The Haematology Laboratory of the Future

BSH ASM April 2025*

*First presented at Gallifreyan Society for Haematology 3025

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BSH Laboratory Specialist Interest Group

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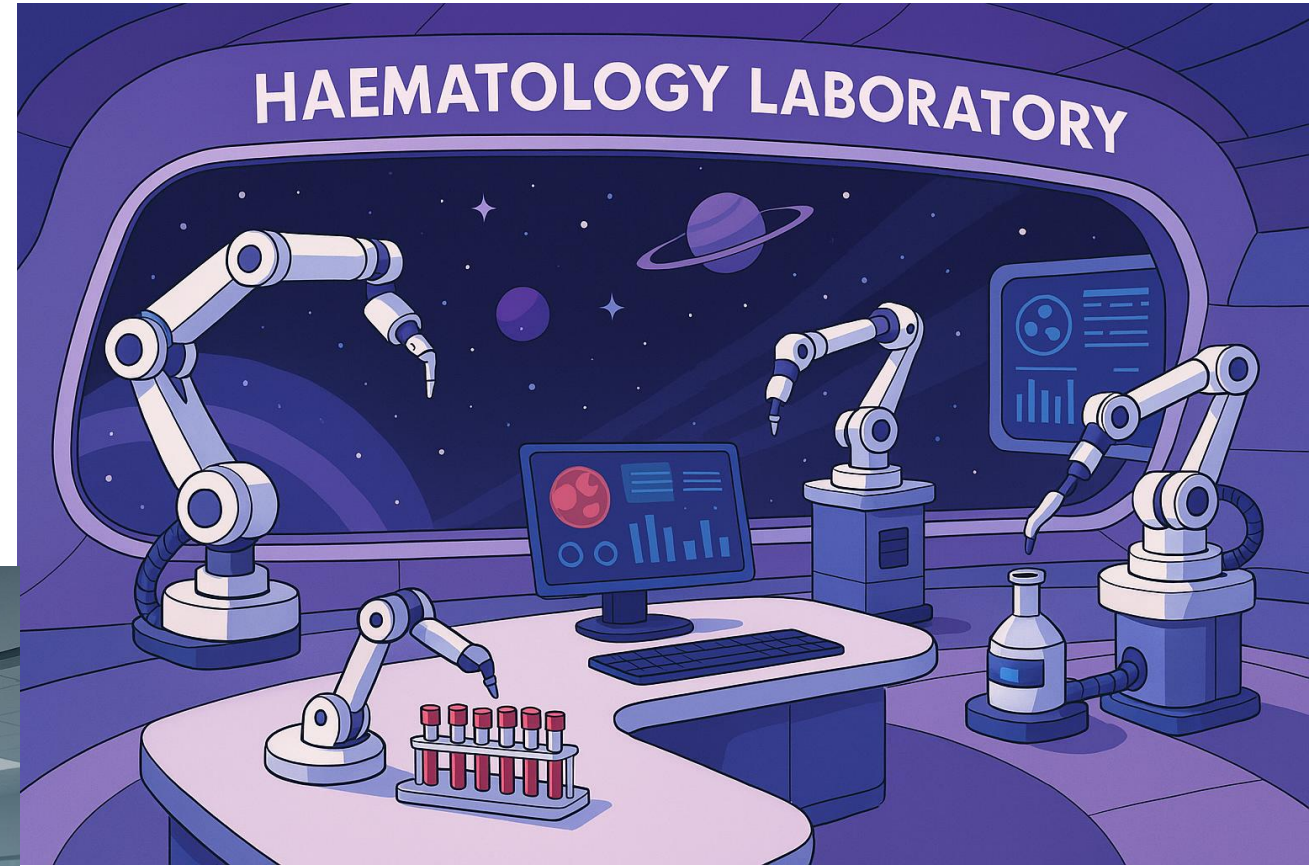
The Haematology Laboratory of the Future?

If in doubt, ask a nine-year-old…



The future is already here — it's just not very evenly distributed[1]

1. William Gibson

- Haematology: the cutting edge of personalised/precision/stratified medicine
- We have a duty to promote equity of care
- We want to learn
- **We are already living in the future**

bloodcancer.org.uk

- Blood cancer is the UK's third biggest cancer killer
- Blood cancer is the fifth most common cancer in the UK, with over 41,000 people diagnosed annually
- There are about 250,000 people living with blood cancer in the UK
- One in every 16 men and one in every 22 women will develop it at some point
- It is the most common type of childhood cancer

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We've been living in the future for a while....

Those that fail to learn from history are doomed to repeat it[1]

History of Laboratory Haematology prior to WWII[2]	
1628	Discovery of the closed circulation of blood by Harvey (St Bartholomew's Hospital)
1660s	First (unsuccessful) blood transfusions
1674	Description of RBCs by van Leeuwenhoek
1770-4	Discovery of WBCs, fibrinogen, the first anticoagulant (Glauber's salt), and the fundamentals of blood coagulation and lymphatic circulation by Hewson
1818	First successful transfusion of human blood to a patient by Blundell
1852-76	Development of RBC and WBC counting by hemocytometer by multiple investigators
1868	Discovery of the role of the bone marrow in hematopoiesis by Neumann and independently by Bizzozero
1868	Virchow describes leukemia, thrombosis, and embolism
1901	Discovery of blood groups, A, B, AB, and O (C) by Landsteiner
1910	First description of sickle cell disease by Herrick
1929	Hematocrit technique refined by Wintrobe, along with introduction of RBC indices MCV, MCH, and MCHC
1929	First description of sternal puncture to obtain bone marrow by Arinkin
1934	Classification of anemias based on RBC indices by Wintrobe
1935	Development of the PT by Quick
1937	Identification of a globulin fraction of plasma as containing the antihemophiliac factor (later factor VIII) by Patek and Taylor
Lots after WWII..	

1. Winston Churchill
2. Coller B Blood at 70: its roots in the history of hematology and its birth *Blood* 2015 Dec 10;126(24):2548-60

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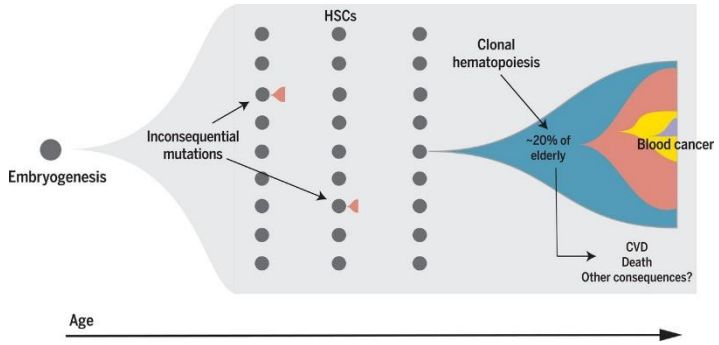
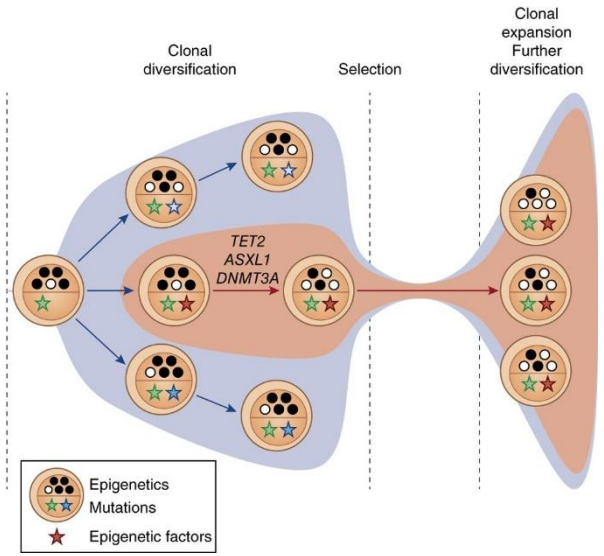
Why is Haematology at the cutting edge of precision medicine?
Biology of blood cancers make them easy to study and target

- Biology of blood cancers relatively simple:
  - BCR::ABL1 positive Chronic Myeloid Leukaemia (1960)
  - Acute Leukaemias, MPNs, lymphomas
- Younger age of some patients
- Aging and **clonal haematopoiesis**:
  - Stem cells
  - CHIP, MGUS, MBL
  - CHIP: Importance for cardiology and medical oncology?
  - What is normal?
- Evolution of subclones, **resistance and relapse**
- Each patient's cancer and **MRD target** is unique?
- **Inherited diseases**:
  - Haematologists pioneered molecular medicine and treat the most common inherited disorders (sickle cell, thalassaemia, haemophilia, haemochromatosis)
  - Blood cancers with inherited predisposition: increasingly defined entities





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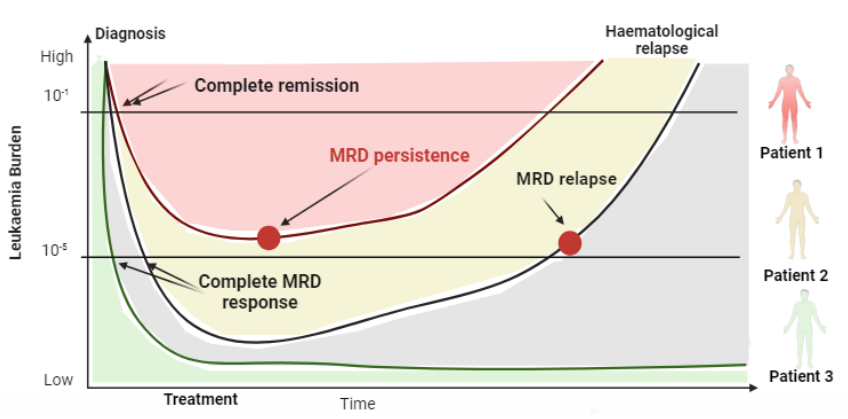
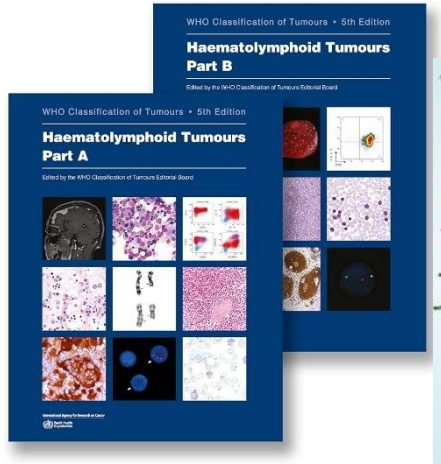
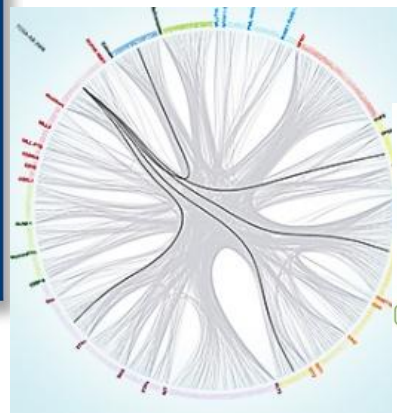
Haematological malignancies:

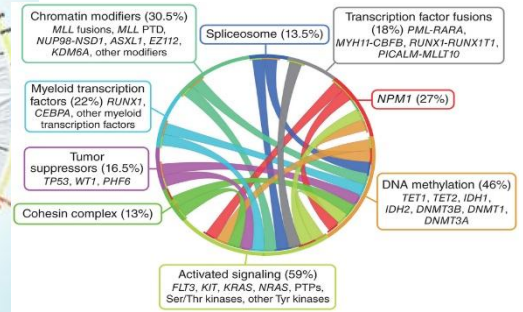
Why is Haematology at the cutting edge of precision medicine?

- Haematology medics *and* scientists: **Pathologists *and* Physicians *and* Researchers**
- **Access to samples** is easier for research and treatment
- **Treatments/actionable targets:** Chemotherapy, TKIs, immunotherapy (SCT, CART, IMIDs), multicentre trials, gene and cellular therapies
- **Personalised treatment/Precision Medicine:** Measurable Residual Disease (MRD), Genomic prognostication, Diagnostic classifications driven by genomic discoveries
- **Integrated diagnostics**





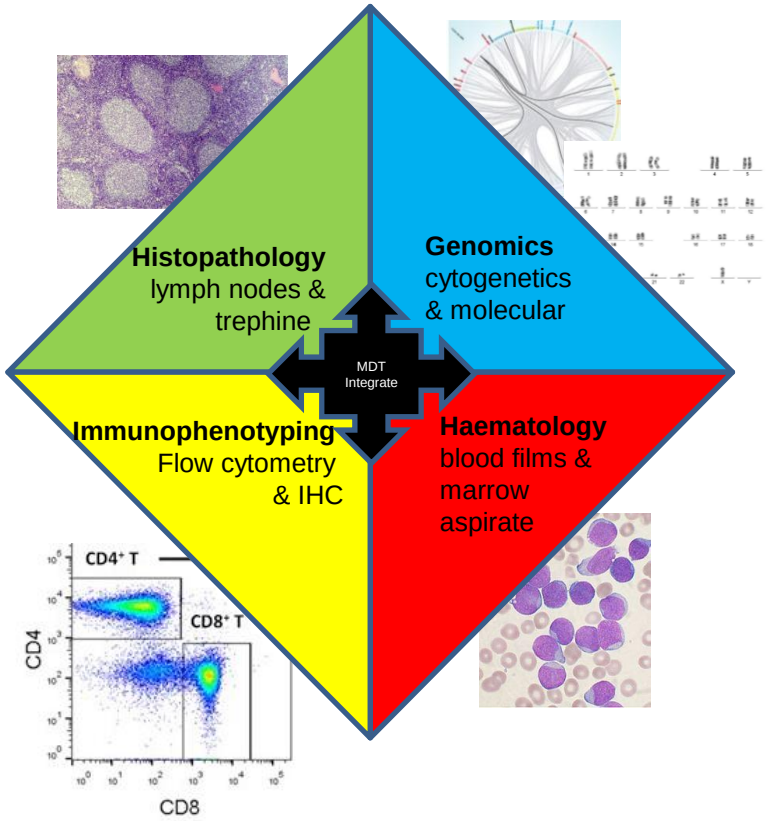




SIHMDS: NICE guidance on integrated diagnosis

Specialist Integrated Haematological Malignancy Diagnostic Services

- **"Improving the consistency and accuracy of diagnosis is probably the single most important aspect of improving outcomes in haematological cancer"[1]**
- Key concept is integration: no single modality answers the diagnostic question
- Studies suggest that 5–15% of blood cancers are misdiagnosed outside an SIHMDS setting
- A relatively small investment in pathology at the beginning of the pathway: greater effect on the patient and on the NHS than high-cost drugs
- Demand optimisation of high-cost tests
- Cancer MDT alignment
- **The model for blood cancers has also informed integrated reporting in solid tumours[2]**



1. Ireland R. Haematological malignancies: the rationale for integrated haematopathology services, key elements of organization and wider contribution to patient care. *Histopathology* 2011;58:145–154

2. Royal College of Pathologists. *Standards for Integrated Reporting in Cellular Pathology*: www.rcpath.org/uploads/assets/442fcdc1-af22-401f-8fcd1b4b65603810/G155-StandardsIntegratedReportingCellPath-Jan17.pdf

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Challenges to integrated diagnostics:

Inequity across UK
Focus on different parts of pathway

- **Coordination and investment:** Need for single specimen reception and collocated laboratories at a single site; Multiprofessional staff work within a single quality management system; Single IT system to produce an integrated diagnostic report; National genomics IT system and national tariffs: not yet realised
- **Collocation** is main recommendation of NG47[1]: *1.1.1 Take into account that recommendations … are most likely to be achieved if the component parts of the specialist integrated haematological malignancy diagnostic services (SIHMDS) are located at a single site*
- Implementation of all 32 recommendations across single-entity or *collocated* SIHMDS is more achievable than *networked* SIHMDS that send tests to a different lab[2]. **Networked models are inherently less efficient and accurate** than single site models: challenging integration, turnaround times, reflex testing and increasing costs.
- **Differences in Culture, Training, Governance, Communication silos**: Haematologists *vs* Histopathologists *vs* Scientists *vs* Clinical Geneticists. Pathology Networks *vs* GLHs.
- **Patients don't tell you they might have a blood cancer: '**Backdoor' lymphomas. Leukaemia diagnosis usually happens via emergency routes. Need to design systems that can diagnose patients from EDs or GPs, not coming via planned 2ww/FDS pathways.

