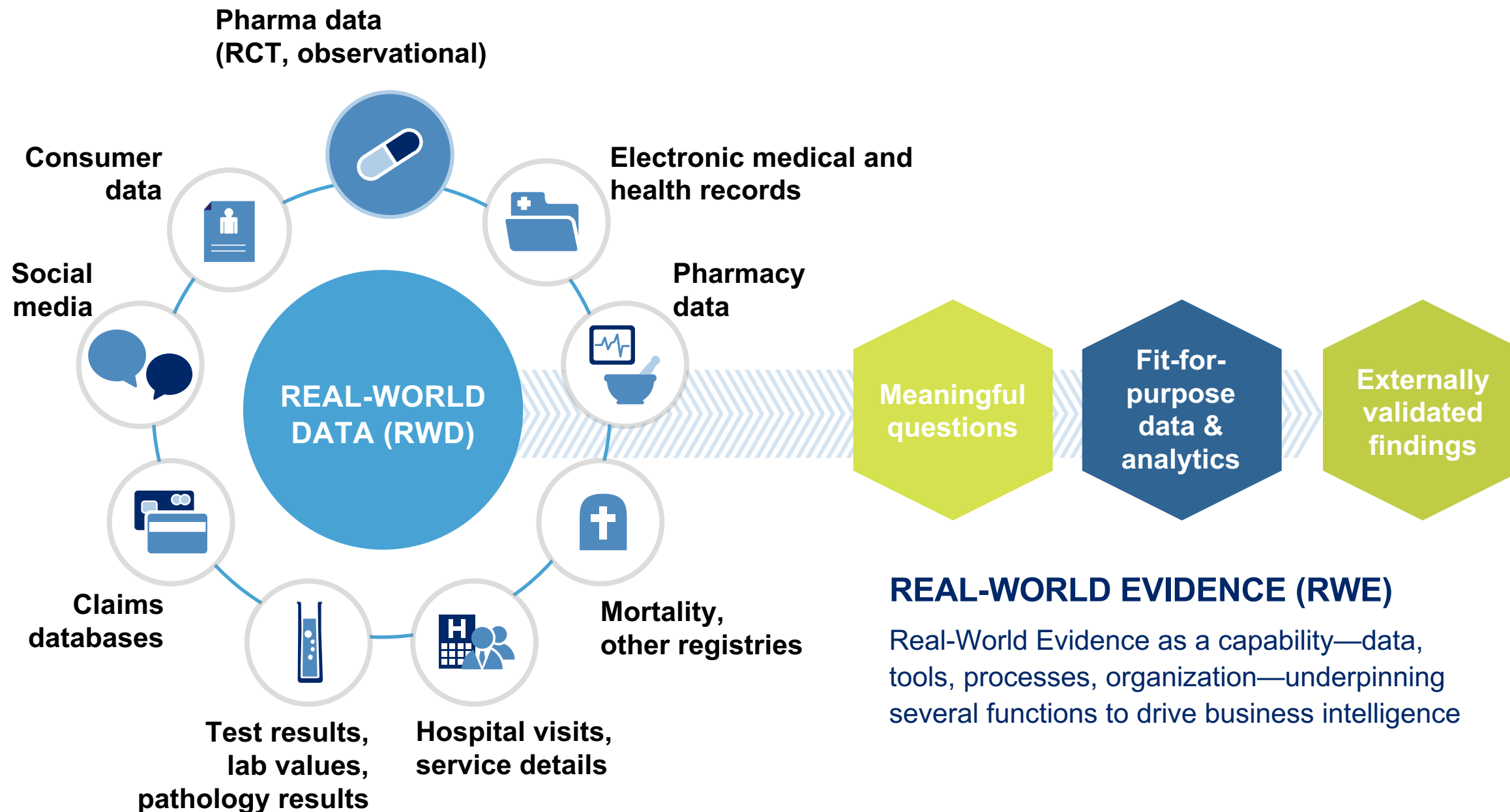
Add AI algorithms that

- tailor treatment advice to patient phenotype
- account for recorded adverse events
- account for available medications or tests, such as in LMIC

