An innovative blood test that may spot more than 50 types of cancer will be piloted by the NHS in a world-leading programme, announced by NHS chief executive Sir Simon Stevens on November 27th.

The Galleri blood test, developed by GRAIL, has the potential to detect early stage cancers through a simple blood test, and will be piloted with 165,000 patients in a world-first deal struck by NHS England.

Research on patients with signs of cancer has already found that the test, which checks for molecular changes, can identify many types that are difficult to diagnose early, such as head and neck, ovarian, pancreatic, oesophageal and some blood cancers.

If the NHS programme shows the test also works as expected for people without symptoms it will be rolled out to become routinely available.

The test could help meet the NHS Long Term Plan goal of increasing the proportion of cancers caught early, which can be the key to reducing cancer mortality.

The GRAIL pilot, is due to start in mid-2021.
It will recruit 140,000 participants aged 50 to 79 who have no symptoms but will have annual blood tests for three years.
People will be identified through NHS records and approached to take part.
Anyone with a positive test will be referred for investigation in the NHS.
Another 25,000 people with possible cancer symptoms will also be offered testing to speed up their diagnosis after being referred to hospital in the normal way.

Results of these studies would be expected by 2023, and if outcomes are positive, then they would be expanded to involve around one million participants across 2024 and 2025.

More information on the roll out of the pilot will be shared in the new year.

https://www.england.nhs.uk/2020/11/nhs-to-pilot-potentially-revolutionary-blood-test/

GRAIL : Multi-cancer early detection test

The earlier that cancer can be found, the higher the chance of successful treatment and survival. Yet, too often cancer goes undetected until it has progressed to an advanced stage.
In studies, the Galleri test has shown the ability to detect multiple cancers through a simple blood draw.
Most of these cancers cannot be detected through current screening paradigms.
When cancer was detected, the Galleri test localised the cancer signal with high accuracy, helping inform next steps to diagnosis.
https://grail.com/galleri/

Liu et al (2020) Annals of Oncology : Volume 31, Issue 6, June 2020, Pages 745-759 : Sensitive and specific multi-cancer detection and localization using methylation signatures in cell-free DNA (cfDNA)

Early cancer detection could identify tumors at a time when outcomes are superior and treatment is less morbid.
Circulating cell-free DNA (cfDNA) refers to extracellular DNA present in body fluid that may be derived from both normal and diseased cells. Abnormalities, such as those seen in people with cancer, can be detected in cfDNA at an earlier time, thus enabling early diagnosis of disease. This allows for noninvasive assessment of tumor in real time and has real potential for improving cancer diagnosis and monitoring, prognosis assessment, and personalised medication guidance compared with conventional serum markers.

In Liu et al's study 6689 participants were recruited :
2482 cancer patients - more than 50 cancer types including neuroendocrine
4207 non-cancer patients
cfDNA samples were taken and underwent specific sequencing and analysis - and a classifier was developed and validated for both cancer detection and identification of tissue of origin (TOO)

Results
Performance was consistent in training and validation sets.
In validation, **specificity** was 99.3% : 0.7% false-positive rate (FPR)].
Stage I–III **sensitivity** was 67.3% in a pre-specified set of 12 cancer types* (anus, bladder, colon/rectum, oesophagus, head and neck, liver/bile-duct, lung, lymphoma, ovary, pancreas, plasma cell neoplasm, stomach), and was 43.9% in **all** cancer types.

In the pre-specified cancer types* sensitivity was
39% in stage I,
69% in stage II,
83% in stage III,
and 92% in stage IV.

In **all** cancer types sensitivity was
18% in stage I,
43% in stage II,
81% in stage III,
and 93% in stage IV.

Tissue of origin (TOO) was predicted in 96% of samples with cancer-like signal; of those, the TOO localisation was accurate in 93%.

cfDNA testing, through this process, detected more than 50 cancer types across the different stages.
Liu et al concluded that "Considering the potential value of early detection in deadly malignancies, further evaluation of this test is justified in prospective population-level studies."

Terminology :

Tissue of Origin (TOO) - where the cancer has started / primary site.

Specificity measures the proportion of true negatives (e.g. the proportion of those who truly do not have the condition who are correctly identified as not having the condition). A test that is 100% specific means all healthy individuals are correctly identified as healthy, i.e. there are no false positives.
A specific test is used for ruling in a disease, as it rarely misclassifies those WITHOUT a disease as being sick. A perfectly specific test therefore means no healthy individuals are identified as having that disease.
Specificity = True Negatives / (True Negatives + False Positives)

Sensitivity measures the proportion of true positives that are correctly identified (e.g., the proportion of those who truly have a condition who are correctly identified as having some condition). A test that is 100% sensitive means all individuals with a specific disease are correctly identified as having that disease i.e. there are no false negatives. A sensitive test is used for excluding a disease, as it rarely misclassifies those WITH a disease as being healthy.
Sensitivity = True Positives / (True Positives + False Negatives)