1. *Haematological Cancers: Improving Outcomes*. *NICE Guideline NG47*. www.nice.org.uk/guidance/ng47

2. Cartwright A, et al. J Clin Pathol 2022;0:1–6. doi:10.1136/jclinpath-2021-208075

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Haematology at the cutting edge of precision medicine

SIHMDS and Haematology laboratories:
Centres of excellence, driving innovation, taking us into the future

- Pioneering introduction of **latest genomics and other diagnostics techniques into mainstream NHS care**
- Pioneering **digital pathology and AI** in analysing blood counts, flow cytometry, images, genomic data
- Requirement for **integrated diagnostics**
- Pressure for **faster** and **more sensitive** genomic tests
- Genomic and diagnostic technology is changing rapidly
- Lab SIG and HMDS Network: **supported by BSH**
- **The Future is already here, it's just not very evenly distributed**

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HMDS Network

Supporting a network of Haematological Malignancy Diagnostic Services in the UK, working with other national organisations

Aims

Collaboration, Communications, Liaison, Education, Training, Workforce Planning, Audit, Peer Review, EQA, Research, Epidemiology, Clinical Advice, Equity of Access

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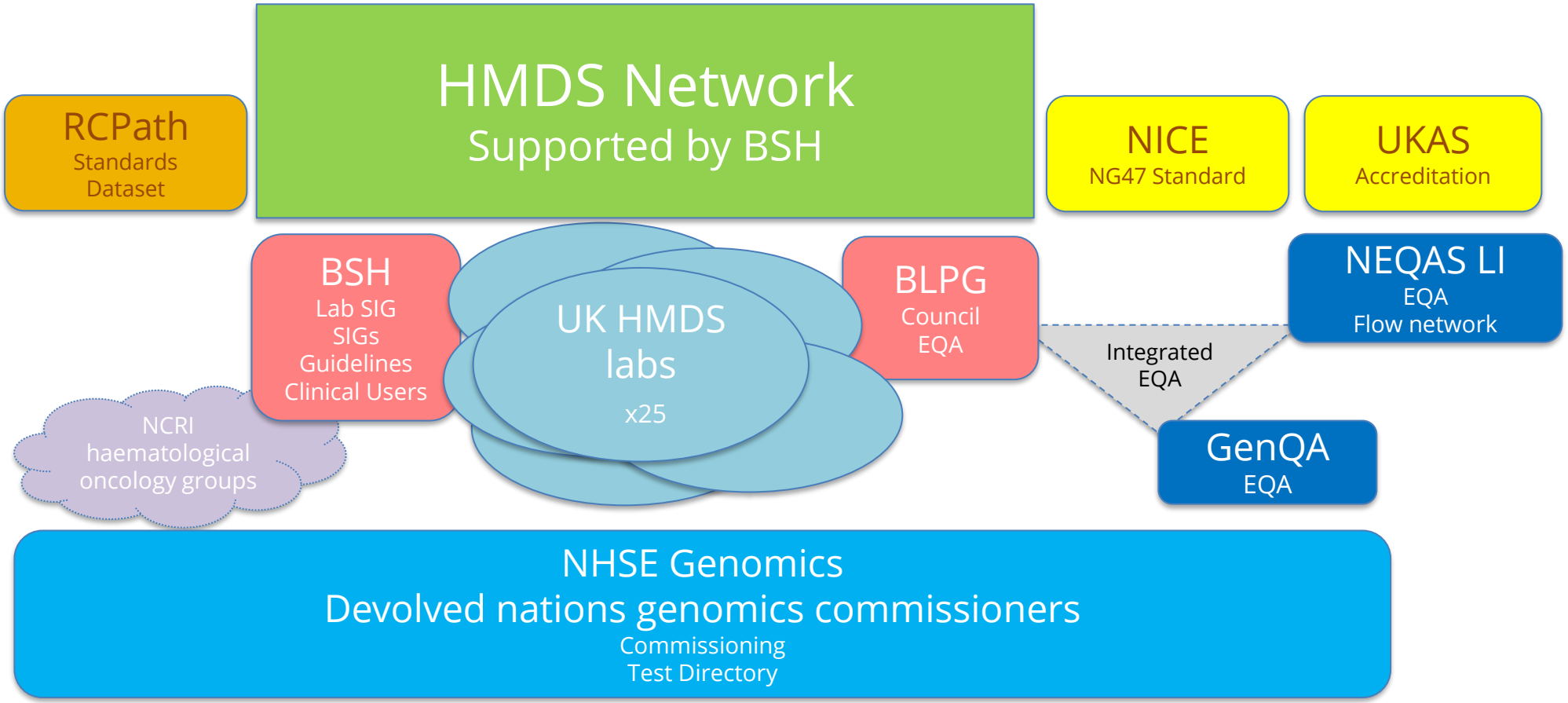

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HMDS Challenges: New GMS Haem-Onc TAT targets:

Clinical need is for faster turnaround times for relatively small number of variants + higher sensitivity

Urgency Category	Clinical Scenario	Suggested Test Method	TAT (days)	Examples (Please note these are for indicative purposes)
Very urgent	Very urgent diagnostic / treatment determining	RT-PCR / targeted mutation testing e.g. fragment analysis / FISH	3[a]	*PML::RARA*
				MYC translocation in Burkitt lymphoma
				BCR::ABL1 for ALL
				FLT3 / NPM1 mutation testing in AML
				CBF FISH testing in AML
	Urgent upfront treatment determining (including at relapse)	Targeted mutation detection / Limited NGS panel	7	*TP53* in AML / selected lymphomas (e.g. HCL, LPL if morphological uncertainty) / (rarely *TP53* in CLL)[c]
		FISH	7[b]	ALL / AML / (rarely CLL)[c]
		Karyotype	7[b]	ALL / AML / CML (including in transformation) if being used to stratify treatment upfront / other
	Urgent monitoring	Chimerism	7[b]	Post-BMT when concerns re relapse / decision re DLI
		FISH / Karyotype	7[b]	AML / ALL concerns re relapse / required to plan imminent treatment
		(RT)-qfPCR	7[b]	AML / ALL concerns re relapse / required to plan imminent treatment

Urgency category	Clinical scenario	Suggested Test Method	TAT (days)	Examples (Please note these are for indicative purposes)
Urgent	Urgent diagnostic pathway	RT-PCR / FISH	7[b]	*BCR::ABL1* in CML / FISH in DLBCL if being used to alter 1st cycle of treatment / FISH in MCL
		Clonality	7	B cell / T cell clonality in suspected aggressive lymphoma where clonality is being used to determine diagnosis

Urgency category	Clinical scenario	Suggested Test Method	TAT (days)	Examples (Please note these are for indicative purposes)
Routine	Diagnostic[d]	FISH	14	Lymphoma
		NGS panel / targeted mutation testing	21[b]	MPNs
		Clonality[e]	21	indolent lymphoma
		FISH	14	Additional AML FISH e.g. MyeChild extended panels / cryptic targets / myeloma if treatment determining
		FISH	21	Myeloma if being performed for prognostication

"Technology is constantly changing: NGS is getting cheaper and quicker, and the drive will be towards local SIHMDS rapid NGS testing as new treatments depend on results that may be needed in 24-72h. "

NGS panel targets increasingly needed sooner, limited single gene PCR for rapid tests becoming obsolete method:

- Some tests **needed in a few hours**
- *NPM1/FLT3:* **needed in <72h**
- NGS targets:
  - *IDH1/2….?*
  - *TP53….?*
  - *Next variant….?*
- Same genomic platforms and staff needed for urgent and routine wet work and analysis, duplication is inefficient

Pressure to decrease TAT as new treatments require knowledge of actionable variants

Pressure to increase MRD **sensitivity** whilst decreasing MRD TAT

NHS Genomic Medicine Service Testing Strategy

By 2035, genomics are predicted to be part of over 50% of all healthcare episodes and used across a patient's lifetime

Non-invasive pre-natal diagnosis

~650k babies born in England each year screened for treatable rare conditions

Early diagnosis and intervention for childhood onset conditions

Early identification of adults at high risk e.g. inherited cancer/ cardiovascular disease

Avoid adverse drug reactions e.g. in stroke care/better tailored medicine dosing based on genetic risk profile (PGx)

Early diagnosis, tailored treatment and improved monitoring for cancer

Identification of adults at high risk of developing conditions more common in later life e.g. dementia

Three big shifts – Forthcoming NHS Ten Year Plan – the time is now

Moving more care from hospitals to communities

Moving from an analogue to a digital NHS

Moving from sickness to prevention

How will it be delivered?
Cancer

- ✓ Integration into the patient cancer pathway
- ✓ Centralised testing
- ✓ Delivering rapid testing
- ✓ Cost effectiveness
- ✓ Automation
- ✓ Stratified data interpretation
- ✓ Close working with Cellular Pathology and SIHMDS
- ✓ No bottle necks

Core services

Move from targeted NGS gene panels (DNA/RNA)

- Solid tumours: DNA exome sequencing*
- HaemOnc: Rapid WGS with extended exomes for FFPE tissue*
- RNA sequencing for fusions and expression
- Expanded targeted monitoring assays

* (including clinical trial targets) and PGx

Benefits

- ✓ Increase genomic knowledge for each cancer patient
- ✓ Provide earlier access to trial where appropriate
- ✓ Provide germline pharmacogenetics findings from one sample/one test
- ✓ Increase scope of fusion testing through extensive DNA and non-targeted RNA approach
- ✓ Minimal residual disease information provides opportunities for escalation / de-escalation

Whole Genome Sequencing

- ➢ Delivered by a defined number of GLHs
- ➢ Rapid tumour first approach for HaemOnc
- ➢ Tailored analysis approach based on classification and treatment
- ➢ Implementation of Long Read Sequencing where appropriate for clinical utility

Benefits

- ✓ Decrease turnaround times
- ✓ Opportunity to develop GLH based bioinformatics pipelines as national protocol
- ✓ Integrate a multimodal approach to deliver an appropriate service

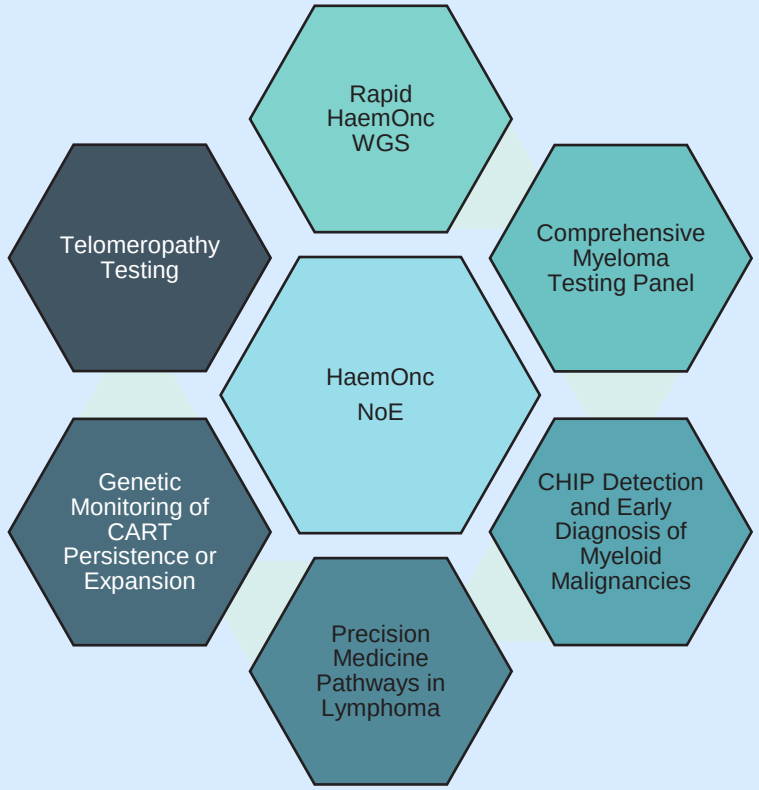
How will it be delivered? *HaemOnc*

Plan for Rapid WGS

- Create a **simplified pathway** for WGS delivery.
- Aim for **7day** TAT.
- Predicated on a **tumour only pathway**, but with option for germline follow up if required.
- Start with **ALL and AML**, and expand to **MDS, MPN and LPD.**
- Utilise current **GEL bioinformatics** pathway.
- Working towards a **suite of clinical indication specific pipelines.**
- **Variant database** to support analysis.

HaemOnc Network of Excellence

Identified gaps in provision and targeted projects



Detection of germline variants & WGS?

- Pathogenicity not always known at time of testing
- Impact over lifetime: genetic risk factors, polygenic risk scores, pharmacogenomics, WGS at birth?
- Impact on family members
- Consent
- Tumour only *vs* germline
- 7-day TAT for WGS, that covers all haem-onc malignancies…?

Prenatal & Paediatrics

- Realise the benefits of fetal sequencing
- Increase number of diseases tested by non-invasive prenatal diagnosis
- Commission non-invasive prenatal testing for common aneuploidies
- Preconception carrier screening to identify potential for high risk pregnancies in defined populations
- Preventation of disease through reproductive choices (prenatal diagnosis and Preimplantation Genetic Testing)

Non-invasive pre-natal diagnosis

~650k babies born in England each year screened for treatable rare conditions

- As evidence is built through the Generation Study, implement newborn screening throughout NHSE to identify affected newborns with treatable conditions
- Generate evidence on clinical benefits of using WGS data of newborns
- Develop safe and useable data systems to support this work
- Lifetime source of genomic data

Pharmacogenomics & Risk stratifcation

- Use pharmacogenetics to identify individuals at high risk of adverse drug reactions and stratify treatments based on metabolic efficiency
- Target groups where drug stratification is effective e.g. mental health treatment
- Build the system to enable calling of PGx drug/gene pairs on all individuals receiving a genomic test
- Work towards high throughput testing, centralised service requiring minimum scientific input
- Develop IT solutions/NHS App to provide the information when required, wherever.

- Presymptomatic testing of high risk individuals e.g. BRCA testing of family members, targeted populations.
- Identification of high risk individuals for developing dementia, suffering from cardiovascular events etc through genomic testing
- Close working with R&D to bring insights into disease development into clinical use
- Use pharmacogenetics to improve understanding of drug interactions in the elderly to reduce hospital events and increase drug effectiveness

23andMe Just Filed for Bankruptcy. You Should Delete Your Data Now.

Updated March 25, 2025

The New York Times

Although the company has promised to continue protecting customer data amidst a possible sale, California's attorney general has advised 23andMe users (15 million people) to consider deleting their information.