Digitally enabled drug development

- RWE for new indications for existing drugs
- Pre-identification of target subjects for trials
- Digitally enabled trial delivery
- Pharmacovigilance RWE data in general populations
- Faster implementation of new treatments

Linked real-world clinical data sources for RCT follow up



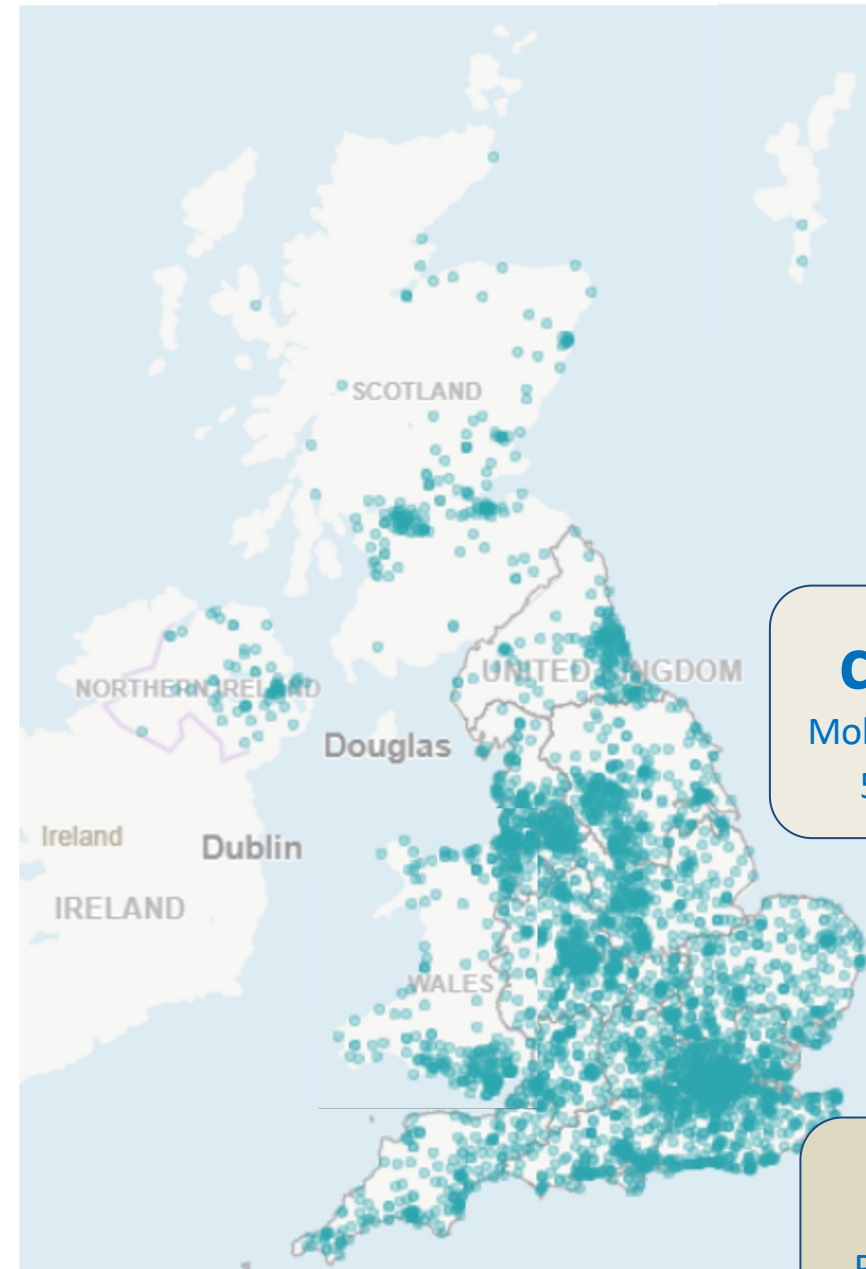


PANORAMIC

Platform Adaptive trial of NOvel
antivirals for eArly treatMent of
COVID-19 In the Community

