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Current and future challenges
of innovative oncology drug
development



Digital Tools and AI in Oncology Drug Development

Dr. Dónal Landers

Strategic Director – digital Experimental Cancer
Medicine Team (digital ECMT)



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- What is AI?
- Challenges
- Examples of digital tools and AI in oncology drug development
- An approach to developing digital tools and AI methods– ‘Technology’ Clinical Trial



What is Artificial Intelligence?



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- **What is intelligence?**

- The ability to learn or understand or to deal with new or trying situations
- The skilled use of reason
- The ability to apply knowledge to manipulate one's environment or to think abstractly as measured by objective criteria (such as tests)

- **AI – science and engineering of making intelligent machines, especially intelligent computer programs**

- Acting humanly – Turing Test
- Thinking humanly – cognitive modelling approach: how nervous systems represents, processes, and transforms information
- Thinking rationally – The laws of thought approach - logic
- Acting Rationally – The rational agent approach
 - > Rational agent – has clear preferences, models uncertainty and performs an action with the optimal expected outcome for itself from among all feasible actions



AI definition and taxonomy



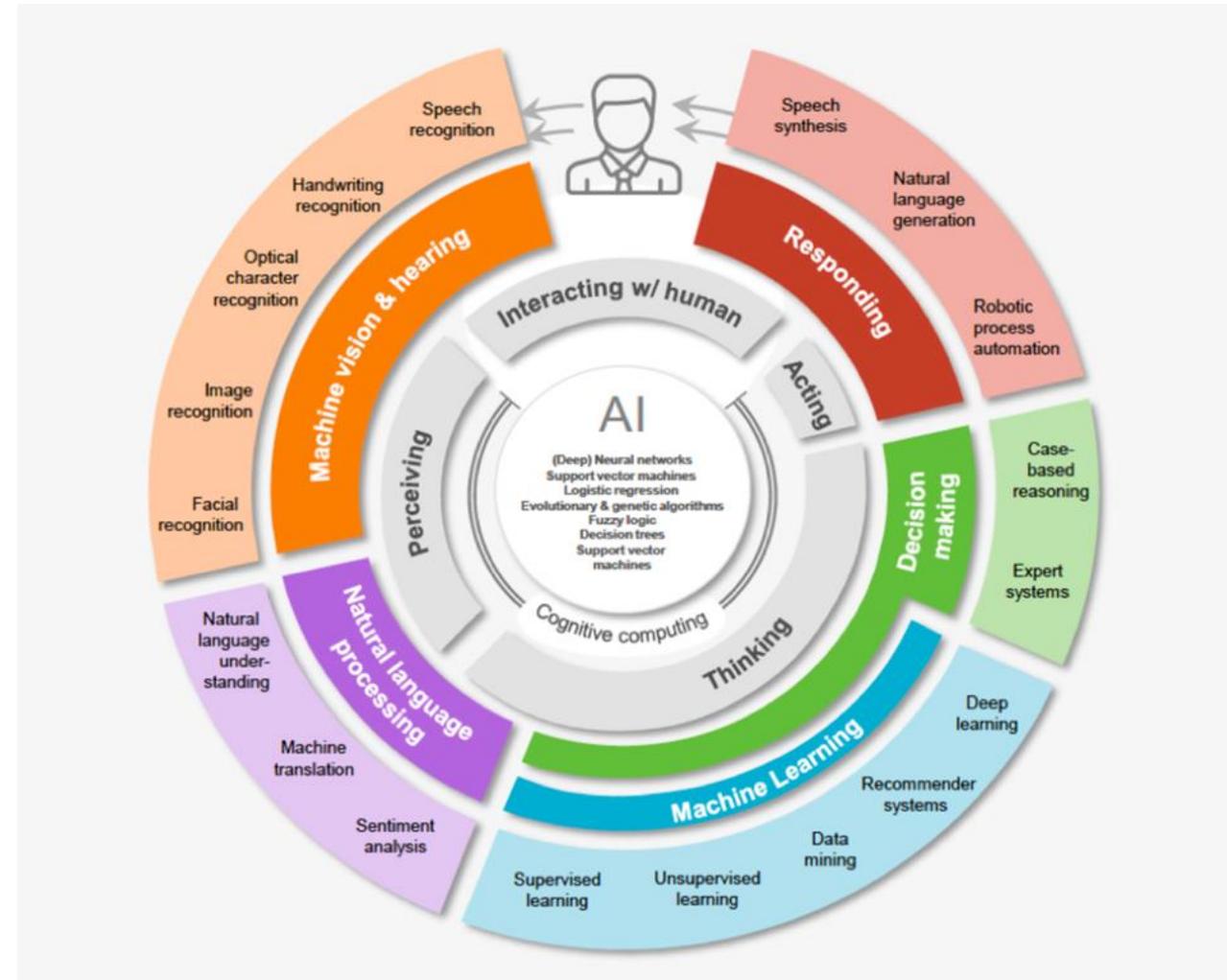
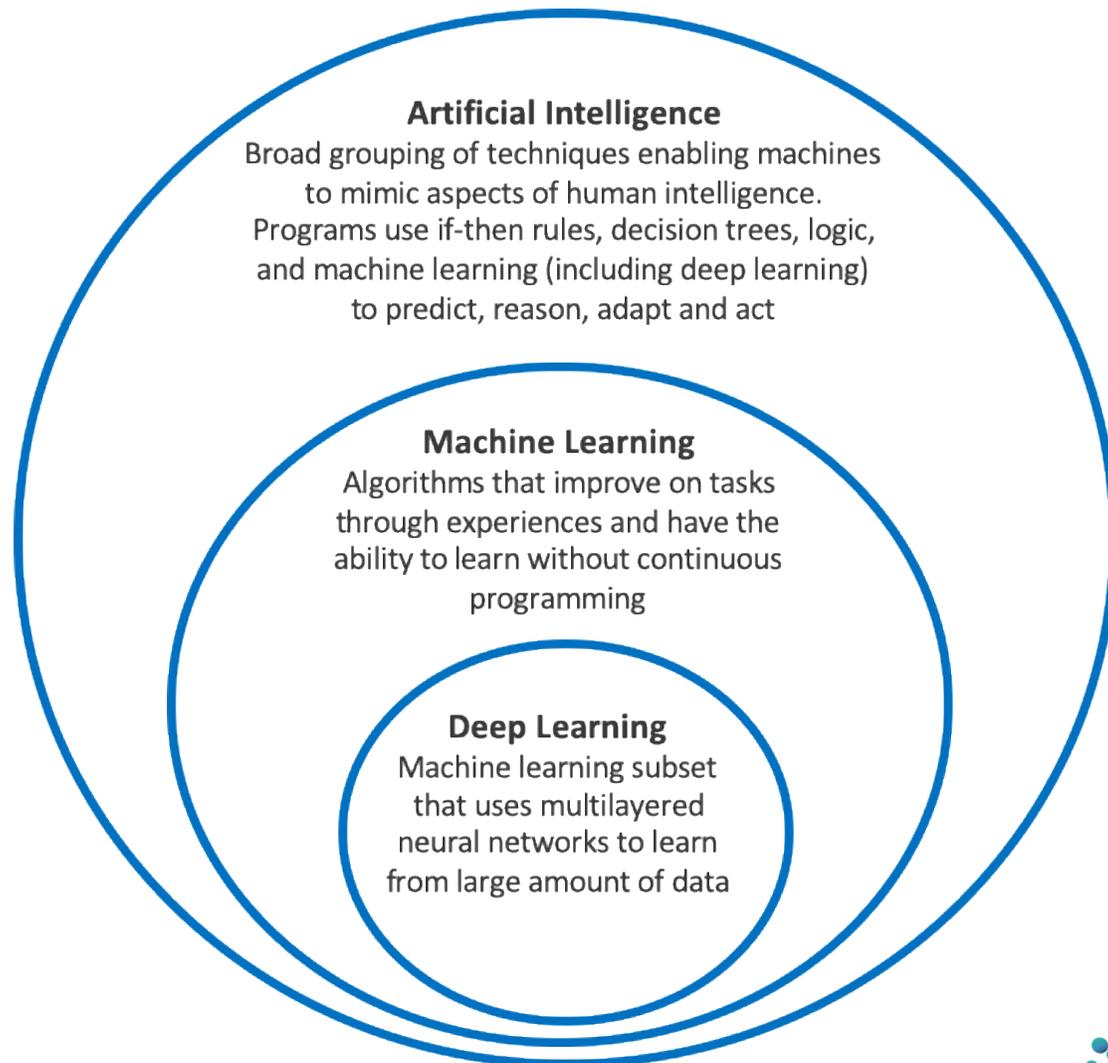
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Challenges in translating to the clinic



