



Digital Health: Catapulting Personalised Medicine Forward

STRATIFIED MEDICINE

CRUK Stratified Medicine Initiative

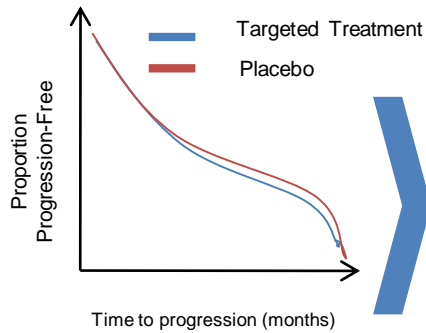
Somatic mutation testing for prediction of treatment response in patients with solid tumours:

- It was already happening and demand was predicted to increase
- Funding was not well established and therefore access is variable across the UK
- Published data from quality assurance schemes suggested that there were issues with the reproducibility and accuracy of results
- Further work was needed in formalin-fixed, paraffin embedded tissue for large-scale routine NHS testing
- There was no clear consensus on who to test, how to test, what to test or how to report results

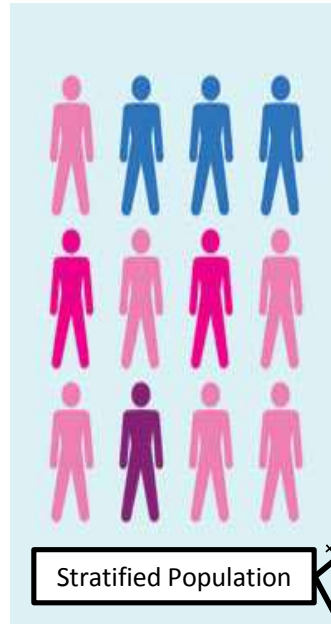
Stratified Medicine



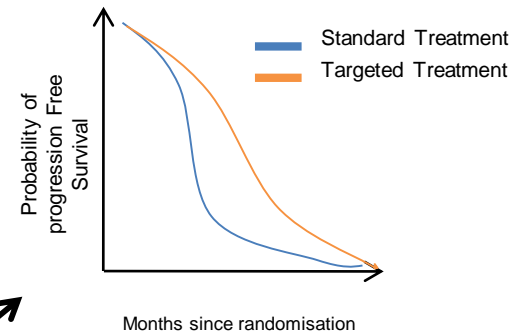
Targeted treatment no more effective than placebo overall



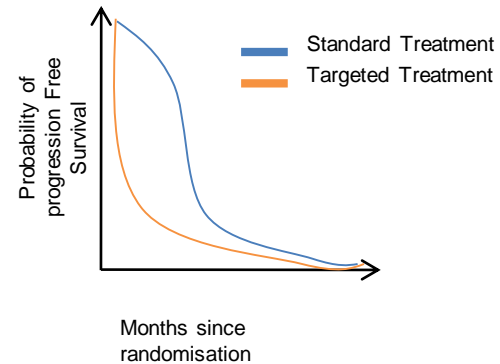
Unstratified Population



Targeted treatment more effective than standard treatment if mutation is present



Targeted treatment less effective than standard treatment if mutation is not present



