The AHSN Network

Genomic innovation: technologies for personalised medicine

Executive summary

This is an overview of a report researched, written and produced by the PHG Foundation for the AHSN Network

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Introduction

This 2020 review for the Academic Health Science Networks (AHSN) builds on the 2018 report *The Personalised Medicine Technology Landscape* and presents an evidence review of genomics and genomics-related technologies that will have an impact on the delivery of personalised medicine within two to three years.

The aim is to support the AHSN's thematic programme on personalised medicine, which has been established to support the implementation of novel diagnostic and treatment approaches that make use of genomics and other 'omics technologies. This review has been informed by desk-based research and analysis of public sources of information including grey literature, peer reviewed literature, and interviews with expert stakeholders.

Innovative genomic technologies in the NHS

With the 2019 launch of the Genomic Medicine Service and National Genomic Test Directory in England, genomics and other technologies that make use of genomics approaches are having an increased impact on the delivery of healthcare in the short to mid-term.

Personalised medicine will continue to develop and drive change away from the 'one size fits all' delivery of care. The rate of development of healthcare innovation is increasing, as is the cost and the expectations of the public for improvements in NHS services.

Given these developments, and the genomics focus of the AHSN's personalised medicine work programme, technologies with an 'omics component were selected for analysis in this report. Each technology presents an opportunity for the AHSN Network to support innovation adoption and spread.

Circulating tumour DNA testing for cancer

Circulating tumour DNA testing is a fast moving technology area, and one type of companion diagnostic testing is already available for lung cancer treatment via the National Genomic Test Directory. In the next three years there is potential for implementation of further companion diagnostic testing in other cancers, and the use of ctDNA testing as a monitoring tool is also showing great promise.

Recommendations

- Given that the available evidence for use of ctDNA testing varies broadly across different cancer types, as well as across different applications, approaches to assess the clinical validity and utility of ctDNA tests will need to be considered on a case by case basis.
- Further work is needed to determine the most clinically and cost effective way of using EGFR ctDNA testing for non-small cell lung cancer in the UK health system. When new tests become available with improved sensitivity and specificity, they should be evaluated against current tests to ensure that the most suitable technology is used and implemented across the health system.
- For clinical indications where there is an unmet need and a ctDNA companion diagnostic test has been identified, consideration should be given at an early stage of test development to gathering the evidence required to support best practice and integration of the test into clinical pathways.
- Further work is needed to support gathering of evidence around the clinical utility of ctDNA monitoring approaches, through clinical research studies and trials.

Pharmacogenomics testing

Pharmacogenomics testing is anticipated to be included in the National Genomic Test Directory in the near future, and there are a number of pilot projects currently underway exploring which gene-drug pairs are most ready for clinical implementation. The main opportunities in this area will come once the pilot projects are complete and plans can be progressed for the implementation of pharmacogenomics in the NHS.

Recommendations

- With pharmacogenomic information interpretation of results is not always straightforward and requires careful consideration. The most up to date evidence from databases and recent guidelines should be used to support clinical decision making.
- Further work is needed to determine for which situations reactive or pre-emptive pharmacogenomics testing will best meet the needs of patients and the health system and how such approaches could be delivered.
- Consideration needs to be given to the evidence requirements to support implementation of pharmacogenomics testing, and on supporting test developers to understand these requirements.
- Support for collaborations that facilitate sharing of resources and data are needed to underpin the information networks required to enable correct prescribing.
- Clinical decision support systems for pharmacogenomics testing are a key area that requires further development and support.

Transcriptomics

Transcriptomics is another ‘omics technology where three tests are already available to support clinical decision making in women with breast cancer. There are a number of other clinical areas where further support and evidence gathering is needed; for example, in rare disease diagnosis.

Recommendations

- Further support is needed for evidence-gathering of clinical utility of gene expression profiling tests, particularly in terms of patient outcomes.
- Ongoing research is required to identify the most promising applications for transcriptomics in rare disease, and these should be supported in terms of gathering evidence of clinical effectiveness.
- Consideration should be given to how current DNA sequencing pipelines and infrastructure can be utilised and altered to support RNA sequencing efforts, should further evidence for its use arise.
- Support for research into standardisation of RNA analysis methods is key to ensuring that evidence gathered is reproducible, accurate and reliable.

Near patient testing to support antimicrobial stewardship

Forms of near patient (and point of care) testing, including rapid diagnostic testing for infectious disease, is an area of varied and intense activity in terms of technology development and application. In particular, technologies that support antimicrobial stewardship have the potential to contribute to global efforts to mitigate antimicrobial resistance. Disease areas where there is already potential to support innovation and implementation efforts include influenza, urinary tract infections and sepsis.

Recommendations

- With the use of their existing networks and by close collaboration with patient safety collaboratives, AHSNs are well placed to support the identification, implementation and dissemination of new diagnostic tests as part of their work programme on AMR.
- The AHSNs could help support further implementation and broader use of influenza point of care tests, through supporting dissemination and implementation of tests with sufficient evidence, and helping generate new evidence where needed.
- In order to support the timely and effective implementation of point of care tests, test developers should work with the health system to understand evidence requirements early in the development process. This will require not only understanding the test performance evidence required, but also consideration of the health economic impact and changes to service models.

Genetically modified regenerative medicines

Genetically modified regenerative medicines (GMRMs) are a subset of regenerative medicines that involve an element of genetic modification - they are complex and technical innovations. There are a number of GMRMs that have been approved for use on the NHS, including innovative CAR-T therapies for blood cancers, and a gene therapy for a rare immuno-deficiency disorder, ADA-SCID. The opportunities to support innovation include further developments in gene therapies, and longer term, in genome editing approaches.

