

Diagnostics Forum 2013 report

Fast-tracking the evidence for
implementing diagnostic tests

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NICE National Institute for
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Technology Strategy Board
Driving Innovation



UNIVERSITY OF
OXFORD

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This report presents the key findings from the 2nd UK Diagnostics Forum held at the University of Oxford on 2nd of May 2013, supported by the Technology Strategy Board, the British In-Vitro Diagnostics Association (BIVDA), the National Institute for Health and Care Excellence (NICE), and the University of Oxford Nuffield Department of Primary Health Care's Centre for Monitoring and Diagnosis (MaDOx).

This one-day conference brought together leading experts from the UK diagnostics industry, health economists, clinical diagnostic researchers, NICE, and the Technology Strategy Board.

Following on from the recommendations of the 1st Diagnostics Forum, the meeting addressed three key priority areas for improving the evidence base for diagnostic tests:

1. What tests are needed?

Where are the gaps in the diagnostics market? What are the most efficient ways to find out what diagnostic tests clinicians and commissioners of services need?

2. How much evidence is enough to demonstrate clinical effectiveness?

What does NICE and others involved in procurement want? What kinds of studies are essential, and what are the most efficient ways of designing research for diagnostics? When can evidence be used across different countries and/or settings?

3. Modeling evidence and cost-effectiveness of diagnostic tests.

When is it necessary to consider the cost-effectiveness of diagnostic tests? What are the best approaches and how can we combine different types of evidence? How does NICE consider the cost-effectiveness of diagnostic tests? What input do we need from economic evaluations of diagnostic tests?

Foreward

In vitro diagnostics (IVDs) already play a key role in the NHS. However, I believe the importance of IVDs will increase for three reasons. Firstly, through the growth of stratified medicine and its reliance on accurate and standardised diagnostic testing, IVDs will increasingly be relied upon to identify patients who will respond to these new therapies. Secondly, IVDs can improve the early identification of disease and thereby improve the chances of successful treatment. Thirdly, IVDs can help identify patients who either will or will not respond to a particular treatment; this is increasingly important as the NHS seeks to offer the best treatments within tight budgets. In short, diagnostics' time has come.



Mark Samuels
Managing Director
NIHR Office for Clinical Research
Infrastructure (NOCRI)

In spite of this, introducing new IVDs into widespread NHS practice has not always been easy. When developing new tests, companies have sometimes not given full consideration to clinical utility at an early enough stage. For the NHS to buy and use new IVD tests, high quality evidence of clinical utility is vital. This does not always mean an expensive randomised trial, but at times good alternatives have not been evident to industry. There is no simple checklist for this. Sound health economics are crucial too. Health economic methods for IVDs, however, may not be the same as for drugs. And there is room to enhance the health economic methods by which diagnostics are evaluated. Finally, it is important for an NHS organisation to know how a new IVD test will impact its local budget.

None of these issues are simple for a company to address on its own. For this reason, the National Institute for Health Research (NIHR) has launched four Diagnostic Evidence Co-operatives. These have the expertise to support both NICE and individual companies in generating the right evidence, which will enable better uptake of new IVDs by the NHS.

The UK is building a critical mass of R&D capabilities in diagnostics. This includes world-class expertise in the NIHR's Diagnostic Evidence Co-operatives, as well as outstanding Biomedical Research Centres and Units. In addition, Technology Strategy Board investment will enhance these capabilities through a Catapult in diagnostics. Together, these offer industry world leading know-how in diagnostics R&D.



Fast-tracking the innovation process

The process of development, validation and adoption of new diagnostic technologies is recognised as being a lengthy process, and one that does not always fulfil initial expectations. This experience contributes to increasing attempts to fast-track the innovation process in many healthcare systems, e.g. the Innovation, Health and Wealth programme in the NHS, and the recently funded NIHR Diagnostics Evidence Cooperatives, are part of an agenda focussing on quality, productivity and prevention, aiming to bridge this translational gap.