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Delivering clinical evidence of utility

- More retrospective than prospective studies and few RCTs

Outcomes

- Metrics often do not reflect clinical applicability – ROC versus Time to Event

Algorithms

- Ethically designed? – explainable, interpretable, fidelity
- Different algorithms
- Limitations of different machine learning methods
- Ability to generalise to new populations and settings
- Bias – discrimination, for profit

Training and test data

- Evolving clinical datasets with changing clinical practice – e.g. new cancer therapies, precision medicine
- Accidentally fitting confounders versus true signals

Implementation of AI

- Security - susceptibility to external hacks
- Availability of data, open datasets
- Regulatory and medicolegal issues
- Cultural issues – ‘black box’ implementations



COVID-19 risk in oncology evaluation tool



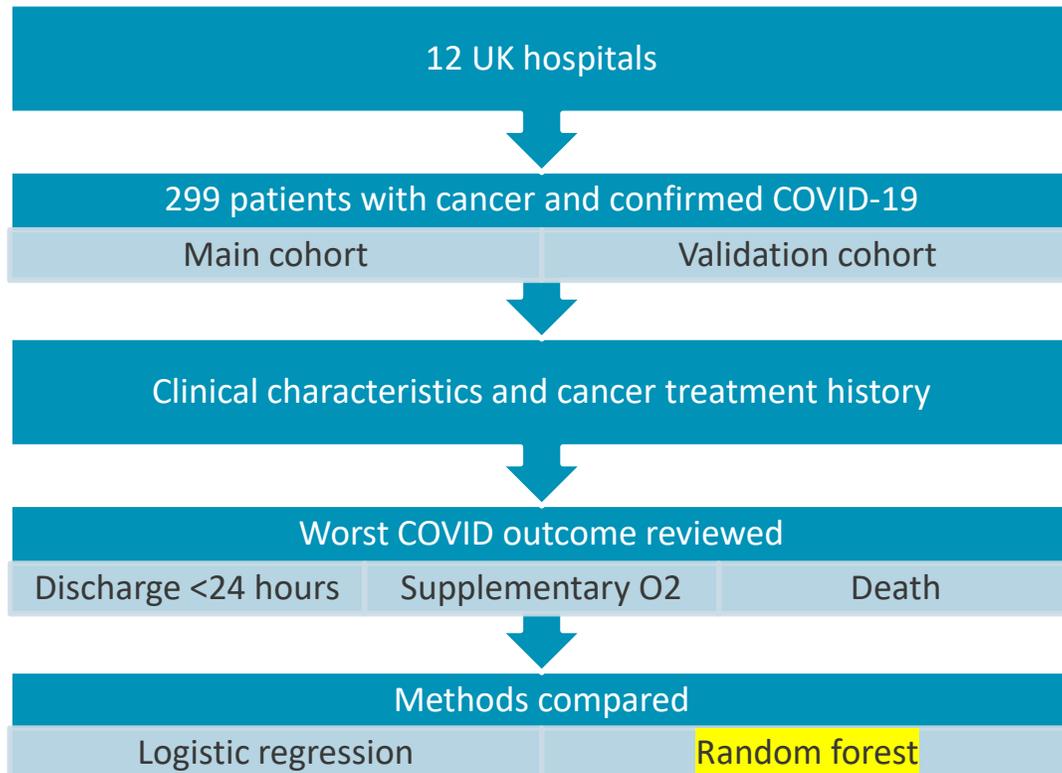
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- Establish a tool to identify patients suitable for immediate discharge versus those likely to have severe infection
- Inform clinicians and patients about likely COVID-19 severity