Due to the rare nature of many of the diseases treated with regenerative medicine, consideration should be given to evidence requirements and collection, which can take time with small patient numbers. This will also have an impact on specialised commissioning approaches for these rare therapies.

Recommendations

- Consideration needs to be given to the levels of evidence required on the clinical effectiveness of therapies that treat diseases with low patient numbers and how that evidence can support specialised commissioning of these therapies.

Understanding the challenges ahead and building on opportunities

Supporting the implementation of the technologies that can deliver more personalised medicine will require a coordinated approach across the NHS, including NHS England, the AHSNs and other stakeholders within and outside the health system.

Each technology not only has to be considered on its own merits, but also as part of an integrated healthcare system. The desire to use an increasing range of new technologies and interventions to improve population health means that the health system should have oversight and consider the implications on how care is delivered when these changes are implemented across the system.

Formal programmes of activities will be required to implement these new innovations into practice when appropriate. These efforts will focus on specific care pathways, but there is also a requirement to consider the system impacts and the necessary infrastructure and resources that will be required to deliver the changes.

The future challenges include:

Understanding evidence requirements

Industry should work more closely with NHS services in order to develop interventions and applications which best meet specific NHS needs. In addition, NHS and NICE evidence requirements need to be addressed in order to facilitate effective and systemic health system adoption of innovation.

NICE, AHSNs, Academic Health Science Centres, the NIHR Community Healthcare MedTech and *In Vitro* Diagnostics Co-operatives, and other bodies such as the MHRA already provide support for commercial developers, in terms of study design and how to obtain the necessary evidence. However, NHS commissioners of services are crucial to the widespread implementation of innovation within the health service, and should assist in defining the nature and level of evidence they require for their decision making.

This will require working with services to understand the clinical problem which the technology has been designed to address, and the types of evidence necessary to demonstrate clinical utility and cost-effectiveness. There will be different requirements depending on the nature of the intervention, the target population, expected costs and benefits and impact on certain care pathways.

Considering health system needs will provide clarity for all stakeholders including those involved in evidence generation and evaluation, and enable more effective implementation of new technologies.

Engagement of commissioners

Effective engagement is essential to support understanding of the nature of new technologies, how they can benefit patients and clinical services, their requirements, and specific implementation approaches to achieve the desired outcomes.

Planning is needed on how to best to achieve this. Informing commissioners about innovations will help to ensure that opportunities for implementation are not missed. Commissioners should also be provided with the specific details and requirements of new technologies in the form of implementation support in order to ensure successful use and avoid unintended consequences for patients and health services.

As some new innovations require complex infrastructure change to support their use, the implementation support needed will also be greater. The NHS digital infrastructure is increasingly unable to support the innovations being considered for implementation and, if not addressed in a timely manner, will become a barrier to the uptake of certain new evidence-based interventions.

Pathway transformation

Whilst less disruptive interventions can be incorporated into established care pathways, some new technologies may necessitate transformational change to deliver the expected benefits. In each situation, special attention and coordinated effort is required to implement new interventions in healthcare. Without taking these steps there is unlikely to be equitable access to these new interventions.

Many innovations provide an active opportunity to transform clinical pathway design and make changes to referral pathways, rather than being added into current pathways as an additional step. One example of where this could occur is where technologies are moved out of specialised services and into secondary and primary care. This might include point of care testing or monitoring (e.g. for cardiac conditions) carried out in a GP surgery. However, the resources and leadership required to implement such system changes should not be underestimated.

Workforce engagement and training

Workforce preparedness is vital. In terms of genomics, this should continue through the ongoing efforts of Health Education England to embed genomic literacy in the workforce. Engagement for other technology areas should be considered.

There are a number of ongoing workforce educational initiatives, such as the Health Education England genomics education programme, which has a number of online courses and offers a Master's degree in genomic medicine. Efforts such as these, which aim to embed genomic literacy in the health workforce, are vital in terms of ensuring that genomic medicine is integrated into clinical practice, and will include equipping clinicians with the skills needed to interpret and act upon the outputs of genomics technologies.

For the other technologies highlighted in this report, further actions are required in order to support the workforce and keep them suitably informed about new innovations. In particular, as plans are made to transform care, greater effort is needed to ensure that a balance is struck in terms of pre-implementation knowledge and on the job training.

As new interventions and diagnostics are deployed, the roles of clinical scientists and other healthcare providers will need to be considered, and appropriate provision made to ensure that they can utilise new technologies appropriately in different healthcare environments.

Delivering on the promise of personalised medicine

Getting all the key elements in place for successful implementation of innovative genomic technologies for personalised medicine as outlined above will provide a range of important advantages:

Benefits for patients

- More precise diagnosis and prognosis
- More targeted treatment
- Fewer side effects and improved clinical outcomes

Benefits for the health system

- More efficient use of resources
- More streamlined care delivery
- Improved health outcomes

The implementation of healthcare services based on the new technologies in development will be occurring in a health system that is also undergoing technological transformation and infrastructural change. Further developments in major digital services and infrastructure will be vital to ensure their successful uptake.

As the single biggest integrated healthcare system in the world, the NHS is uniquely placed to transform healthcare at a population level, ensuring equitable access to these new health services. There is therefore a valuable opportunity for the AHSN Network to play a central role in supporting the clinically appropriate, systematic implementation and spread of personalised medicine technologies in this new landscape, and thereby helping to realise the benefits to patients and the NHS.

The **AHSN** *Network*

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