After a 2023 data breach in which attackers gained access to information from close to 7 million customer profiles, 23andMe's stock price plummeted

As a geneticist, I will not mourn 23andMe and its jumble of useless health information

Adam Rutherford

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Technology

23andMe users struggle to delete their highly sensitive data

The computer systems of 23andMe have been struggling to cope with the sheer volume of customers racing to delete their data, after the DNA-testing company announced that it was filing for bankruptcy protection.

The firm says it has now resolved the IT problems caused by increased traffic on its website at the start of the week.
But users have reported ongoing difficulties as they scrambled to protect their genetic information, health histories, and ancestry details.

Direct to Consumer Testing (DTCT)

- Direct-to-consumer testing (DTCT) refers to commercial laboratory tests initiated by laypersons without the involvement of healthcare professionals [1]
- Improving test accessibility and choice for consumers. Reducing delays, logistics, and costs associated with clinical consultation
- Overutilization of healthcare resources through confirmatory testing and downstream clinical visits
- Huge variations in usage and regulation around the world

1. Direct-to-consumer testing as consumer initiated testing: compromises to the testing process and opportunities for quality improvement. An opinion paper from the EFLM DTCT-Taskforce. P Shih et al *Clin Chem Lab Med* 2024 Aug 14.

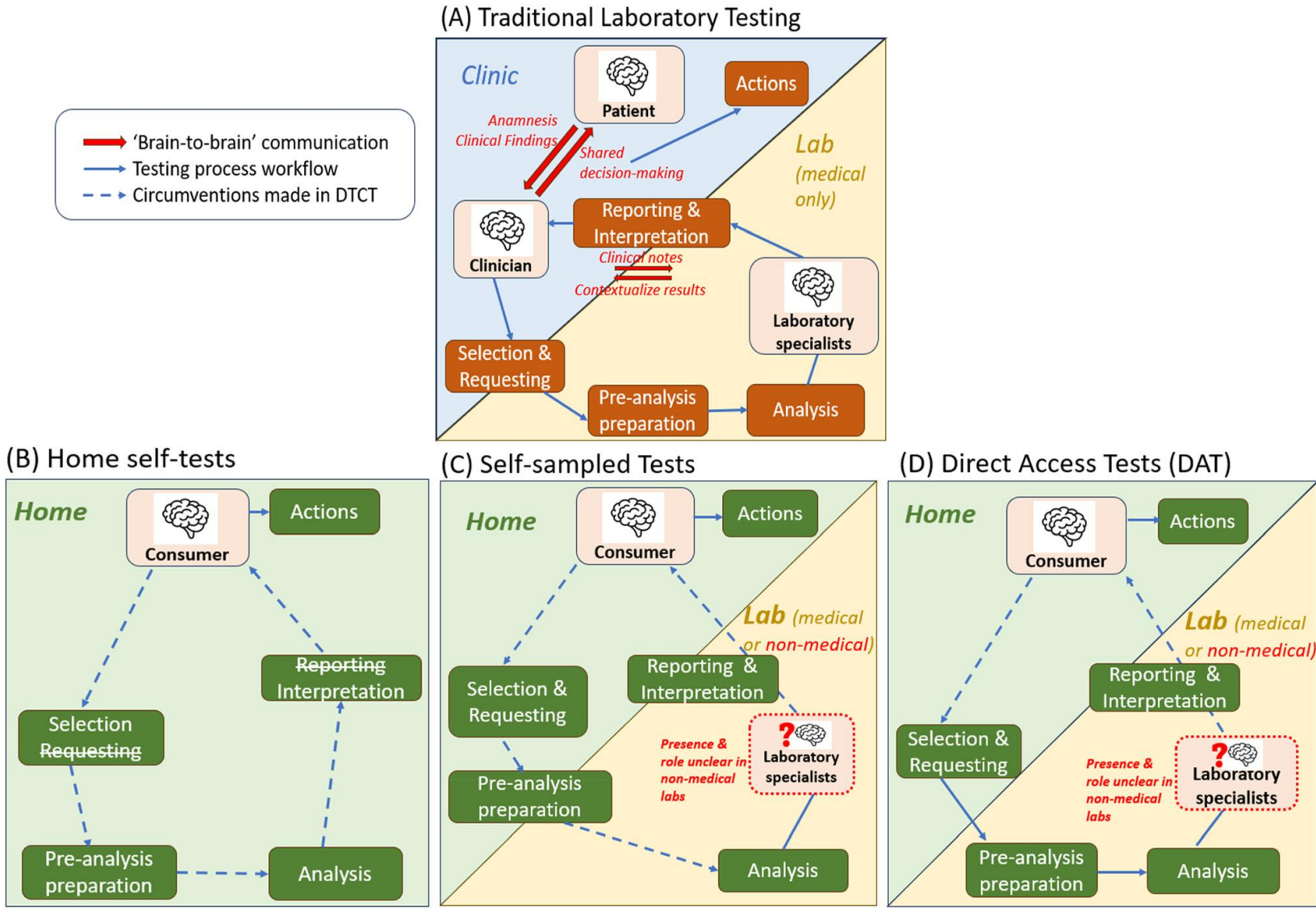
Direct to Consumer Testing (DTCT)

- The DTCT market is expanding rapidly, growing 20-fold between 2010 and 2020, and expected to worth US$6.32 billion by 2032
- growing number of DTCT are now conducted in non-medical, non-accredited laboratories, which are not regulated under the same performance standards applicable to medical laboratories
- Non-evidence-based tests or tests still under research and development are also being sold directly to the public
- To avoid regulation as medical tests, some products are described as promoting ‘wellness’ and a ‘healthy lifestyle’

Traditional testing
Collaborate closely with clinicians and patients in a ‘brain-to-brain loop’ of communication and decision-making

The absence of clinicians in DTCT creates gaps in information flow. Any errors in test selection, pre-analysis, analysis, and post-analysis will eventually impact on consumers’ health outcomes

DTCT introduces a fundamental circumvention to the total testing process by making consumers the sole human agent responsible for almost all decision-making in testing



1. Direct-to-consumer testing as consumer initiated testing: compromises to the testing process and opportunities for quality improvement. An opinion paper from the EFLM DTCT-Taskforce. P Shih et al *Clin Chem Lab Med* 2024 Aug 14.

Circumventing the total testing process: potential benefits and harms of DTCT

- The movement away from traditional clinical testing to consumer-initiated testing is purported to empower, not harm consumers
- Gives consumers more control of the process, this should complement, not add burden to the healthcare system

But

- The diversity of DTCT modalities and the uneven way in which they are regulated causes confusion for consumers and health professionals alike
- Need to look beyond the attributes of test accessibility and personal choice. Ensuring higher quality in the whole testing process must be paramount
- **Establishing dedicated regulation will be a right step in this direction**

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Point of care testing, non-invasive testing, DTCT

theranos

one tiny drop changes everything.

At Theranos, we're working to shape the future of lab testing. Now, for the first time, our high-complexity CLIA-certified laboratory can perform your tests quickly and accurately on samples as small as a single drop.

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Theranos founder Elizabeth Holmes loses fraud appeal

Mallory Moench

BBC News

Point of care testing, non-invasive testing, DTCT

Salat-Tora et al Point-of-care BCR::ABL1 transcript monitoring using capillary dried blood in chronic myeloid leukemia patients *Leukemia* . 2024 Aug;38(8):1822-1824

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Point of care testing, non-invasive testing, DTCT

- Darzi report 2024[1] suggested three ‘big shifts’:
  - Moving from analogue to digital
  - **Shifting care from hospitals to community**
  - Moving from sickness to prevention

- UKAS accreditation of POCT
- Pathology Network Maturity and POCT

1. Independent investigation of the NHS in England
Lord Darzi's report on the state of the National Health Service in England.

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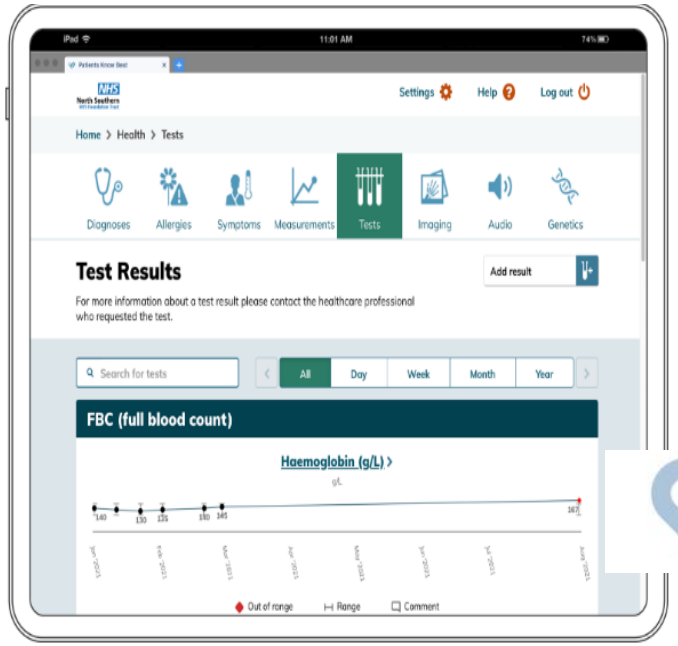
Patient empowerment and access to pathology results

- Patients: the greatest untapped resource in healthcare
- ‘co-production’ and ‘co-design’
- **Patients are accessing their results online**
- **Patients often see their results before clinicians**
- Delays built in for release of sensitive tests (cancer, sexual health)



Current and past data

View up-to-date information about a patient’s current or ongoing conditions, along with any past medical history, live care plans and discharge summaries.

Understand changes that have occurred over time and make more accurate assessments with all the information in front of you.

PATIENTS KNOW BEST®
MANAGE YOUR HEALTH

Lab Tests Online® UK
Peer-reviewed Non-commercial Patient-centred
A public resource on clinical lab testing from the laboratory professionals who do the testing

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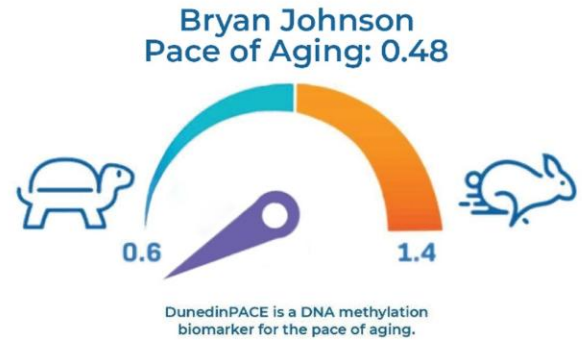
Humans are changing….

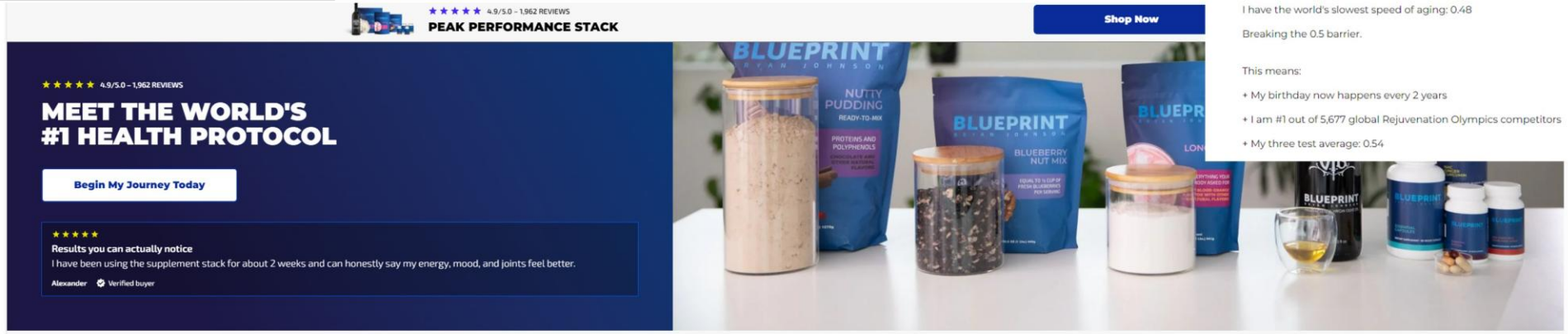
- Anti-CD38/CD47 mAb: interfere with transfusion/flow cytometry
- Gene therapy: Haemoglobinopathies, Haemophilia, ……
- ESA doping & new diabetes treatments causing raised HCT

- **Crazy rich people** are doing crazy things, but some of those crazy things might be innovations….?

I have the world's slowest speed of aging

Written by: Bryan Johnson | Published on: March 11, 2025





I have the world's slowest speed of aging: 0.48

Breaking the 0.5 barrier.

This means:

+ My birthday now happens every 2 years
+ I am #1 out of 5,677 global Rejuvenation Olympics competitors
+ My three test average: 0.54

72 DAILY HEALTH ACTIVES • 3RD PARTY TESTED • BE AT THE TOP 1% • BACKED BY SCIENTIFIC RESEARCH • PRECISION DOSING • 72 DAILY HEALTH ACTIVES • 3RD PARTY TESTED • BE AT THE TOP 1% • BACKED BY SCIENTIFIC RESEARCH • PRECISION DOSING

BRYAN JOHNSON'S LIFE CHANGING RESULTS

Bryan's commitment to his rejuvenation protocol has placed him in the top 1% across key health metrics, proving what's possible.

MUSCLE MASS Top 0.5% whole body muscle and fat via MRI	**HEART HEALTH** Top 1.5% of 18 year olds in cardiovascular capacity	**SLEEP** Top 1% in sleep performance and recovery
INFLAMMATION	**PACE-OF-AGING**	**BONE HEALTH**

BUSINESS

‘No benefits detected’ from swapping blood with son, Bryan Johnson says

By Shannon Thaler

Published July 11, 2023, 11:47 a.m. ET

34 Comments

The anti-aging-obsessed tech mogul who used his teenage son as his personal “blood boy” said he won’t be swapping plasma with his child again because there were “no benefits detected.”

Bryan Johnson — the 45-year-old fanatic who **spends $2 million a year on a regimen that includes counting his nighttime erections so that his organs, including his rectum, function like a teenager’s** — tweeted last week that he was stopping the blood swaps.

Johnson had enlisted his 17-year-old son Talmage two months ago for a tri-generational blood-swapping treatment that included his 70-year-old father Richard.

Anti-aging guru Bryan Johnson shared his latest trick in his efforts to stay young.

X/ @bryan_johnson

"TPE removes all of my body's plasma and replaces it with Albumin," Johnson wrote on social m

"The therapy objectives are to remove toxins from my body. The evidence is emergent."

US NEWS

Anti-aging zealot Bryan Johnson brags about his 'liquid gold' plasma as he reveals new blood exchange therapy

Johnson, 47, who funnels $2 million a year into his quest for eternal youth, said on Monday he underwent a total plasma exchange that would take that fluid from his body and replace it with pure albumin, a protein found in a person's blood plasma.

Defining disease entities: analogue to digital

- Darzi report 2024[1] suggested three ‘big shifts’:
  - **Moving from analogue to digital**
  - Shifting care from hospitals to community
  - **Moving from sickness to prevention**

1. Independent investigation of the NHS in England
Lord Darzi's report on the state of the National Health Service in England.