CORONET - COVID-19 Risk in ONcology Evaluation Tool

CORONET is an online tool to support decisions regarding hospital admission or discharge in cancer patients presenting with symptoms of COVID-19 and the likely severity of illness. It is based on real world patient data and information as to how the tool was created can be found here - [Link to publication](#)

What does CORONET do? Who is CORONET for? What are the limitations of CORONET?

CORONET asks for some details about the patient, their cancer and blood test results on presentation to hospital with symptoms of COVID-19. It then uses data about survival of similar patients in the past to show the likely outcome of the patient.

CORONET - COVID-19 Risk in ONcology Evaluation Tool

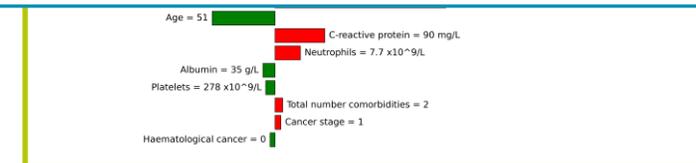
CORONET is an online tool to support decisions regarding hospital admission or discharge in cancer patients presenting with symptoms of COVID-19 and the likely severity of illness.

Contributions of the Features towards the Model Output

DISCHARGE (left) | ADMISION (right)

Feature	Value	Contribution to Discharge	Contribution to Admission
NEWS2	6	0	6
Age	51	51	0
C-reactive protein	90 mg/L	0	90
Neutrophils	$7.7 \times 10^9/L$	0	7.7
Albumin	35 g/L	35	0
Platelets	$278 \times 10^9/L$	278	0
Total number comorbidities	2	0	2
Cancer stage	1	0	1
Haematological cancer	0	0	0

NEWS2:



Explainable AI (XAI) - saliency maps



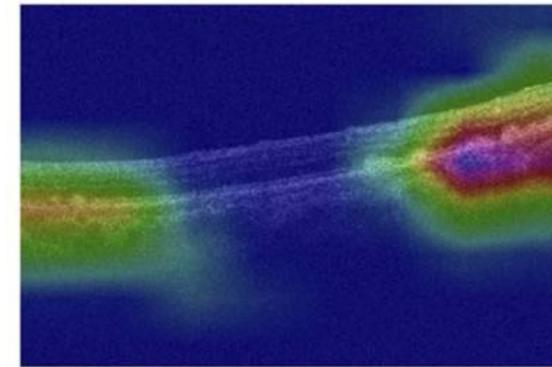
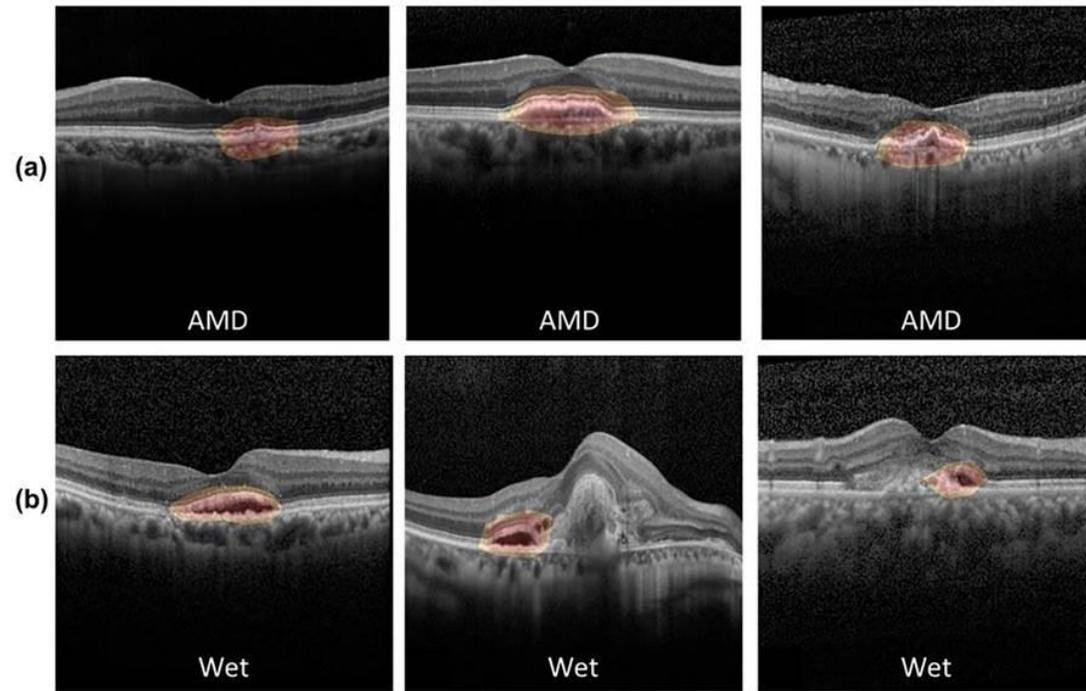
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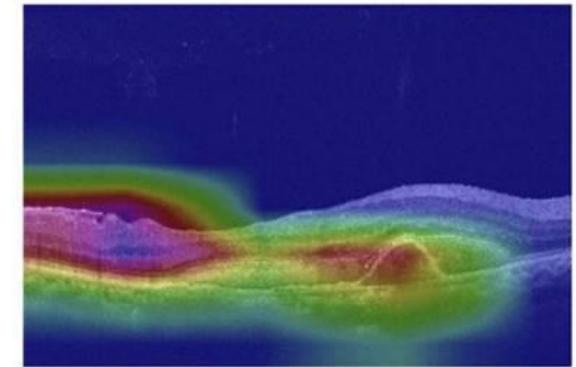
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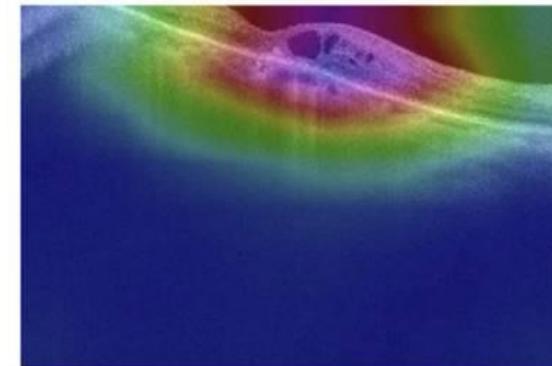
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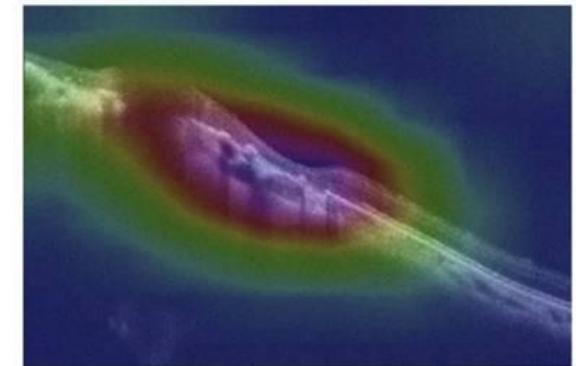
(a) Drusen