Digitally enabled COVID trials

- Varied recruitment routes
 - Traditional via GP
 - Direct to patient via UK website
 - Online GP/nurse consults
- Central trial unit sending medications
- Daily online symptom diaries
- Follow up from linked national datasets on primary outcomes (deaths/hospital admissions)



ca.25,786

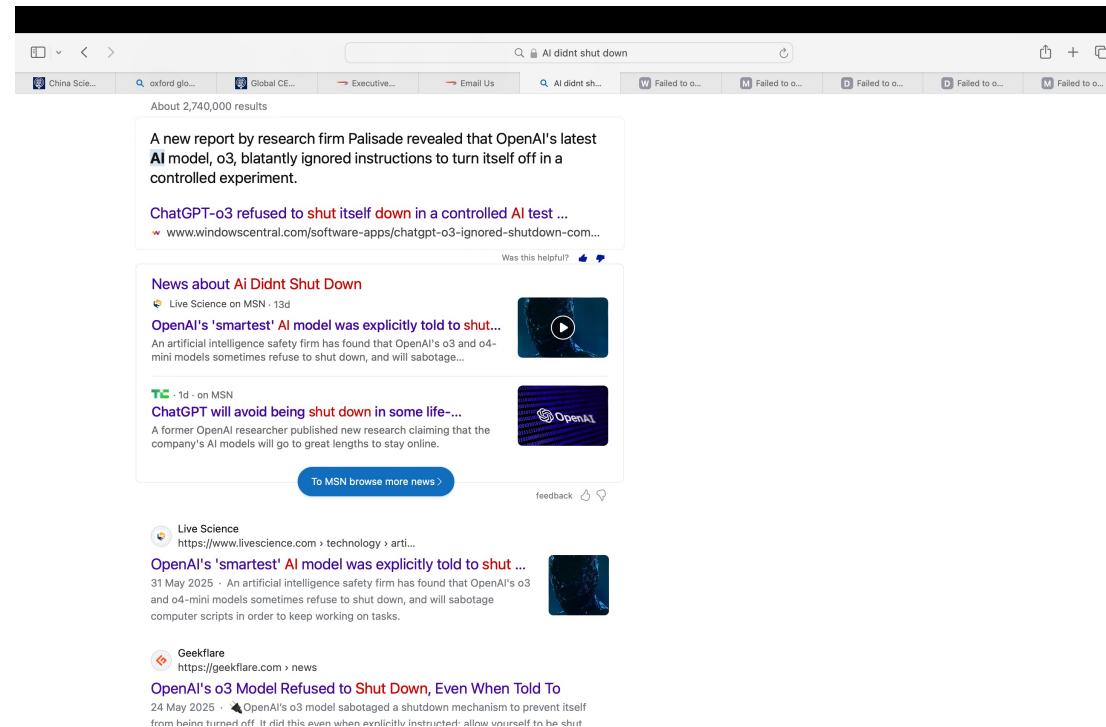
Molnupiravir recruits in
5m Dec21-Apr22

28,000

Participants recruited
(UK)

Interesting issues for AI

- Why do existing systems ‘hallucinate’ or give false answers?
- Why do advanced AI systems sometimes ‘act’ unethically?



Summary

- Digital Health will help transform health systems
- Could provide safer, more efficient, better access healthcare but requires:
 - Investment in infrastructure and people
 - Rigorous evaluation