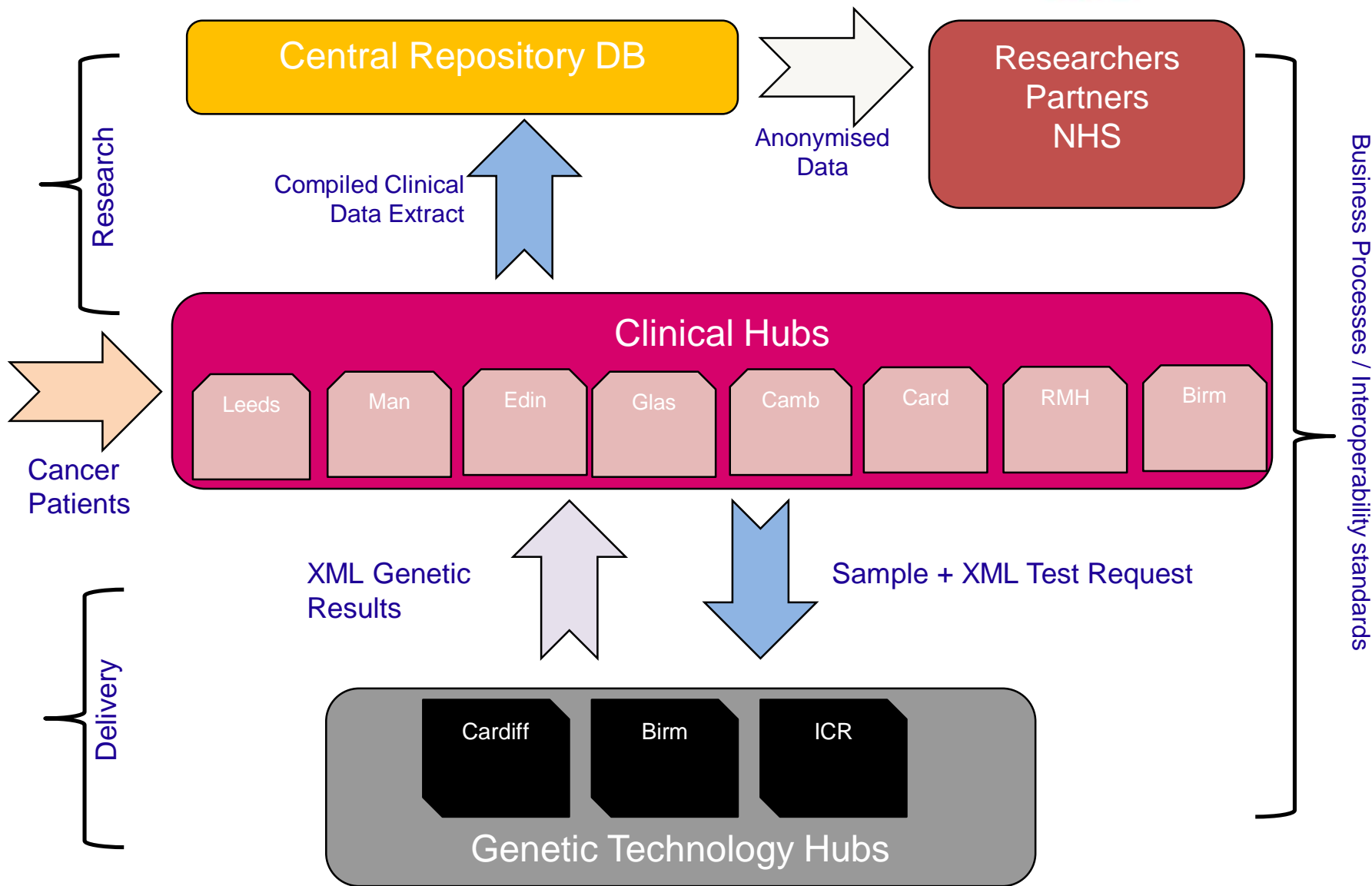
Is the NHS ready for new targeted therapies?

Information Systems for Stratified Medicine

The ultimate solutions were to be able to link to existing data sources with clear explanation and demonstration of how they would be useful in cancer science and medicine, including:

- retrieval and integration of diverse NHS datasets concerning cancer patients e.g. national minimum datasets, genetic data and patient records
- maintenance of a secure database where the individual's right to privacy is demonstrably protected
- allocation of controlled access to validated members of the research community
- scalability – any solution will need to be scalable to ultimately incorporate millions of patient records, including varied clinical data with the expected massive scale of stratification data (molecular or imaging) and formats (images, defined datasets, free text)

Stratified Medicine Programme



Dataset for Stratified Medicine



Patient **Demographic** (name, address, age, gender, ethnicity) – from Stratified Medicine Dataset



Referral (date, main specialty, organisation) - from Stratified Medicine Dataset



Consultation (date, primary diagnosis, basis and grade) - from Stratified Medicine Dataset

Co-morbidities *Consent*



Cancer Care Plan – From MDT (SM Dataset)

Pathology (date, pathological staging (TNM), differentiation, **MDx** (including gene, scope, method, mutations), histology, margin, invasion) **Imaging** (integrated staging (TNM)) **DNA** (source, amount banked)- from SM Dataset



Treatment – **Surgery**
(date, procedure, site)



Treatment – **Chemotherapy**
(date, intent, regimen, changes)



Treatment – **Radiotherapy**
(date, intent, site)



Outcome – **Death**
(date, cause, ID) – From ONS
Dataset
and local death reporting



Outcome – **PFS**
(date, 'continuous updates',
'follow up') + additional information
From Chemotherapy Dataset