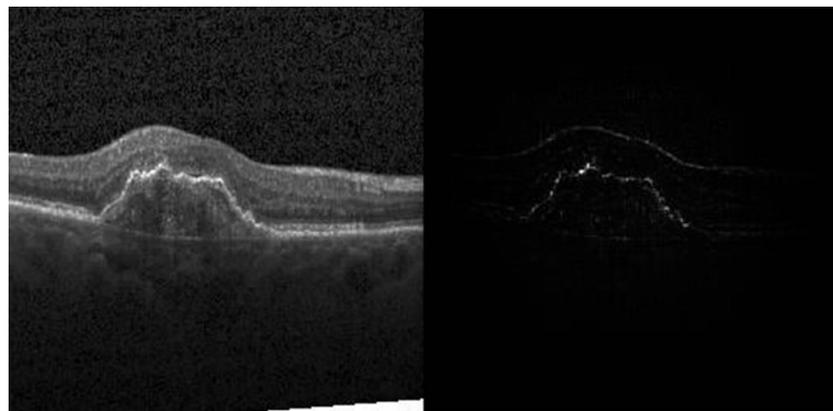
(b) Thickening of retina and PED



(c) Macular edema



(d) Retinal atrophy



An AI system is explainable if it is intrinsically interpretable or if the AI system is complemented with an interpretable and faithful explanation – ‘post hoc’ explainability

'Technology' clinical trial – positioning digital tools and AI



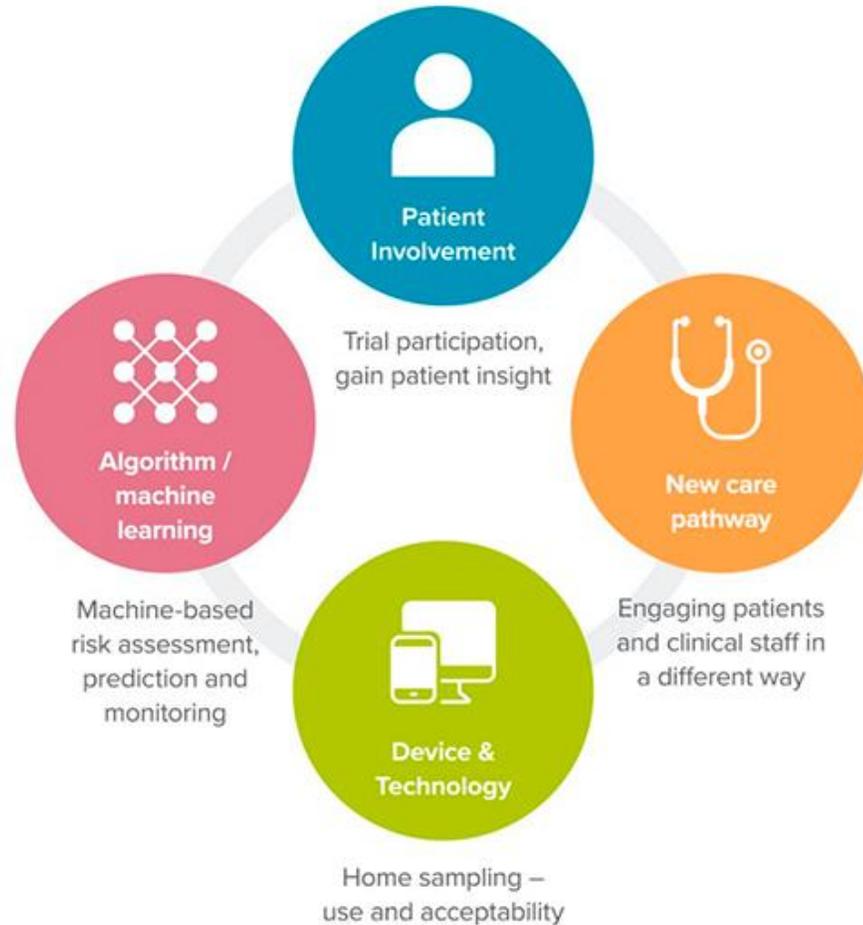
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Driver – augmenting clinical decision making to benefit the patient