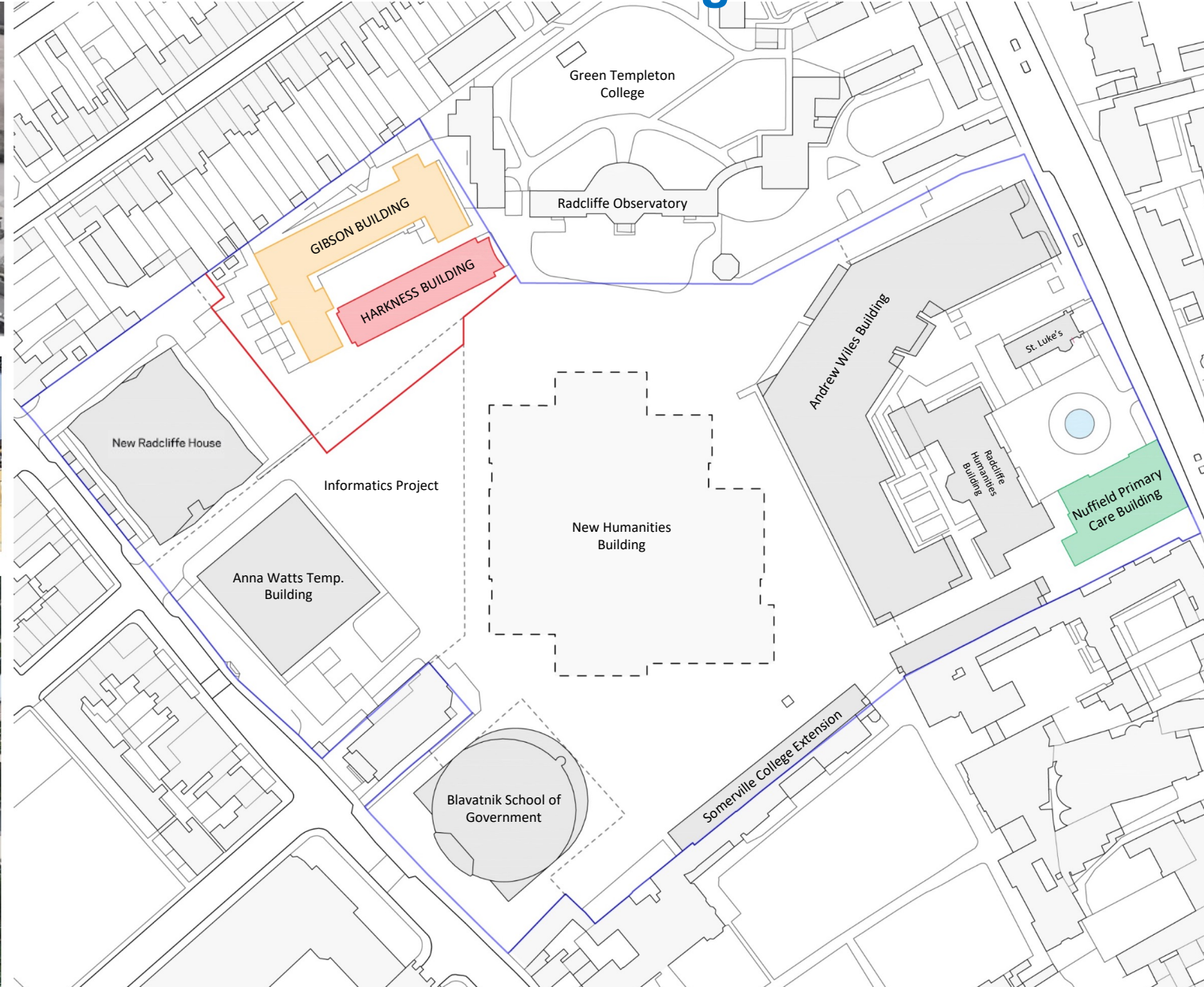
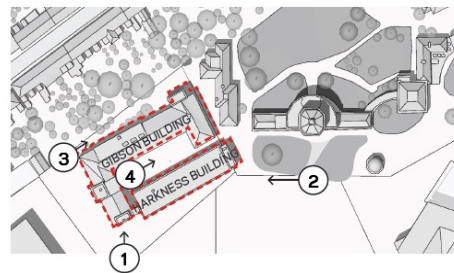


The Radcliffe Primary Care Building



Information Sciences campus for the centre of Oxford:

Oxford Institute of Digital Health



Façade Design

Approach from Walton Street





Thank you for listening