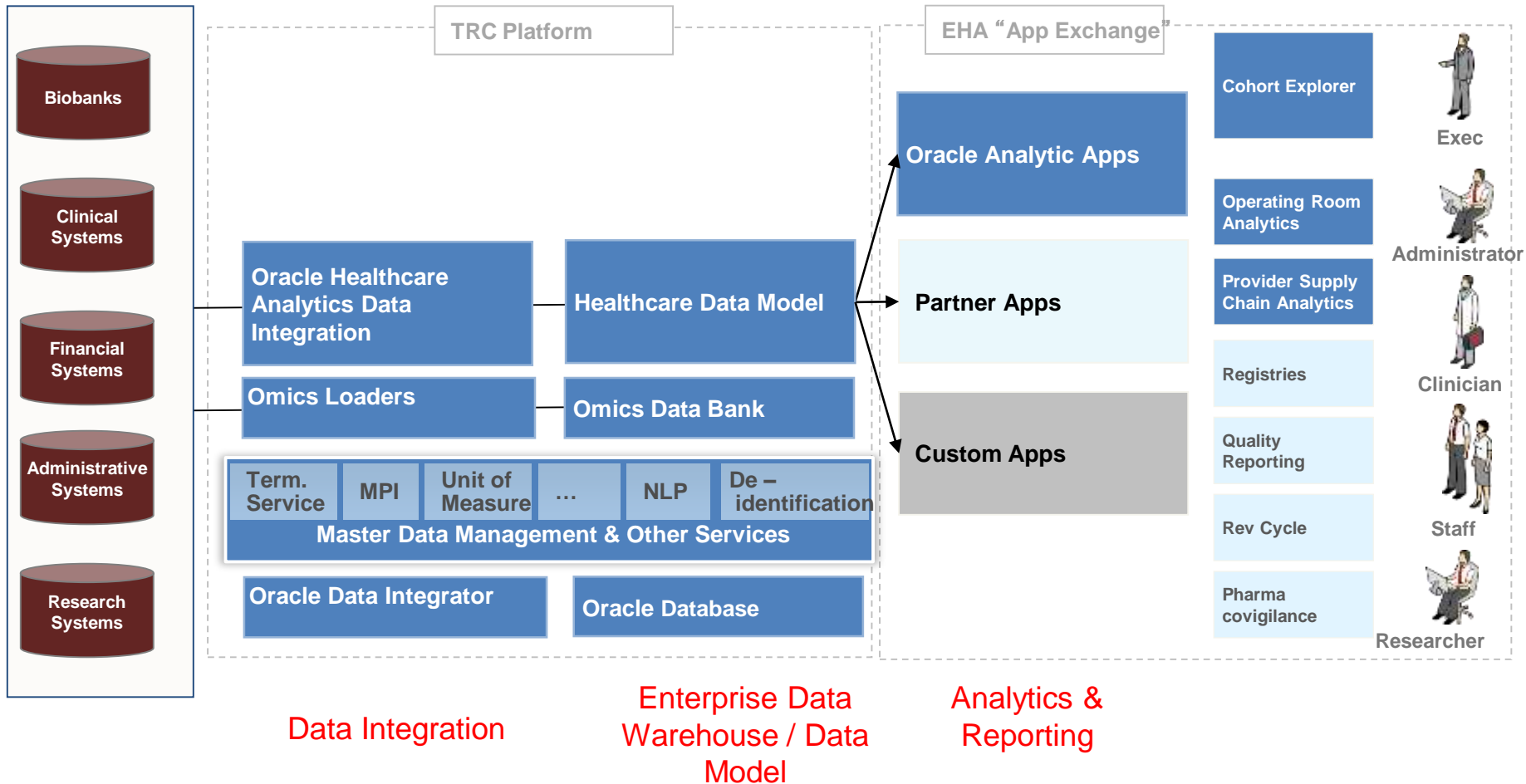
Outcome – **Relapse**
(A&E, Outpatient and Inpatient activity
which can be used as an indication of
relapse)
– From HES

Analysis and Reporting



- Collation of all data extracts in central repository - Cambridge
- Installation of research database and Cohort Explorer - Oxford
- Export of Stratified Medicine cohort (approx 9000 anonymised patient records – clinical, pathology and genomic data)
- Requirements for both fixed reports and ad hoc analysis; user licences for clinical and technology hubs
- Community of knowledge to explore the potential further using data export
- Developmental use for further analysis and ‘proof of concept’ for Next Generation Sequencing (NGS) molecular diagnostics