Innovation in healthcare results from a collaboration between clinicians, scientists, entrepreneurs and commercial organisations – as well as managers and policymakers in healthcare. Defining present standards of care and utilising new technology to redefine products and services will allow new best practices to be implemented and audited across healthcare systems (Figure 1).

“There’s a finger-prick blood test that allows patients on anticoagulation therapy to self-monitor their blood clotting time. It’s effective, convenient, and in the end, cheaper for the NHS. But still, less than 2 per cent of the 1.25 million people in the UK on long-term anticoagulation therapy are self-monitoring. This is happening with a whole host of drugs and treatments. It is a massive missed opportunity – and in so many ways it’s out-of-kilter with the spirit of the NHS.”

David Cameron, UK Life Sciences Speech 2013

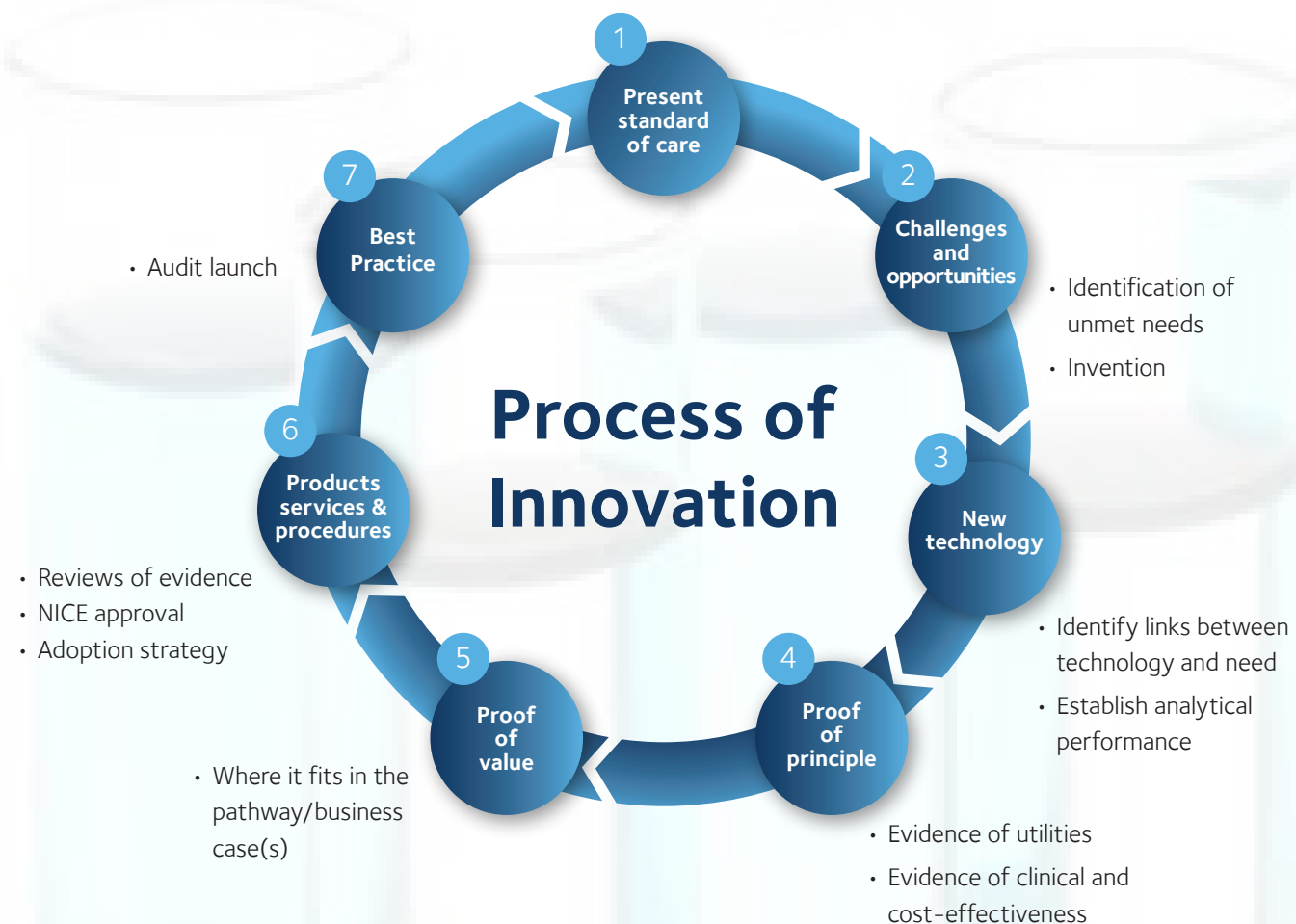


Figure 1: The cyclical process of innovation

Involving stakeholders

One of the central points to recognise at the onset of the innovation process is the number of stakeholders with an interest and investment in the adoption of new technologies. Innovation can stall if stakeholders such as those listed below are not included in the process:

- patients and their families/caregivers
- commissioners of services and clinical commissioning groups
- primary care clinicians
- secondary and tertiary care clinicians
- social care providers
- secondary and tertiary care provider organisations
- laboratory professionals (and equivalents in other diagnostic modalities)
- governmental agencies, including regulators and quality monitors
- diagnostics industries

NICE Health Technologies Adoption Programme

The HTAP at NICE facilitates the adoption of selected NICE-approved health technologies across the NHS, through engaging with front-line NHS staff and services – It does this to understand and assess the factors that will promote access to, and increase the sustainable uptake of, evidence-based health care technologies, within routine NHS care.

Identifying unmet testing needs in healthcare should be an important driver of innovation, with the expectation that a new diagnostic technology that fulfils a current 'gap' is more likely to be adopted. However, different stakeholders may perceive different needs, and may not actively be engaged in the priority setting:

Patients:	There is currently no 'one stop' forum for identifying their needs, so industry may use several consumer groups to help identify needs. Special interest patient groups may also provide input into highlighting needs. Sometimes guidelines (e.g. NICE guidelines) may identify priority unmet testing needs from patient perspectives.
Clinicians:	Identifying clinicians with time or expertise to contribute to needs assessment may be difficult. New tests may lead to new or different workloads in an already pressured system. Protective practices mean there may be a reluctance to change, maintaining the status quo.
Commissioners of healthcare:	Responsibility for most efficient use of resources, which may be driven by short-term needs to reduce expenditures. May also be difficult to selectively disinvest in existing diagnostic services, or other elements of the care process that become redundant.

In some cases these different perspectives can create potential conflicts of interest, which may vary according to different health systems. Moreover, different values and preferences may lead to wide variability among stakeholders on perceived needs, depending on their individual attitudes towards risk, uncertainty, over (and under) diagnosis and costs. Eliciting the variability in perspectives may further shape the innovation process.

Current needs

Recommendation 1: Whilst innovation is the result of collaboration between researchers, clinicians, and commercial organisations, there needs to be a transparent and systematic elicitation of the needs of different stakeholders.

Recommendation 2: NHS trusts should have a dedicated clinician or healthcare manager to deal with stakeholder issues related to diagnostic innovation involving patients, clinicians and commissioners.



Identifying the problem

Medical tests can potentially be used to solve many different problems (not just one – for example, diagnosing, monitoring, assessing prognosis). Furthermore a test alone, without an accompanying change in clinical management, is unlikely to improve health outcomes.

The starting point for successful innovation is specifying ‘what is the problem?’ and how a medical test might be able to help resolve the problem. Or, put another way, unmet needs are probably best addressed by employing the basic approach to quality improvement and system redesign:

1. Where could clinical outcomes be improved?
2. Where could processes be improved?
3. Where could resource utilisation be improved?

It is then important to determine how the test will be used, i.e. what decisions can be made, actions taken by use of the test, and how the new test would fit in the overall patient flow organisation.