Analogue to Digital

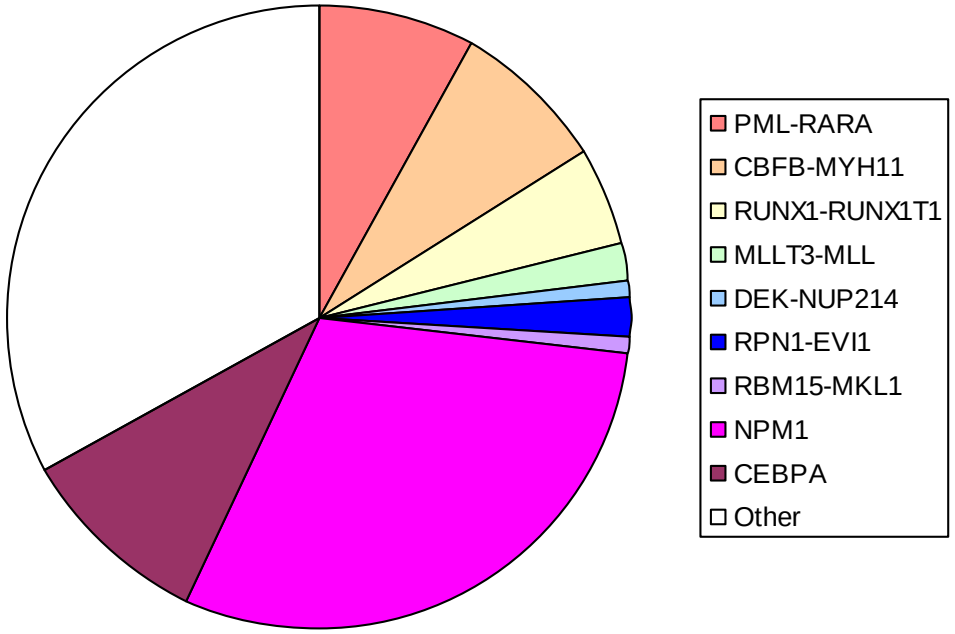
Histopathology

Histopathology 2025, 86, 158–170. DOI: 10.1111/his.15353

REVIEW

Future directions in myelodysplastic syndromes/neoplasms and acute myeloid leukaemia classification: from blast counts to biology

Matteo G Della Porta,[1] Jan Philipp Bewersdorf,[2] Yu-Hung Wang[3,4] & Robert P Hasserjian[5]



- Description of newer technologies used in classifying MDS/AML beyond traditional morphology
- Application of molecular technologies to define disease boundaries in myeloid neoplasms
- Acute Myeloid Leukaemia with recurrent genetic abnormalities
- SF3B1 variants vis ring sideroblasts
- *Epigenetics*
- *Proteomics*
- *Imaging Flow Cytometry*

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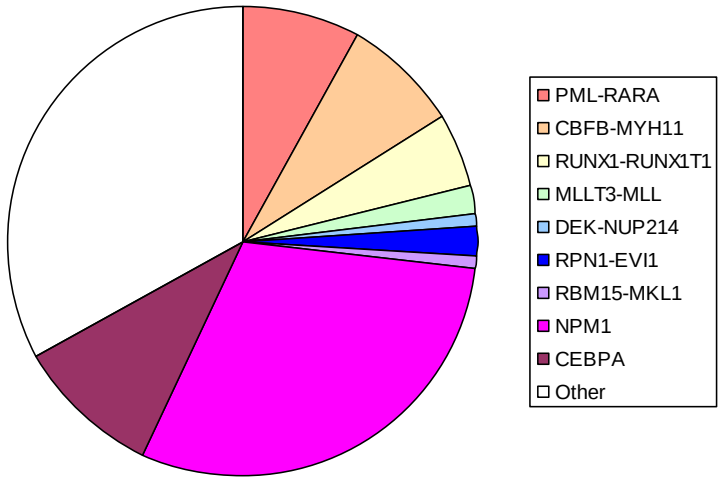
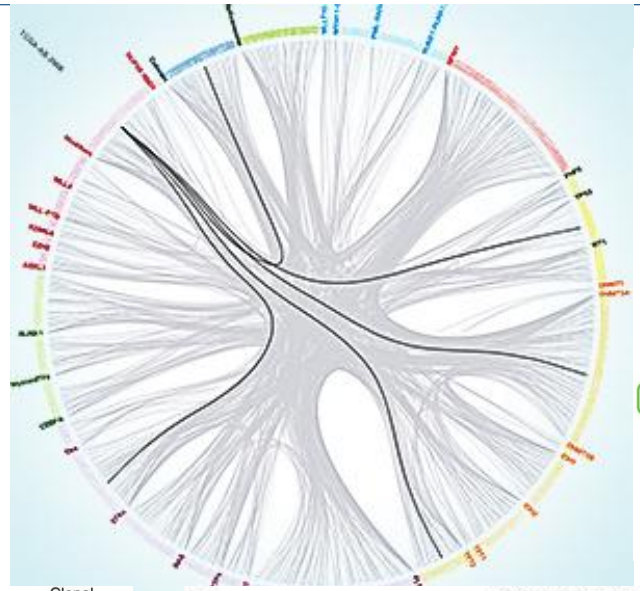
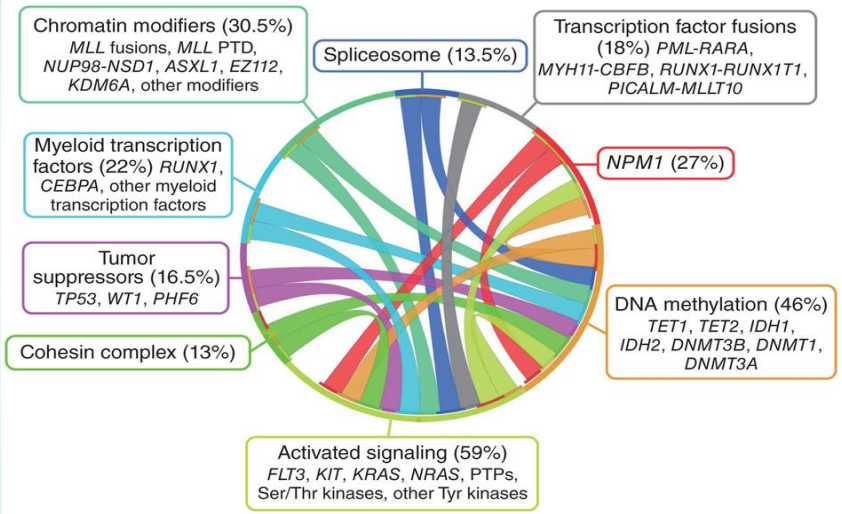
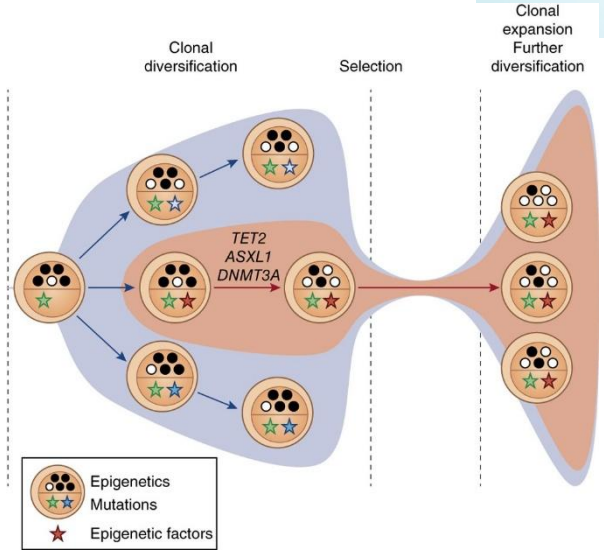
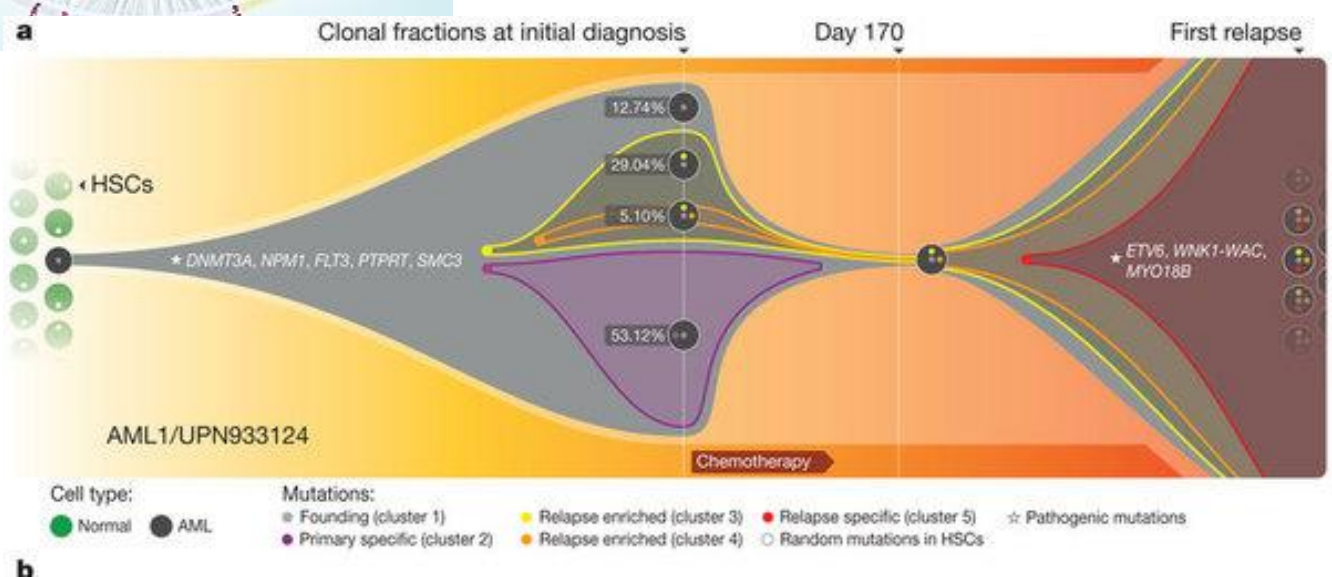
Analogue to Digital?











Algorithms: combining different results for predictive power

- **Fibrosis-4 (FIB-4) Index for Liver Fibrosis**
  - Age, AST ALT, Plt count
- **GAAD score for Hepatocellular carcinoma**
  - AFP, PIVKA-II, age, sex
- **ColonFlag:** web-based machine learning algorithm designed to help identify people at high risk of having colorectal cancer
  - Age, sex, FBC indices

Moving from sickness to prevention?

MGUS? MBL? CHIP?

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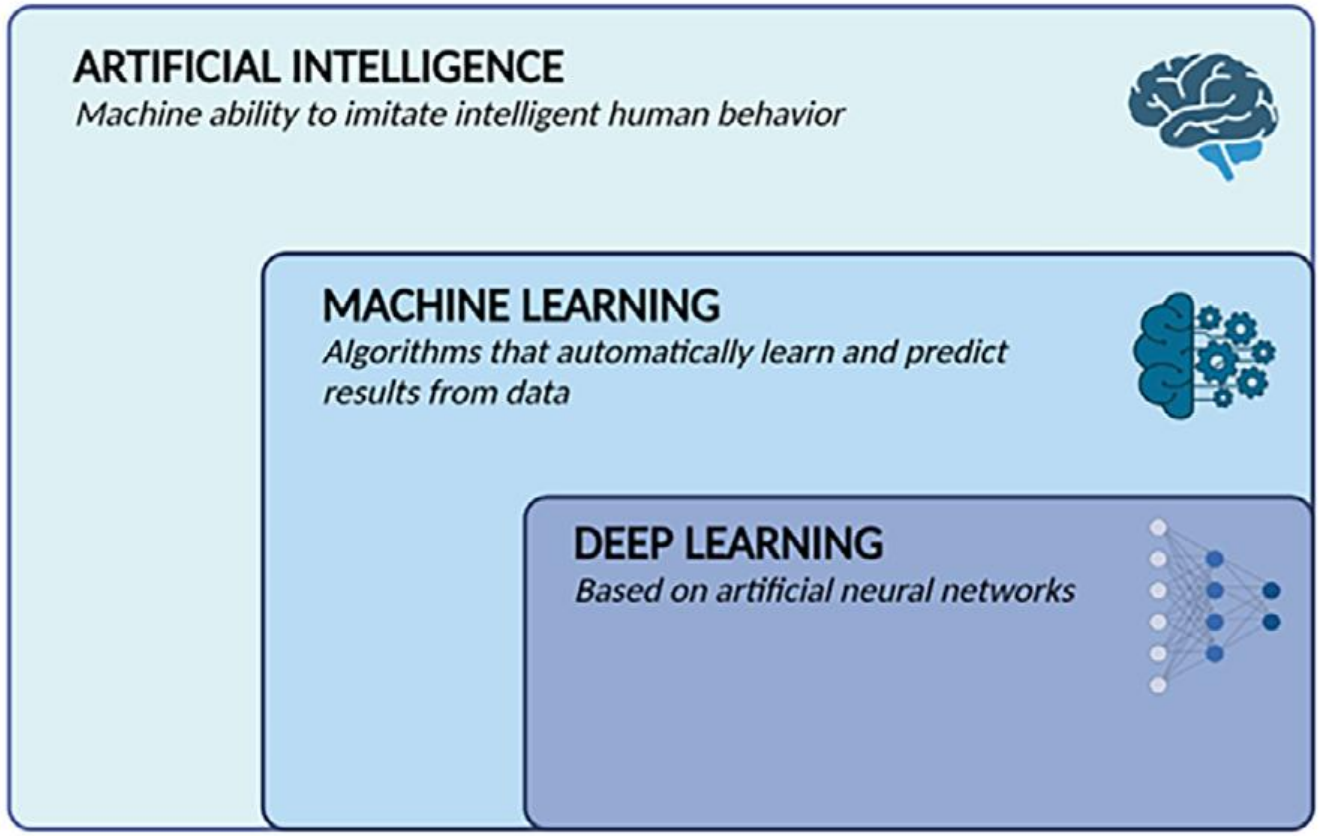
Artificial Intelligence



Histopathology

Histopathology 2025, **86**, 58–68. DOI: 10.1111/his.15327

REVIEW

Role of artificial intelligence in haematolymphoid diagnostics

Charlotte Syrykh,[1] Michiel van den Brand,[2,3] Jakob Nikolas Kather[4,5] & Camille Laurent[1,6]