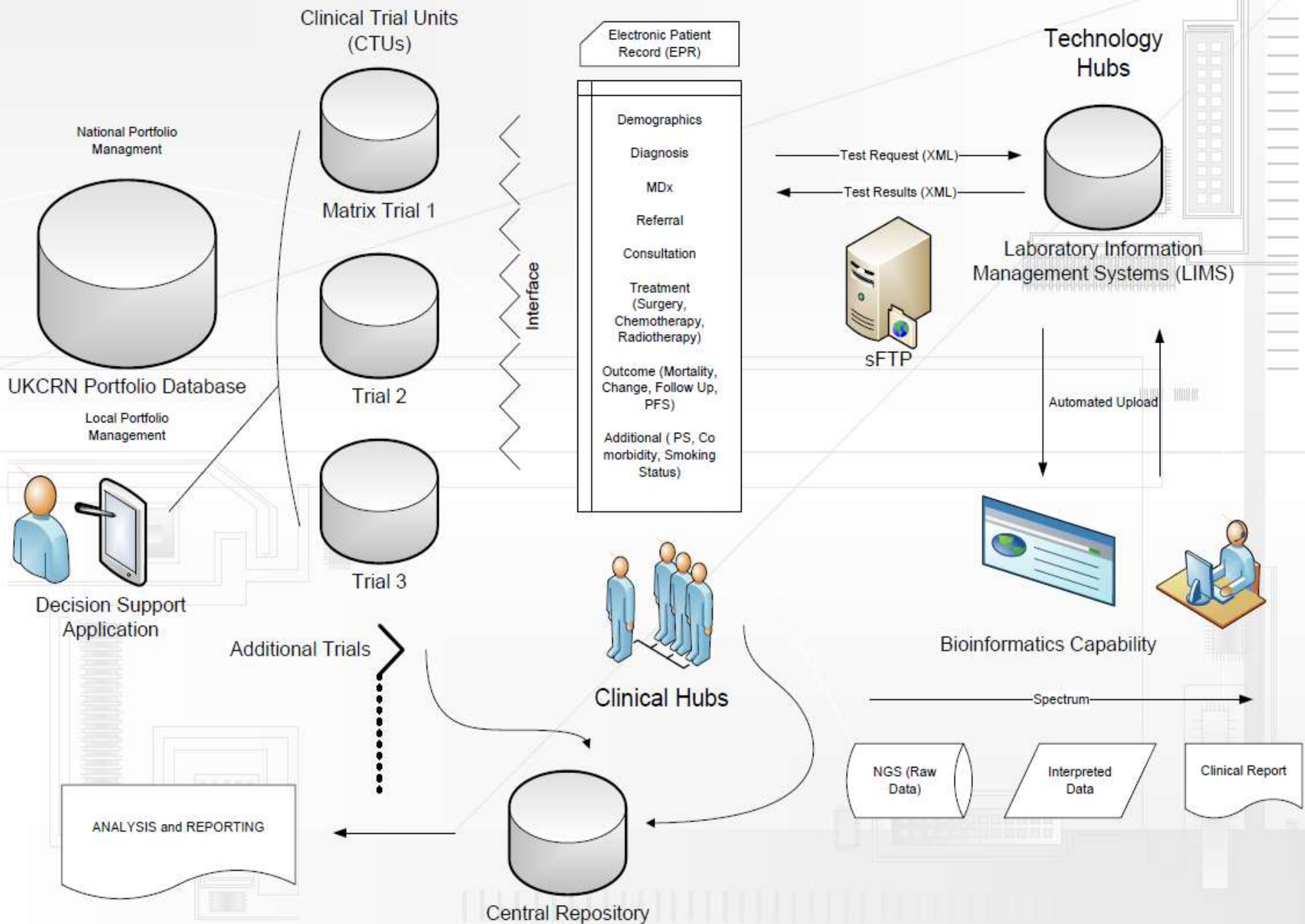
Oracle Enterprise Healthcare Analytics



Challenges Remaining

- Embedding molecular diagnostic testing for multiple markers into patient pathways
- Achieving clinically relevant turnaround times
- Moving towards a single panel approach
- Establishing standards for molecular pathology
- Establishing routine consent of patients and samples for research
- Sufficient resources and clinical support to enable delivery of clinical data for research
- Capability to extract follow up and broader outcomes data

STRATIFIED MEDICINE 2 – ENTERPRISE ARCHITECTURE



Applications of the Clinical Data

- Describing the characteristics of the patient cohorts
- Prevalence of molecular abnormalities in the UK population and comparison to other published data
- Range of mutations seen and other findings e.g. amplification/deletion of genes involved in rearrangements
- Co-existence of mutations in individual tumours
- Clinical correlates of mutation-positive cases e.g. morphology, stage of disease, survival
- Identifying patients who may be eligible for entry to stratified clinical trials
- Informing sample size calculations for future studies in sub-groups with rare mutations

The Impact on Patients

- A service delivery model has now been established for molecular diagnostics in the UK
- The structured interoperability of the systems (using XML messaging) has been key to success and strongly endorsed by clinicians at the hospitals and labs
- Patients tests and results are happening much more quickly and effectively than before
- The accuracy and consistency of reporting these results improves patient safety and access to treatment
- Cohort exploration and analysis is increasing our knowledge and expertise which in turn leads to improving diagnosis, treatment and outcomes

Acknowledgements

- The patients who consented to take part in the Programme
- Investigators and teams at the clinical and technology hubs, and their NHS colleagues
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- Other partners; Oracle, EMC², Roche, BMS

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