Identifying the Problem

There is a drive in several health systems to provide a more patient-centred approach to care, making care more accessible and closer to home. However, there is a shortage of point of care technologies and a lack of understanding of the pathways, which can effectively rule out disorders and safely manage the patient in the home setting.

Recommendation 3: Fast track innovation in diagnostic testing requires a clear understanding of the clinical problem at the outset of the development process.

Identifying unmet needs

There are a number of strategies to identify unmet testing needs, but it is unclear which of different stakeholders use these, and which provide the most useful information. Some of the methods used for needs assessment included:

- Surveys of clinicians, patients and carers
- Focus groups with clinicians, patients and carers
- Identifying research gaps in clinical pathways, e.g. from existing NICE guidelines
- literature reviews
- observational studies of current clinical practice and test use

However, currently it is not clear which of these methods (alone or in combination) are most useful for different stakeholders, and which of these apply across multiple different settings (e.g. primary care, secondary care), and which can be used across different healthcare systems and countries.

Recommendation 4: Develop more effective ways of identifying diagnostic testing needs from different perspectives (patient/carer, clinicians, laboratory services, commissioners, industry).

Demonstrating clinical effectiveness

The 'bar' for how much and what kind of evidence is considered sufficient for adoption are perceived by many (particularly in the diagnostics industry) as being very unclear. There is no universal checklist or agreed set of evidence criteria, and decision-makers across Europe adopt different approaches. In addition, the overall level of understanding (by industry, regulators, and clinicians) about diagnostics evidence and study designs – beyond initial validation studies – is often quite vague. The Conference highlighted the relatively small group of 'diagnostics

methods experts' in the UK, and the difficulties industry has in understanding where 'the bar' for adequate evidence actually sits.

This lack of clarity clashes with the global strategies of companies, who need evidence that will not apply only to the UK healthcare market. In fact, compared to larger markets such as the USA, the UK market is often not seen as a priority, and studies are primarily designed to meet the requirements of wider markets.

There are many different 'hierarchies' or 'levels of evidence' for studies of diagnostic tests. Increasingly there is more attention now being paid to effects of tests above and beyond 'merely' demonstrating test accuracy. Rather than judging a test on its diagnostic properties, emphasis is now increasingly placed on a test's ability to improve patient outcomes. This means that many tests need to be evaluated specifically with respect to the clinical pathway in which they will be used.

This approach causes problems because:

- The clinical pathway may not always be well characterised
- There may be large variability in pathways across different countries, regions, hospitals and clinical practice
- A test may be used for more than one clinical indication, necessitating the evaluation of the test for each clinical indication (e.g. ruling in/ruling out, treatment monitoring, prognosis) and thus each clinical pathway.
- A one size fits all approach does not take into account the different types of tests, patient comorbidities, or patient settings (see below)

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'Me-too' diagnostics, i.e. ones that are simply replacing one test in a defined clinical pathway with another (more accurate, more feasible or cheaper test) are a simpler situation. In this case, assessment based on diagnostic



accuracy and direct costs may be sufficient, because the clinical pathway remains unchanged and the test's impact on patient outcome is likely to be minimal. Considering the current regulatory framework allows such me-too diagnostics to be marketed without much prior evaluation, industry perceives the development of novel diagnostics as risky: why therefore, under the current system of equivalence, invest resources in generating evidence when a competitor can then market a very similar test without the need to collect costly evidence?

Novel diagnostics, with the potential to disrupt current care pathways, are the most complex. Adopting the new diagnostic technology may result in changes to patient outcome and/or processes of care, which should be evaluated before widespread implementation. Where these are also likely to have significant cost implications, they are priorities for cost effectiveness analysis. Studies capable of generating the key evidence required for the determination of cost effectiveness as well as clinical effectiveness are considered desirable before marketing. Moreover, 'downstream' changes to patient outcomes can occur well after the diagnostic test has been used, further complicating evaluation.