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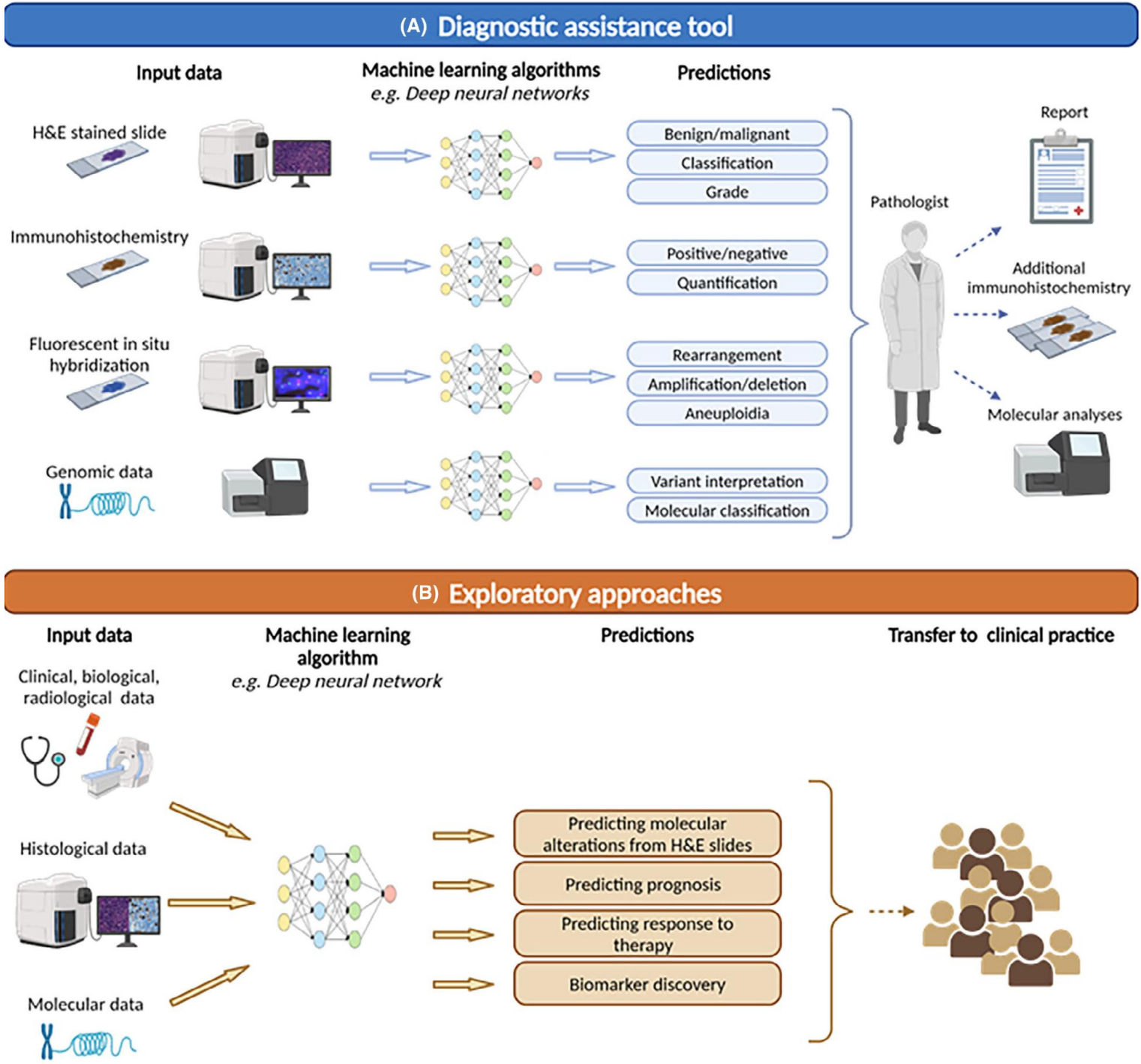
AI in Pathology

- Access to whole-slide imaging offers the possibility to apply AI approaches to high-resolution images to extract features in order to develop diagnostic/classification tools and prediction algorithms

- Could help to overcome the limitations of subjective visual assessment and capture the complexity of tissue architecture that is sometimes undetectable to the human eye



AI in haematopathology

- AI models have shown promising results for the detection and classification of lymphomas from whole-slide images with areas under the receiver operating characteristic curve (AUROC) often exceeding 0.90
- However, all these algorithms focus on only a few subtypes of the most common lymphomas, such as DLBCL, FL and CLL
- AI approaches can also standardize grade assignment (FL) and identify progression/accelerated/transformation (CLL)or aggressive subtypes
- Help standardize Ki67 assessment
- In DLBCL, ML-based algorithms for immunohistochemical classification into COO (Cell of Origin, i.e. germinal centre or nongerminal centre subtypes) achieved better performance compared to the gold standard Hans algorithm

Syrykh et al Role of artificial intelligence in haematolymphoid diagnostics *Histopathology.* 2025 Jan;86(1):58-68

AI in haematopathology: genomics

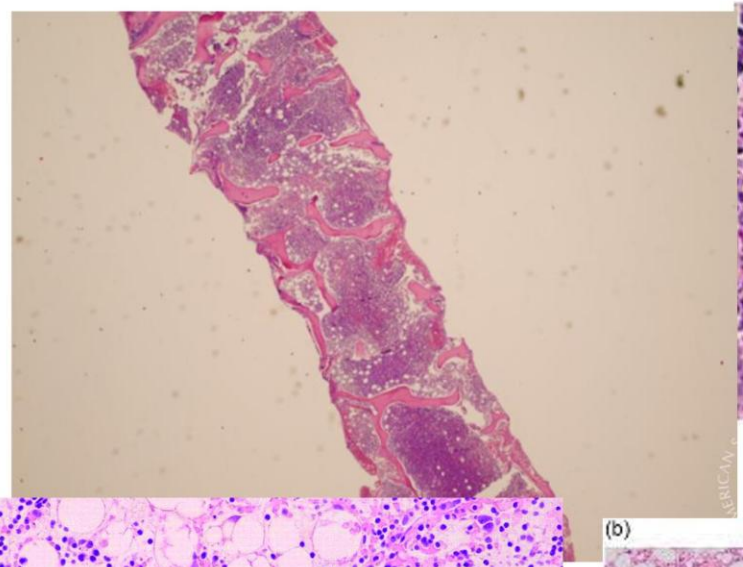
- Automated FISH image capture and analysis systems
- Gene expression data to train ML algorithms to recognize and distinguish different lymphoma entities/subtypes (mostly DLBCL), or predict OS in FL [1]
- *Screening*: In various solid tumours, deep-learning based on H&E images has been used to predict the presence of mutations
- In DLBCL, can predict double/triple hit lymphomas[2] or response to R-CHOP [3]
- Current application is limited by the scarcity of comprehensive databases and the still constrained access to high-throughput sequencing techniques in laboratories

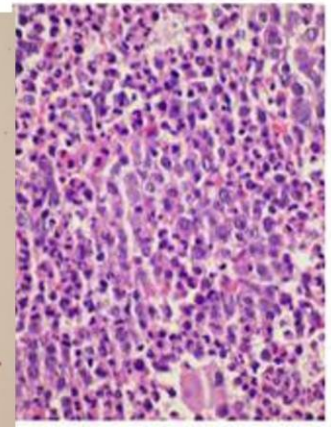
1. Carreras J, Kikuti YY, Miyaoka M et al. Artificial intelligence analysis of the gene expression of follicular lymphoma predicted the overall survival and correlated with the immune microenvironment response signatures. Mach. Learn. Knowl. Extr. 2020; 2; 647–671
2. Perry C, Greenberg O, Haberman S et al. Image-based deep learning detection of high-grade B-cell lymphomas directly from hematoxylin and eosin images. Cancer 2023; 15; 5205
3. Lee JH, Song G-Y, Lee J et al. Prediction of immunochemotherapy response for diffuse large B-cell lymphoma using artificial intelligence digital pathology. J. Pathol. Clin. Res. 2024; 10;

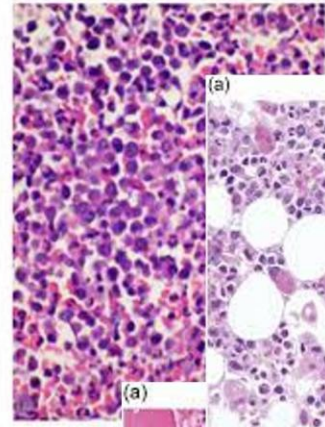
AI in haematopathology: integrative approaches

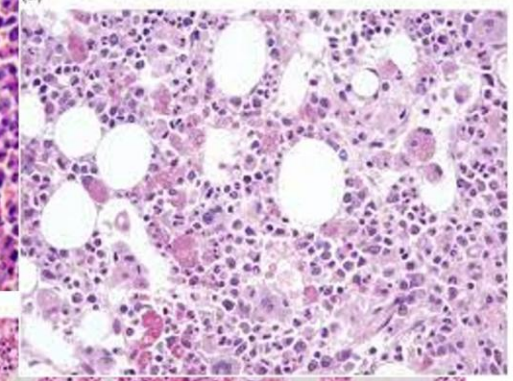
- Integrative analysis of data from different sources for diagnostics, prognostics, prediction
- Simultaneous examination of histopathological images and patient metadata, such as epidemiologic, clinical, radiology and genomic data, as well as therapeutic response
- In high-grade B-cell lymphoma, Kong et al. used machine learning to generate a prognostic model based on data from morphology, immunophenotype, and clinical features[1]
- Another study used data from national lymphoma registries to predict outcome in DLBCL and showed a better performance than the international prognostic index (IPI) score[2]

1. Kong H, Zhu H, Zheng X et al. Machine learning models for the diagnosis and prognosis prediction of high-grade B-cell lymphoma. Front. Immunol. 2022; 13:919012Perry C, Greenberg O, Haberman S et al. Image-based deep learning detection of high-grade B-cell lymphomas directly from hematoxylin and eosin images. Cancer 2023; 15; 5205
2. Biccler JL, Eloranta S, de Nully Brown P et al. Optimizing outcome prediction in diffuse large B-cell lymphoma by use of machine learning and Nationwide lymphoma registries: a Nordic lymphoma group study. JCO Clin. Cancer Inform. 2018; 2; 1–13.





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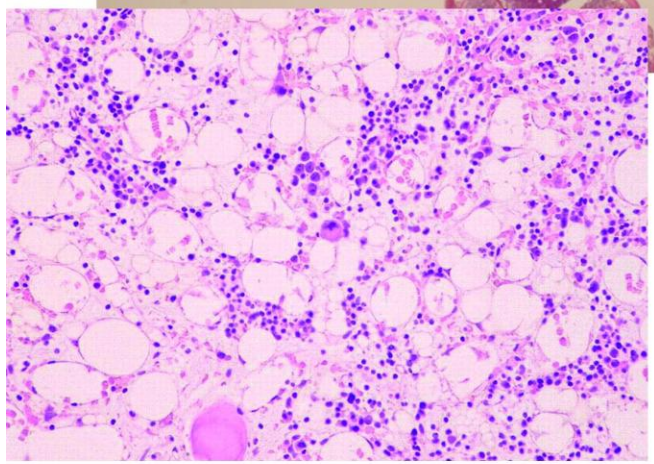
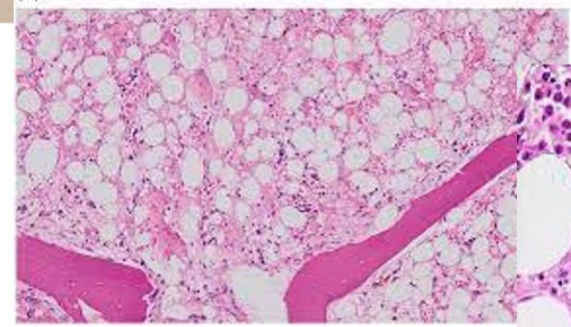
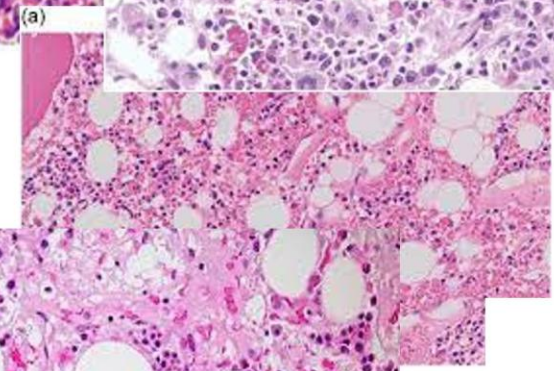



(b)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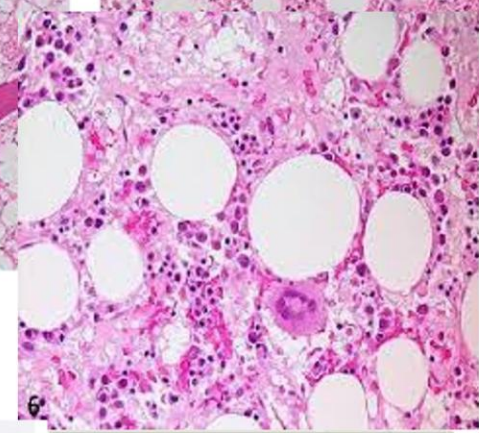
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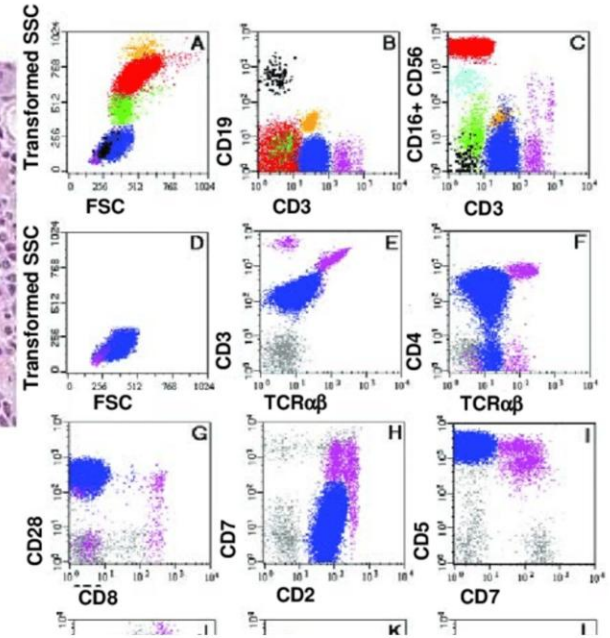
Transformed SSC
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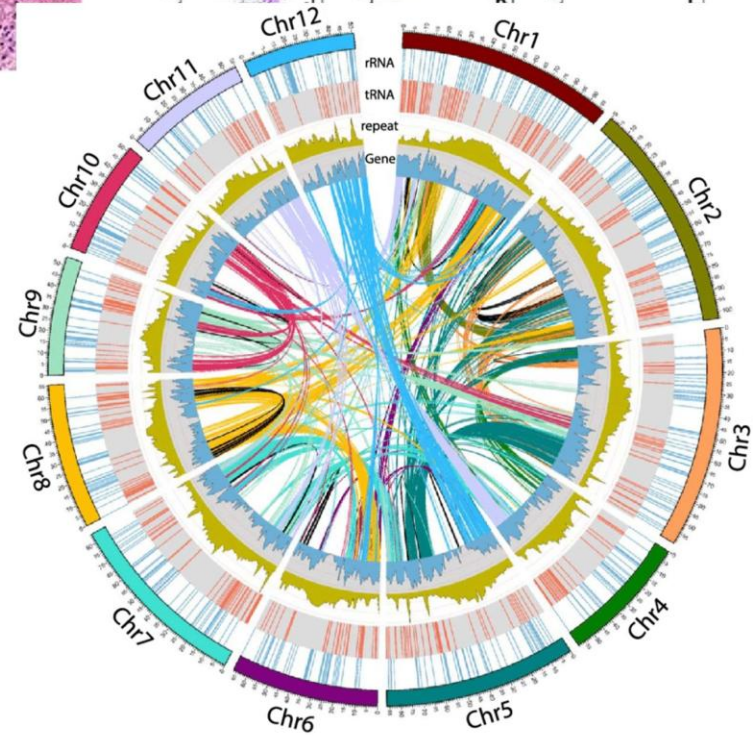
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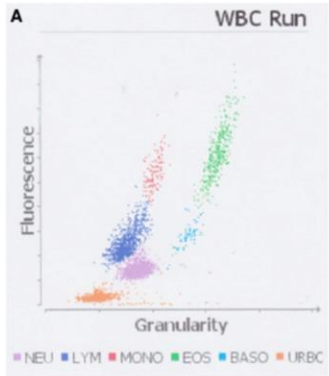
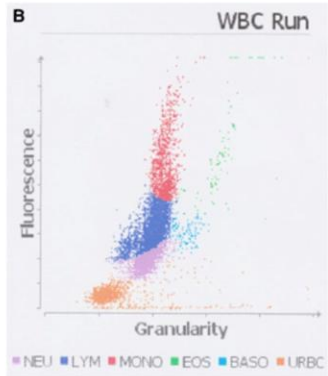

A
WBC Run
Fluorescence
Granularity
NEU LYM MONO EOS BASO URBC


B
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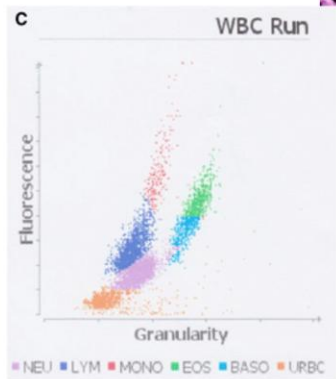
C
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Fluorescence
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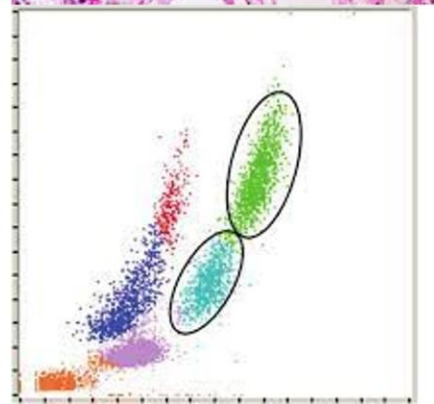

www.bloodcounts.org

BloodCounts!