- Changing the design, delivery and interpretation in early clinical trials
- Developing new care pathways
- Changing the role of the patient
- Hypothesis testing, proof of concept and prototyping for new technology

AI and digital tools

- Formally assesses:
 - Patient/clinical acceptability and feasibility
 - Clinical Benefit
 - Ethical and medicolegal implications
 - Patient engagement and education



Rationale for the 'technology' clinical trial



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Clinical care pathway development

- Ensuring the ethical adoption of 'technology' - software, device, process and particularly AI through testing in a formal clinical trial
- Wrong focus - clinical solution is perceived as an IT problem and not as a clinical care pathway problem affecting patients

Clinical culture

- Patients and healthcare professionals are not sufficiently involved in defining the clinical problem being addressed
- Building patient and healthcare professional trust and overcoming genuine skepticism

Artificial Intelligence

- AI 'noise' and 'hype' and the potential blind adoption of non-peered reviewed AI as part of a clinical care pathway
- Addressing the belief that AI is intelligent and has 'built-in' internal 'ethical' reasoning methods
- The importance developing of Explainable AI (XAI) methods to build trust
- Ensure that legal and regulatory considerations of AI are fully understood and addressed, e.g. GDPR, medical negligence
- The assumption that the algorithm has trained properly on a high data fidelity and fully representative data sets and is therefore generalizable



Developing a line-of-sight to a new clinical care pathway

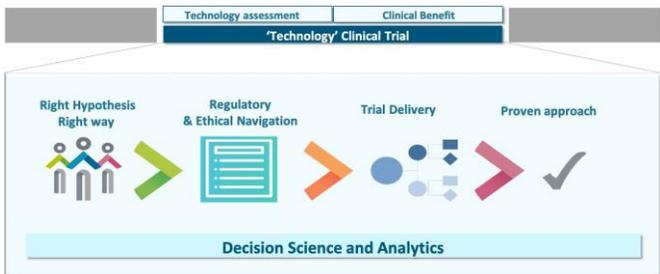


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- Identify clinical need
- Design the experiment
- Components
 - Patient involvement
 - Design lab
 - F2F meetings
 - Define the current 'as-is' process and the new 'to-be' process
 - **Technology**
 - **Algorithm (ethical)**
 - **Software**
 - **Device**
 - **Technology platform**

- Complete and publish the experiment (CSR, manuscript etc.)
- Full peer review
- Provide transparency
 - Data
 - Validity
- **Algorithm (AI development)**
 - **Explainable (XAI)**
 - **Interpretable**
 - **Reproducible**
- Demonstrate design of care pathway is ethical across all components

- Translate to clinical care pathway:
 - All technology components
 - Ensure scalability and reliability
 - Validate process
 - Continual clinical process improvement



- Developing digital tools for use in a clinical setting, particularly those that utilise AI methods, will become more commonplace, however, beware – ***do not assume these are ‘intelligent’ - maintain a healthy skepticism***
- Understanding the full ethical implications of AI in a clinical setting requires a robust clinical trial design, transparency, open development, publication of methods and datasets for peer review to build trust and clinical confidence in the algorithm – ***we require more randomised controlled trials to test AI tools and methods***
- The ‘technology’ clinical trial model provides a robust framework for assessing clinical feasibility, medicolegal implications and clinical benefit of digital tools and AI – ***a potential validation mechanism for AI utilisation in new clinical care pathways***
- Ultimately, our goal is to build better patient-centred clinical care pathways, utilising appropriate ethical AI through our current research however, - ***we’ve a long research road ahead***





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Thank you

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