The data derived from genomic sequencing are transforming our understanding of health and disease thus enabling more accurate diagnosis in rare disease, infectious disease and cancer. The wealth of data in the genome provides enormous potential to improve health and develop tailored therapies. Whole genome sequencing is a single assay that generates vast amounts of data on which several different tests can be run. [There are many less expensive, more focused genomic tests that can provide diagnostic information for many individuals but have less potential value for research.] We welcome the implementation of genomics in the National Health Service (NHS), acknowledging that the quality and standards that apply across the rest of medicine also apply to Genomic Medicine and advocate upholding a set of key principles to maximise benefit and minimise harm as follows:

1. **Equity:** Equity of access to testing & screening, based on clinical need rather than ability to pay, should be a fundamental principle of Genomic Medicine in the NHS. Tests on any NHS recommended list should be equally available across regions and localities and to all members of society.

2. **Evidence-based medicine:** Genomic medicine should be based on sound evidence of clinical benefit. Demonstration of clinical validity and utility is required before genomic tests are adopted by the NHS. Without this, use of such tests should be a research endeavour.

   - **Diagnostic testing** – The likelihood of genomic variants causing disease can vary greatly, based on the context in which they are found. As with other medical tests, genomic testing and results need to be contextualised and interpreted by a clinician, with appropriate expertise, to make them suitable for each individual patient.

   - **Genomic screening** – Many people who are genetically predisposed to a condition will never develop symptoms. Despite extensive research, the full consequence of most variants when found in a healthy person is not known. Before variants are used in screening tests, information about the likelihood of disease developing (penetrance) when the variant is found in a healthy person and its clinical relevance must be available together with data on whether the proposed test meets current NHS requirements for screening.

Failure to adhere to these principles may expose people to unnecessary risk and the NHS to considerable unnecessary expense and resource utilisation.

3. **Safety:** Genomic medicine runs the risk of over-diagnosing and treating conditions that may never manifest, with the possibility of further amplifying any errors through cascade testing of relatives. To minimise harm, tests should only be deployed once they have been evaluated in the population and context in which they are to be used and have an acceptable level of sensitivity and specificity. Quality control of genetic testing and interpretation is essential.

4. **Consent:** Genomic medicine challenges our current understanding of consent for medical treatment as there are implications not only for the patient but potentially also for family members. Knowledge of genomics is evolving rapidly. Education of clinicians and patients is required on specific diseases as well as the evolving nature and possible implications of genetic testing now and in the future; for the individual and family members; the importance
5. **Research:** Each genome contains 4-5 million variants and there is an unprecedented level of complexity involved. There has been great progress, but it will take decades of research to optimise genomic testing and interpretation. Investment in high quality research is a high priority to understand: the biology of disease; the mechanisms of drug action; the interaction between genomic variants, environmental exposures, and random events; and to innovate new treatments.

6. **Patient and Public engagement:** It is essential to engage with diverse groups of the public to discuss the opportunities and limitations of genomic testing: to develop the appropriate use of genomics in medicine, ensuring patient-centred care for individuals and more widely at a societal level. Transparency about data-access/usage and industry involvement is paramount in building trustworthiness. Genomics is often described as much more clear-cut than evidence suggests; public understanding of the complexities and uncertainties will help the appropriate use of genomics in society.

7. **IT and connectivity:** Commissioning of genomic services and attempts to implement an IT system to support this have highlighted key communication and engagement gaps. This requires fit-for-purpose IT and informatics; and ready access to supporting information for clinicians and patients. A new approach involving experts and patients in co-design, would avoid potential disconnect and disruption and produce more innovative, flexible and future-proof systems.

8. **Quality and appropriateness:** Currently, the quality of individual genome sequences is far from perfect, and further innovations in sequencing technology and data interpretation are required to improve this to achieve a truly comprehensive and accurate readout. Genome analysis may not be the most sensitive, specific or cost-effective test in many clinical scenarios; as with all investigations, genomic tests should be used where clinically appropriate.

9. **Training resources:** The ability to develop genomic medicine in the NHS is dependent on adequate training for relevant medical professionals and appropriate genomic medicine training in existing graduates; adequate resourcing of appropriately skilled personnel. Successful implementation of genomics in all branches of medicine requires a strong core of clinical genomics expertise to lead implementation, evaluate when tests are ready to deploy widely and to support other healthcare professionals in their use. Education of doctors, all health professionals and the public requires multifaceted educational tools with key skills indicators. An integrated approach between General Practice and specialist colleagues is important as GPs will be the first port of call for many patients who might be concerned, worried or simply inquisitive about genomic medicine relevant to them.

10. **Setting priorities to support primary providers:** To ensure equitable decisions about recommended tests and access within all regions, the medical Royal Colleges and other professional bodies will feed in to determine priorities for testing based on peer review and inclusive input from members; they will support primary providers in the decision to order...
whole genome testing through regional input and development of clinical pathways for genomics within each specialty.

Due to the rapid pace of genomic science, agile adjustment to: 1) the Test Directory, 2) pathways, and 3) guidelines will be essential as knowledge grows. The Academy is working with the medical Royal Colleges and their affiliate specialist societies to embed genomics in clinical practice across the UK via the Genomics Leads group. The positive expectations of genomics must be tempered with the limitations of our current knowledge and the realities of current workforce pressures and budgetary constraints. There is considerable risk in over-promising the ability of genomic medicine to lead to prevention of disease and personalisation of treatment; there needs to be a balance between hope and honesty about what genomic medicine can realistically deliver.