We use the Full Blood Count test to predict infectious disease outbreaks and for earlier diagnosis of non-infectious conditions.

- We are investigating the use of rich full blood count (R-FBC) data, which is a larger set of data produced by blood analysers. If we can find that computerised analysis of R-FBC data is as good as traditional methods, it would ease the burden on healthcare staff
- It's likely that many blood disorders, especially in their early stages, cause subtle changes in blood parameters that can be detected through R-FBC analysis, but not routine testing
- Certain blood cell abnormalities can appear years before the onset of certain blood cancers
- The information obtained from routine FBC testing, particularly the red cell distribution width, has only limited predictive value
- **We hypothesise that the detailed information provided by R-FBC analysis could improve the accuracy of predictive models for a wider range of blood disorders**

Scopio

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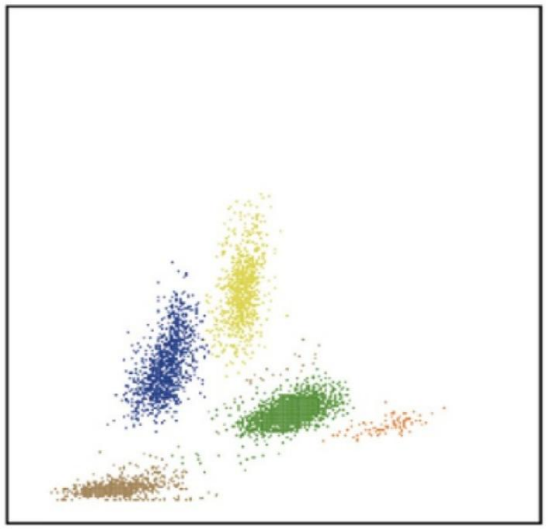
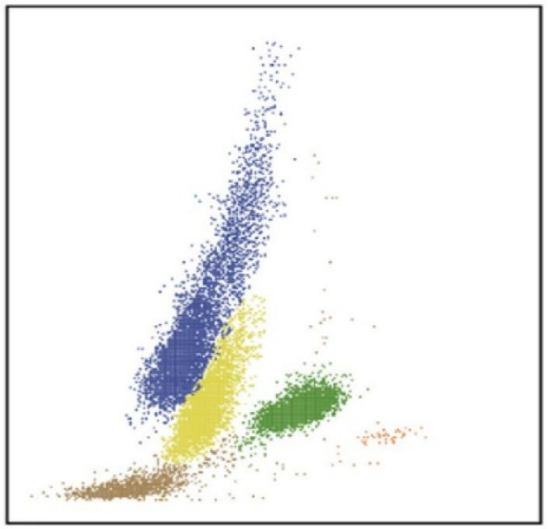
Cell

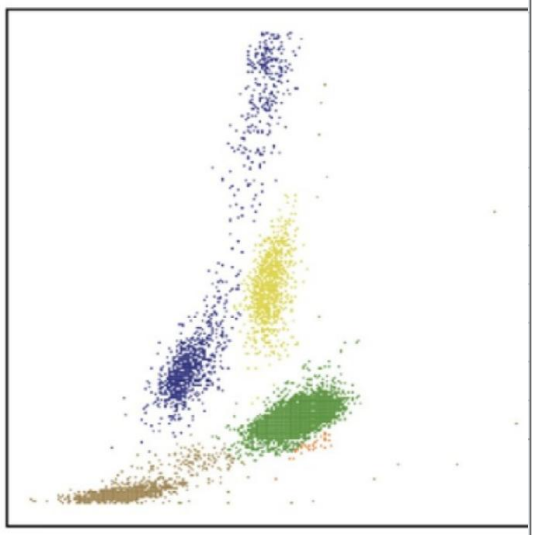
Healthy



Influenza

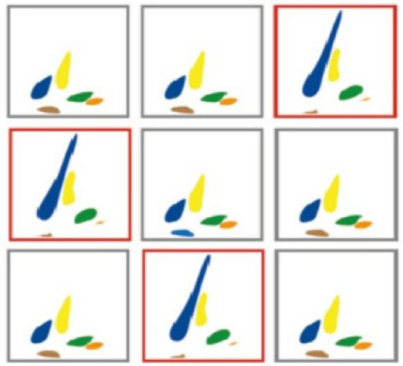


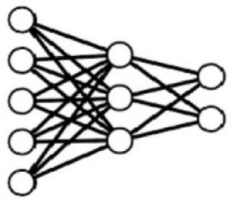
SARS-CoV-2



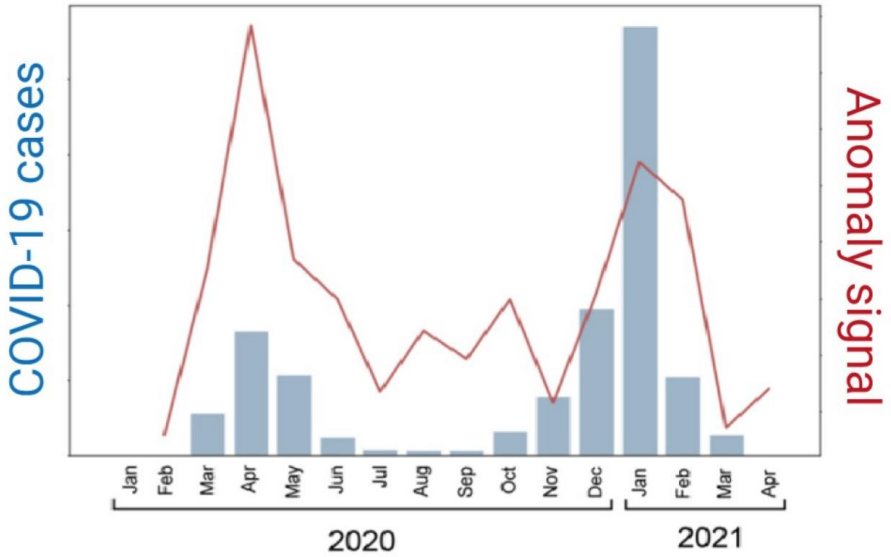
Lab View	14/Apr/2025 16:42 BST
General Haematology	
Haemoglobin	138 g/L
White Blood Count	H 11.4 x10^9/L
Platelet Count	L 46 x10^9/L
Citrate platelet count	44 x10^9/L
Haematocrit	0.40
Red Blood Count	4.80 x10^12/L
Mean Cell Volume	83.1 fL
Red Blood Cell Distribution Width	H 15.0 %
Mean Cell Haemoglobin	28.8 pg
Mean Cell Haemoglobin Concentration	H 346 g/L
Neutrophil Count	H 7.5 x10^9/L
Lymphocyte Count	2.8 x10^9/L
Monocyte Count	0.7 x10^9/L
Eosinophil Count	0.3 x10^9/L
Basophil Count	0.1 x10^9/L
Nucleated Red Blood Cell Count	0.0 x10^9/L
Blood Film Microscopy	Blood Film Microscopy
Registrar Film Comments	
FBC Comments	
Reticulocyte Count	
Reticulocyte Count %	
Urgent Blood Film Microscopy	
Immature Platelet Fraction	33.6 %
Immature Granulocytes	0.1 x10^9/L

Historical Data





Outbreak Detection



www.bloodcounts.org

AI: Future challenges and opportunities

- AI tools in diagnostic practice **require a validated application** that is preferably directly available within the image management system and easy to use
- **Most easily implemented if the workflow is already strongly digitized, which is presently not the case for many laboratories**
- Many new algorithms for digital pathology will complete the implementation phase in the coming years, but at present this number is still limited to ~50 applications with CE certification in Europe and six applications in the field of pathology with FDA approval in the United States: *focused on solid tumours*
- It might be a first step to use H&E slides to predict either the absence (high sensitivity) or the presence (high specificity) of a genetic lesion with a high level of certainty

AI: Future challenges and opportunities

- *Lack of explainability*. Although explainability methods are used increasingly, many AI algorithms are still **black boxes** that are particularly problematic in medicine
- The deployment of AI in clinical settings raises significant ethical concerns and requires the establishment of **robust regulatory frameworks** to ensure patient safety and data privacy.
- The use of AI in clinical decision-making raises questions about the balance between machine autonomy and human supervision. **It is essential to determine the extent to which clinicians should rely on AI rather than use it as a support tool**
- Federated learning (AI models training on data from multiple institutions without the data leaving its original location) and collaborative efforts among research institutions and pathology labs should enable the access to **larger combined datasets** of rare lymphomas

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AI: Future challenges and opportunities

- Combined molecular and computational approaches could eventually provide valuable assistance to pathologists, who are often faced with difficult diagnoses.
- However, the pathologist will always be necessary to validate the performance of the algorithms and control the results they produce
- Automate routine diagnostic tasks, enabling pathologists to focus on complex cases
- **Enhance pathologist expertise rather than replace it**

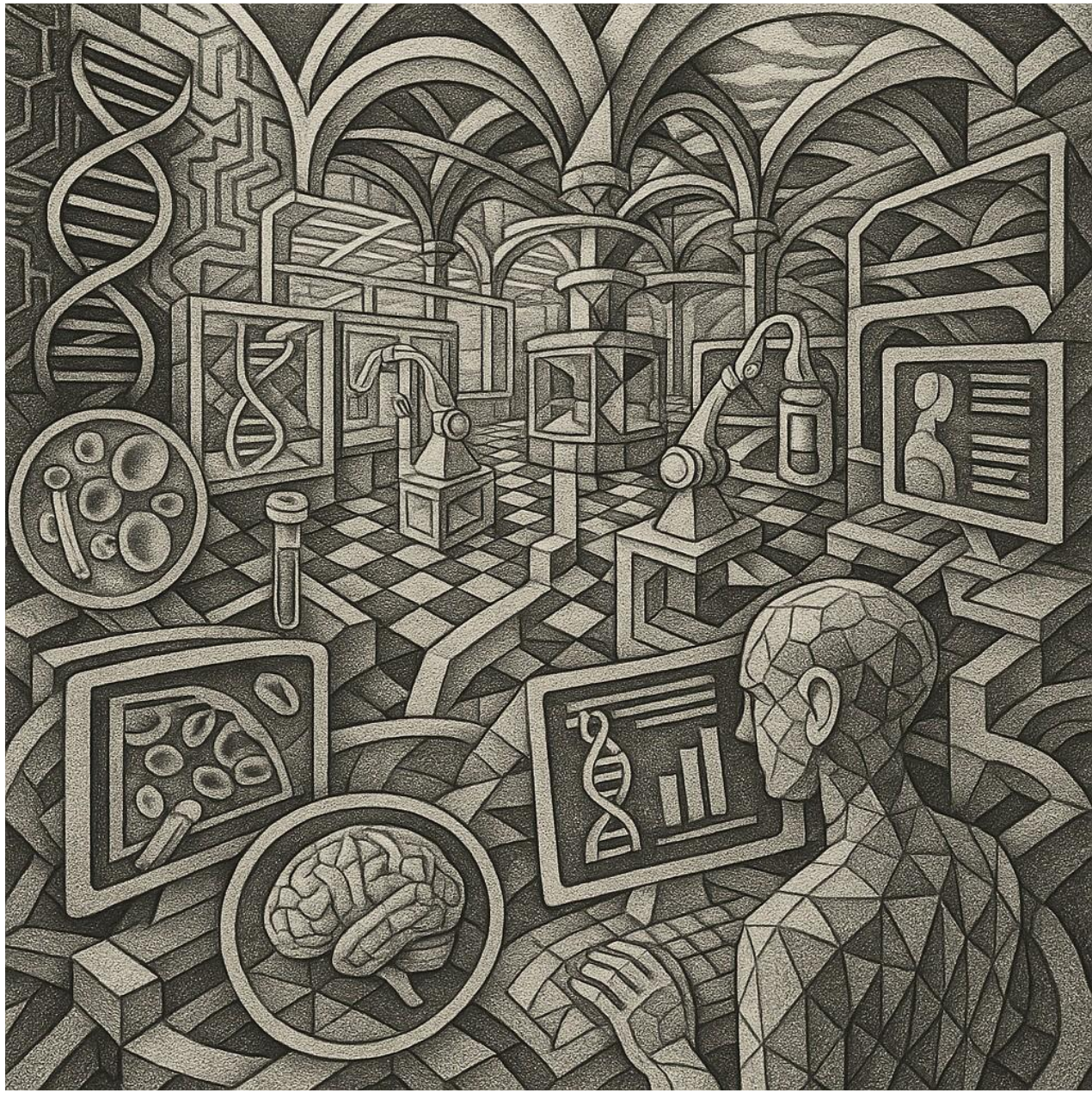
AI generated art: The Haematology Lab of the Future

Based on text within this presentation

- Thanks to:
  - ChatGPT
  - Dr Joe Taylor

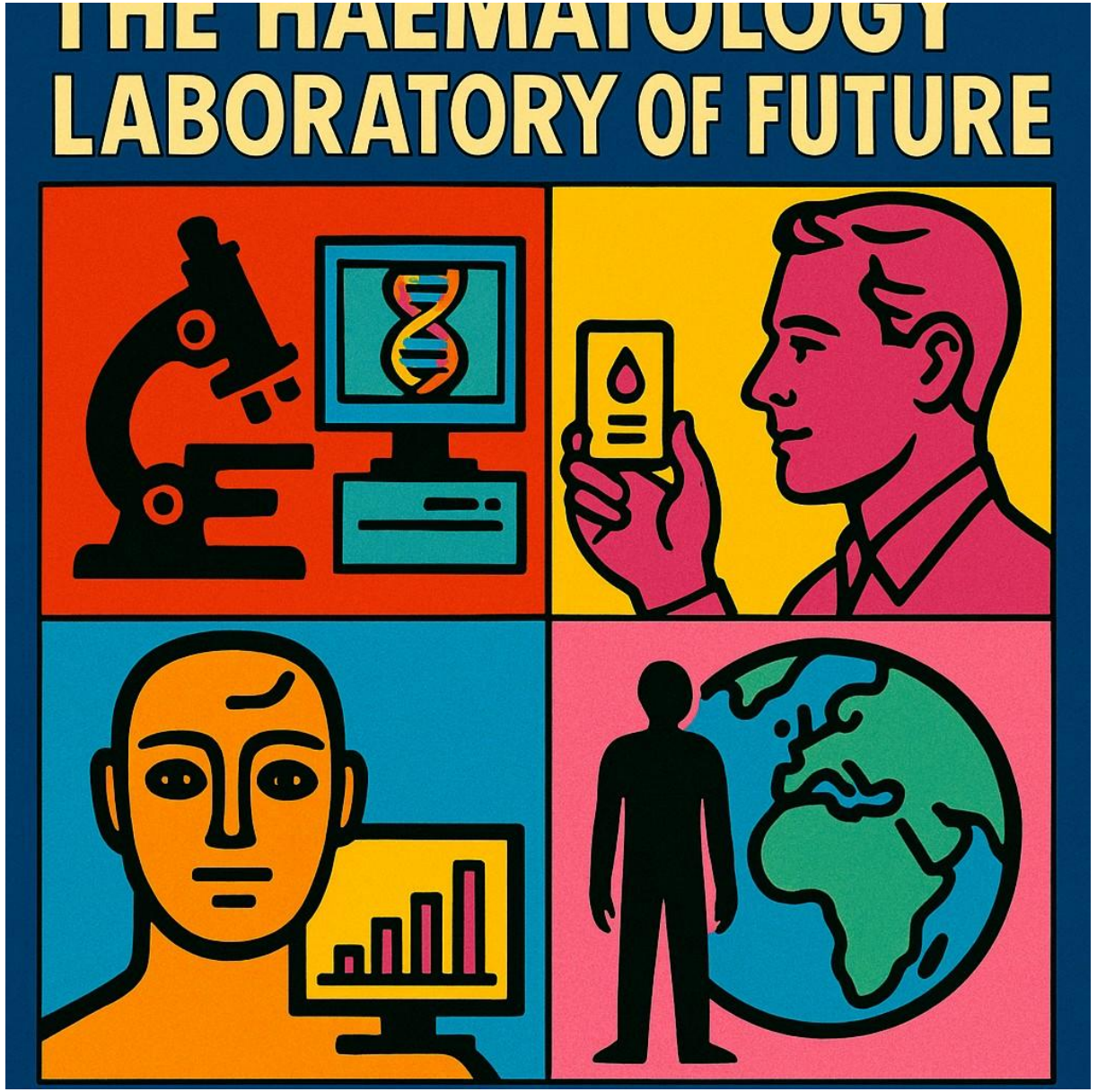
Salvador Dali

Van Gogh



MC Escher

Warhol



Constable

Dark Labs

Asklepios Clinic Bad Oldesloe (Schleswig Holstein) is the first hospital in the world to have two autonomous laboratory robots

www.unitedrobotics.group/en/robots/umobilelab

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Dark Labs

Asklepios Clinic Bad Oldesloe (Schleswig Holstein) is the first hospital in the world to have two autonomous laboratory robots

www.medilys.de/weltpremiere

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Dark Labs

- **Fully automated labs:** Designed to function without regular human intervention, harnessing the power of robotics, artificial intelligence, and advanced data analytics
- **Addressing staff shortages**
- **Enhancing efficiency and speed**
- **Data-driven insights and predictive analytics**
- **Eliminating human errors**
  - Note that 15% of errors occur in analytical phases, vs 62% pre-analytical, 23% post-analytical[1]

Challenges

- Initial setup cost of fully automated systems requires up front investments in vessel moving, robotics, AI technology, and infrastructure. These costs may occur before the reduction in staffing costs due to a hybrid phase while laboratories transition between the two operating models
- Processes such as inventory replenishment, routine maintenance, sample loading and others do not currently have standardized, readily available solutions
- There is also a need for specialized training for the personnel overseeing the automated processes and managing technical issues.

1. Errors in a stat laboratory: types and frequencies 10 years later, Carro P, Plebani M *Clin Chem* . 2007 Jul;53(7):1338-42.

The future is already here — it's just not very evenly distributed[1]

1. William Gibson

- Haematology: the cutting edge of personalised/precision/stratified medicine
- We have a duty to promote equity of care
- We want to learn
- **We are already living in the future**

bloodcancer.org.uk

- Blood cancer is the UK's third biggest cancer killer
- Blood cancer is the fifth most common cancer in the UK, with over 41,000 people diagnosed annually
- There are about 250,000 people living with blood cancer in the UK
- One in every 16 men and one in every 22 women will develop it at some point
- It is the most common type of childhood cancer

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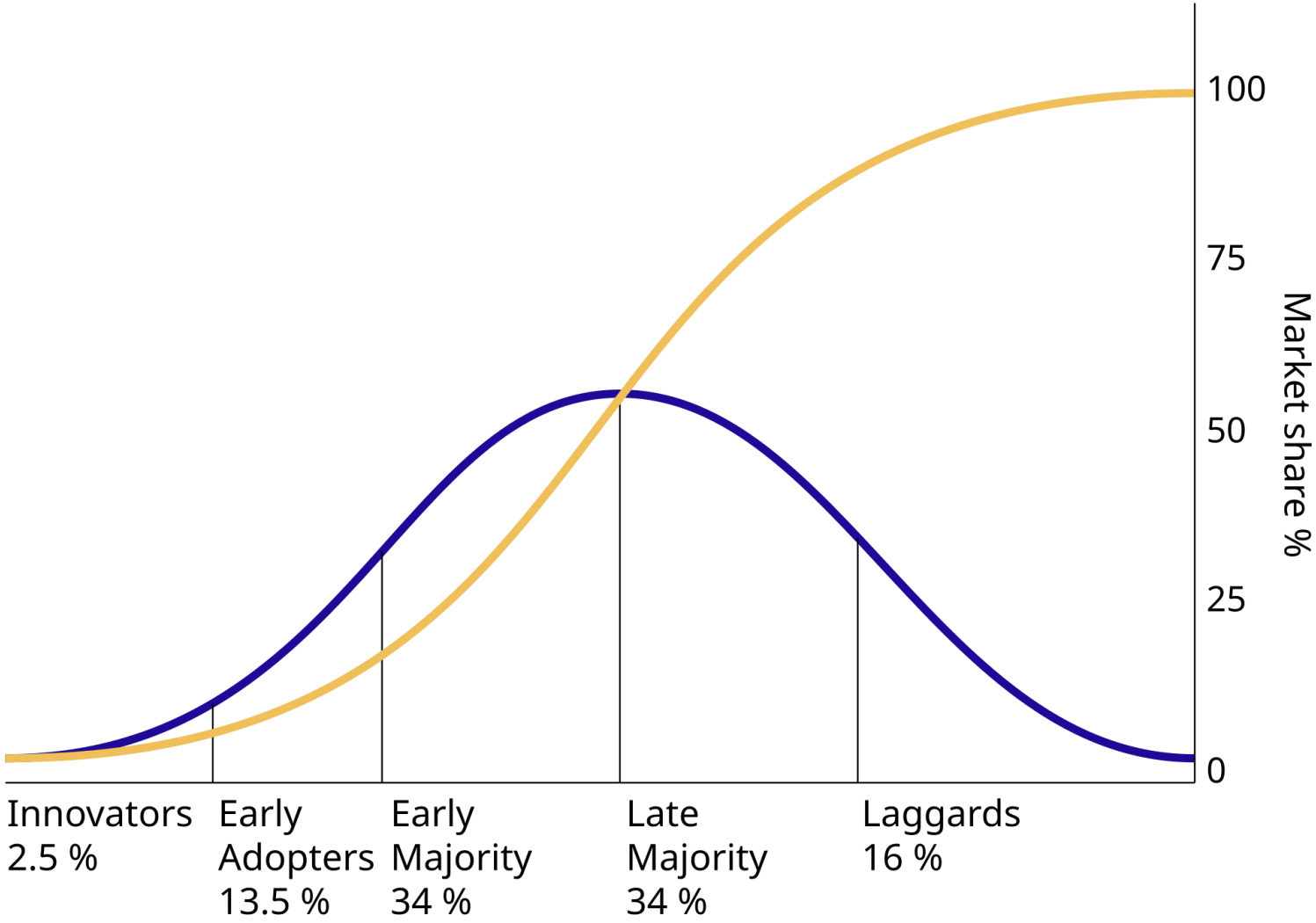
How to distribute the future more evenly?

Diffusion of innovations theory
Everett Rogers 1962



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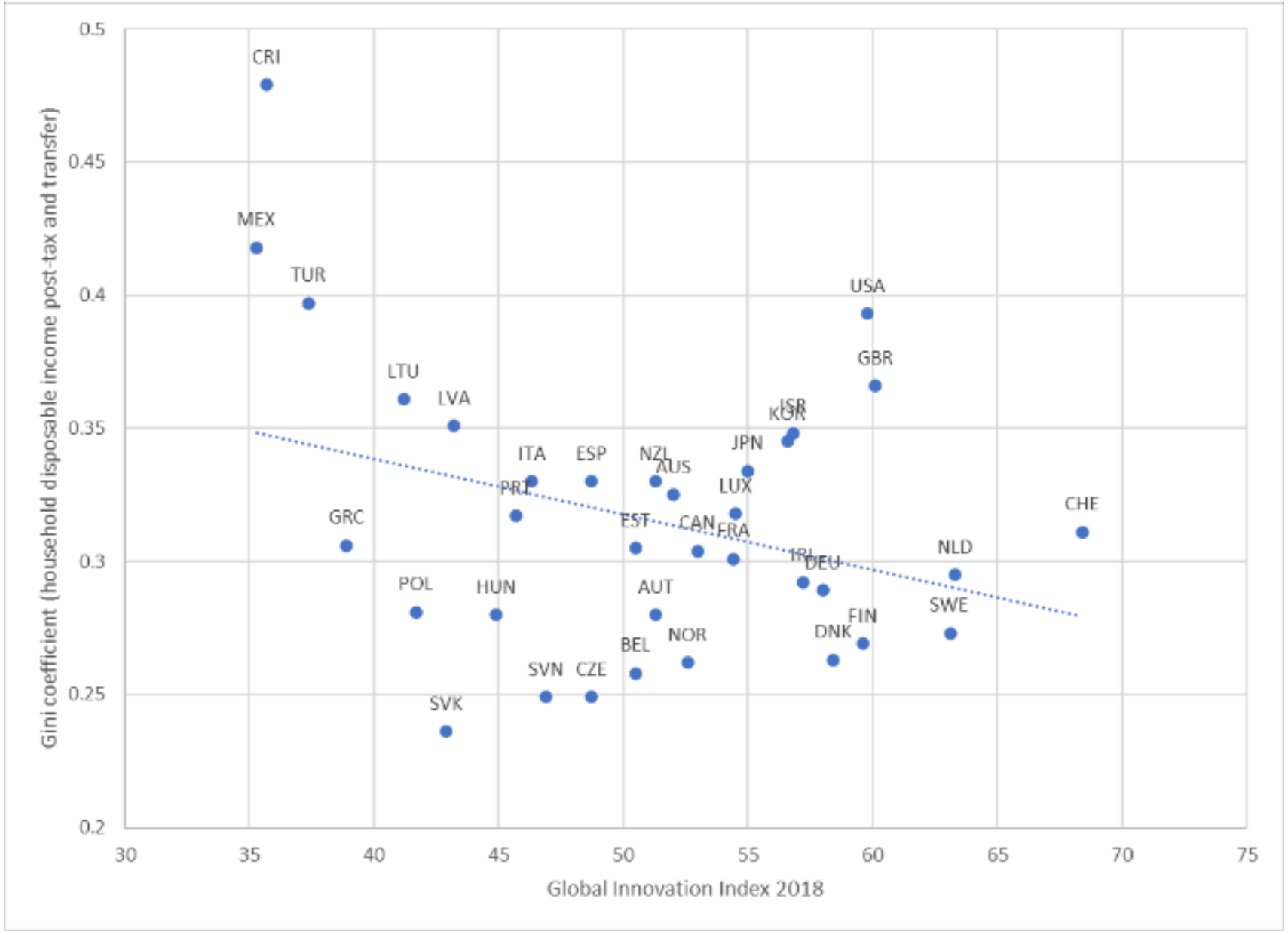


Innovation and inequality:

More equal societies innovate more

Berry, C. and O'Donovan, N. (2023). Entrepreneurial egalitarianism: How inequality and insecurity stifle innovation, and what we can do about it. UCL Institute for Innovation and Public Purpose
Global Innovation Index data from www.globalinnovationindex.org;
Gini coefficient data from stats.oecd.org.

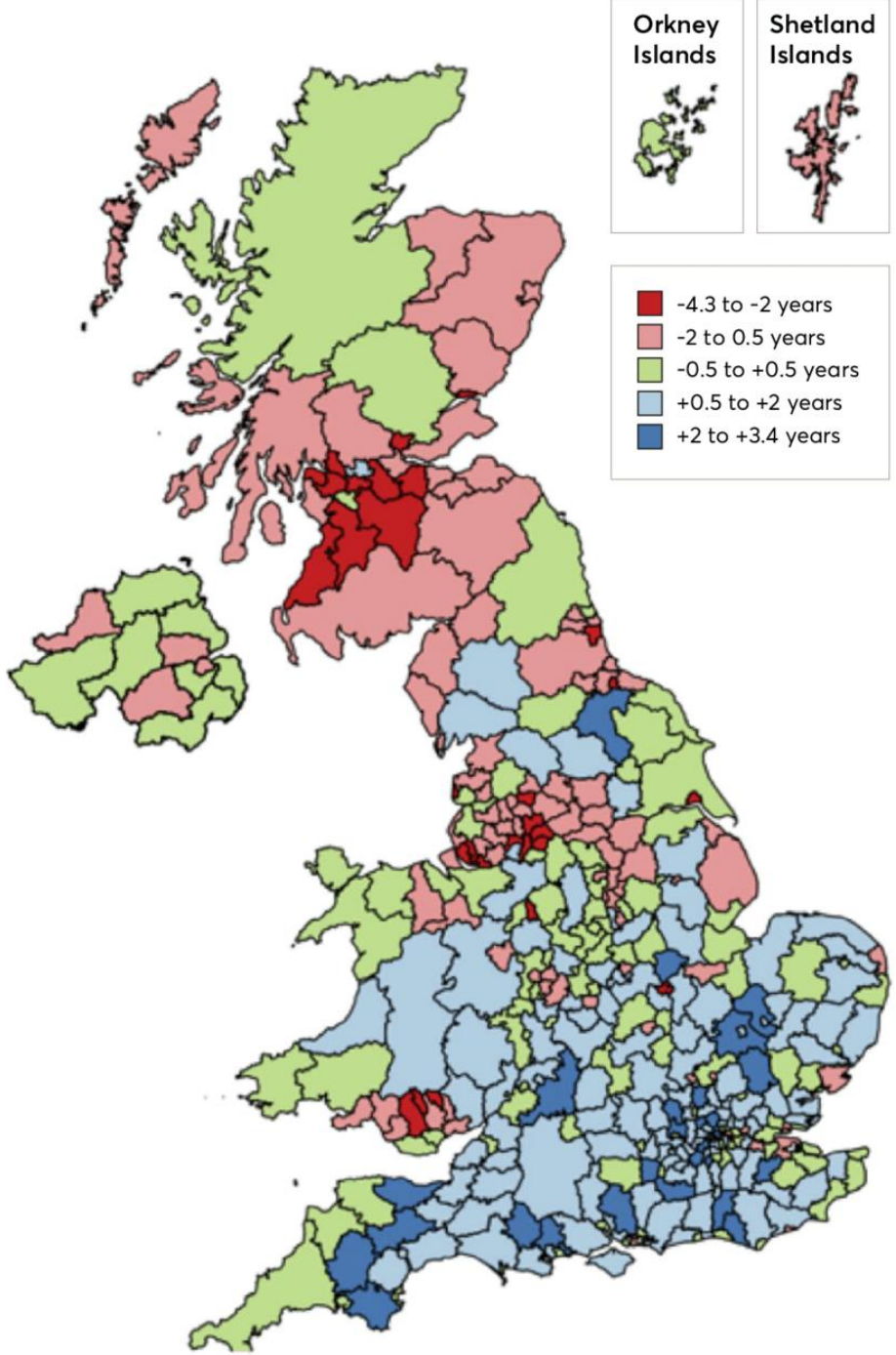
Innovation and inequality

- **Innovation can affect inequalities in many ways** – increasing some inequalities and decreasing others
- Depends on who controls the property rights to exploit the innovation and what they decide to do with it
- **Public sector innovations in medicine and health care are often inequality-reducing, particularly in countries with universal state-provided health care, such as the UK**
- Changes over the last few decades in the technology of production have favoured higher skilled workers
- Innovation increases productivity, thus increasing economic wealth
- Innovation can foster social mobility, decreasing inequality
- The wealthy, including those that have become rich by successfully innovating in the past, can use their wealth to lobby to protect their own markets, for example, by preventing new innovators from entering the market
- **'We need to protect capitalism from the capitalists'**

Aghion, P. and Griffith, R. (2022), 'Innovation and inequalities', IFS Deaton Review of Inequalities

Berry, C. and O'Donovan, N. (2023). Entrepreneurial egalitarianism: How inequality and insecurity stifle innovation, and what we can do about it. UCL Institute for Innovation and Public Purpose

Inequity exists



Regional variations in life expectancy across the UK, by local authority district. Life expectancies at birth, females, 2012-2014

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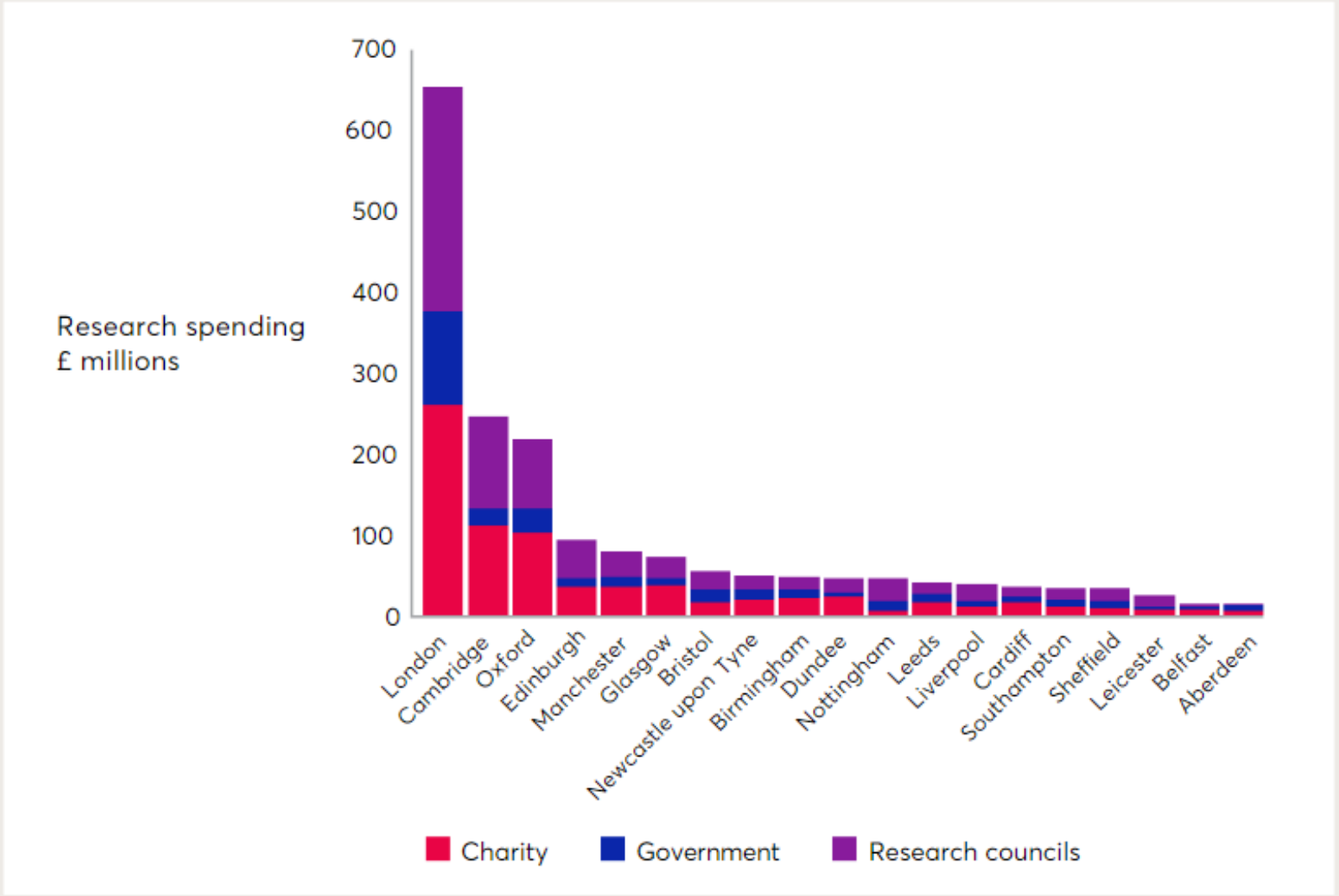
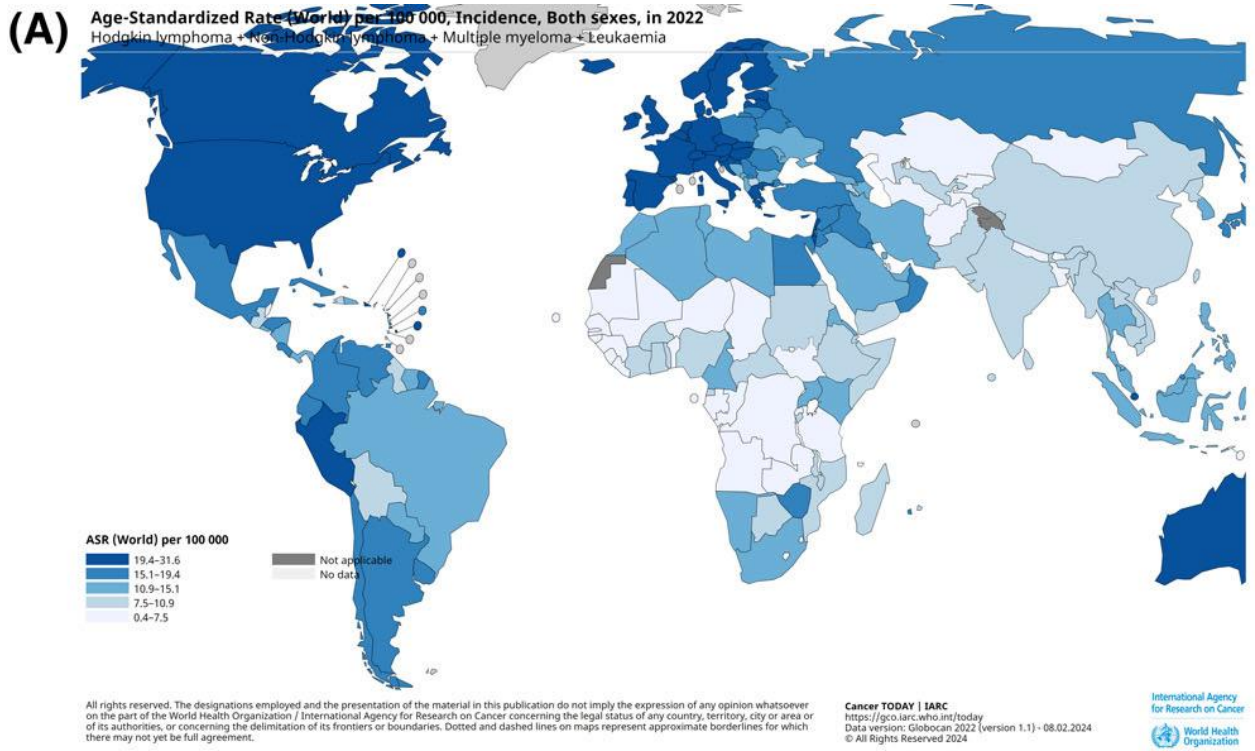
Figure 4.2. Geographical distribution of health-related research supported by government and charities. These 19 cities receive more than 90 per cent of total funding; 55 per cent goes to London, Oxford and Cambridge.

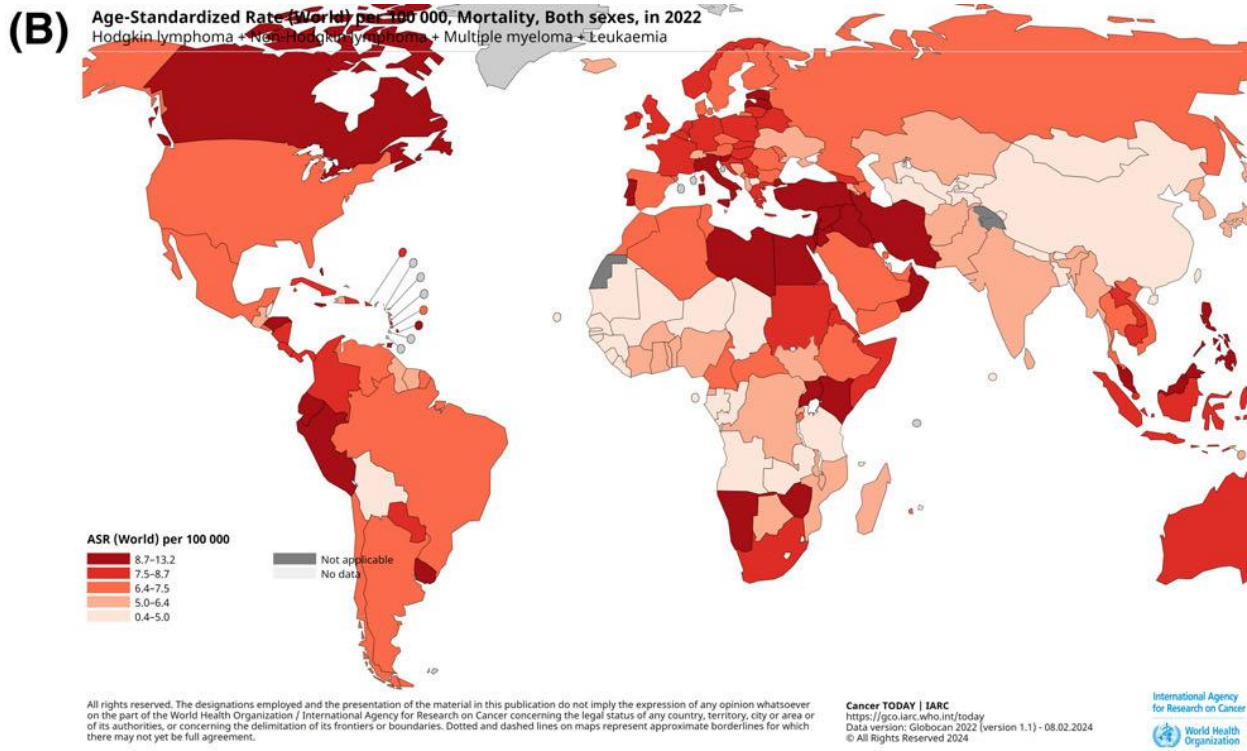


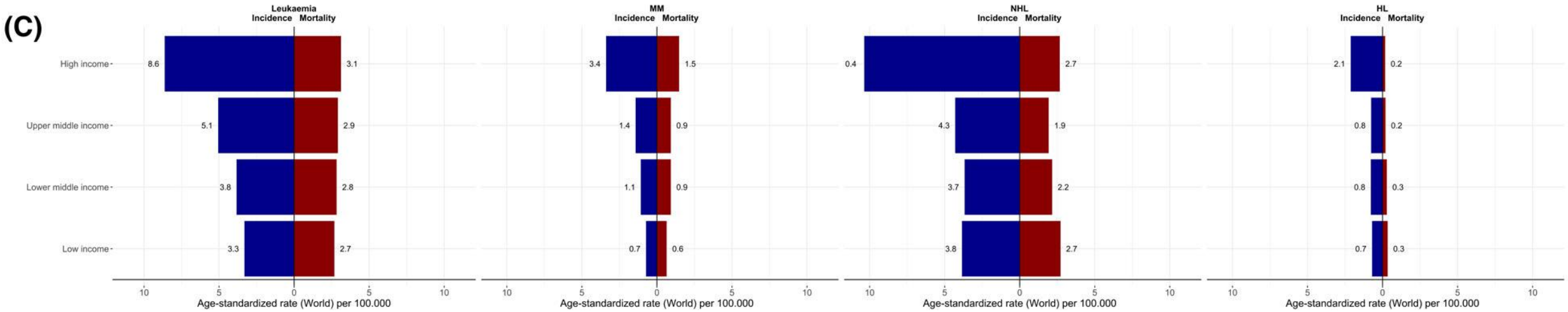
Source: UKCRC 'UK Health Research Analysis 2014'.

Inequity exists

Y Fedoriw , O Silva , A Znaor , E Macintyre
Global view of haematolymphoid tumor classifications and their application in low- and middle-income countries Histopathology 2025 Jan;86(1):6-16







The future is already here — it's just not very evenly distributed[1]

1. William Gibson

- Haematology: the cutting edge of personalised/precision/stratified medicine
- We have a duty to promote equity of care
- We want to learn
- **We are already living in the future**
- **The BSH, BSH Lab SIG, HMDS Network will support us**
- **We all have a duty to innovate and move into the future**

- Blood cancer is the UK's third biggest cancer killer
- Blood cancer is the fifth most common cancer in the UK, with over 41,000 people diagnosed annually
- There are about 250,000 people living with blood cancer in the UK
- One in every 16 men and one in every 22 women will develop it at some point
- It is the most common type of childhood cancer

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The Haematology Laboratory of the Future?

Assuming we have free will...what will you do today and tomorrow?

The future depends on what you do today *Mahatma Gandhi*

The best way to predict the future is to create it *Abraham Lincoln*

When I look into the future, it's so bright it burns my eyes *Oprah Winfrey*

We shall not cease from exploration
And the end of all our exploring
Will be to arrive where we started
And know the place for the first time.

Four Quartets by TS Eliot

Blood tells the future—
Genes, tech, and choice intertwine.
Hope, risk, and wonder.

Haiku by ChatGPT