However, randomised controlled trials of diagnostic tests are not very common; it is estimated that there are only 37 randomised controlled trials of diagnostic tests published each year worldwide, which is a tiny fraction of the overall research on diagnostics. At present there is little incentive for such an in-depth and costly evaluation of diagnostic tests prior to marketing. However without this evidence it is difficult to make a strong business case for adoption. Often tests are marketed first and then evidence in real-life populations is collected, (comparable to phase III trials for pharmaceuticals), which is one of the reasons why adoption is slow or misplaced.

Recommendation 5: Develop an agreed set of evidence criteria for diagnostic tests, which take into account different evidence requirements for different types of tests (e.g. novel tests, replacement tests), which can be understood and implemented by multiple different stakeholders (e.g. regulators, commissioners, industry, clinicians) across Europe.

Recommendation 6: Developing and collecting the body of evidence set out in the agreed criteria should be incentivised by national bodies to promote local market access and facilitate commissioning of novel diagnostic technologies.

Modelling evidence and cost effectiveness of diagnostic tests

Health economic principles should be fundamental to the earliest stages of product design and innovation. Economic scenario analysis can, for example, help define the diagnostic accuracy that a product would require to make it cost effective compared to current practice. Similarly, threshold analysis can be used to estimate the clinical benefit that a diagnostic would need to deliver in order to be cost effective. For example, the effectiveness and cost effectiveness of prognostic markers such as DNA-ploidy in predicting aggressive prostate cancer was modelled to inform forward product development decisions on minimum diagnostic accuracy.

Modelling can also estimate a new test's impact on patient outcome and healthcare processes before the development of costly trials. Linked evidence modelling, in which the evidence on a new diagnostic test (typically diagnostic accuracy) is linked with the evidence on treatment and ultimately patient outcome, can be an alternative strategy. Linked evidence modelling is feasible when there is existing evidence for parts of the care pathway: the key issue being the criticality of the assumptions used. Care pathway assumptions are particularly challenging as practice varies so widely both within and between different healthcare systems.

NICE clinical guidelines are generally used to inform care pathway assumptions in NICE evaluations of diagnostics. However, it may not be straightforward to understand the fine detail of the 'real life' care pathways that patients are subject to – and this fine detail may have significant impact on cost effectiveness. Nonetheless, some elements within a clinical pathway may be similar and evidence may be transferable to some extent. For example, the downstream consequences of treatment may be identical when these

follow internationally-accepted clinical practice. Other elements may require collecting evidence at the country or local level, such as staffing or costs.

Assessing the impact of near-patient testing

The Technology Strategy Board, in partnership with the Department of Health, invested £2.2m in 6 projects to produce new and improved tools, products or capabilities in the field of health economics to assist companies in the design and evaluation of diagnostic clinical trials.

Determining patient response

In a competition concerned with adverse events and non-responders, the Technology Strategy Board and DH also invested in a two-phase competition where companies were asked to develop the economic case to evidence the value of a proposed diagnostic upfront.

With an investment of £1m, 11 companies were supported in Phase 1 and 4 companies, with a further investment of £7.2m, are being supported to develop their products.

Recommendation 7: Investment is needed in economic scenario analysis, which can define the diagnostic accuracy that a product would need to make it cost effective compared to current practice.

Recommendation 8: Detailed mapping of care pathways is appropriate in most cases as an integral part of cost effectiveness analysis.

Recommendation 9: Develop availability of generic economic models for specific scenarios, including estimates on clinical and cost effectiveness that are transferable to different countries or can be adapted to local needs.

How to achieve these recommendations

There is a perception that “innovation is not working”, and there have been innumerable studies illustrating the barriers to innovation. In order to implement the recommendations from the 2nd UK Diagnostic Forum, six barriers need to be taken into account:

1. Lack of an innovation culture

Culture is the characteristics of a particular group of people, so without taking into account the broadest range of stakeholders, innovation uptake is likely to be slow and ineffective. **Recommendation 1** highlights the need for a stronger and more transparent process of collaboration between researchers, clinicians, and commercial organisations, taking advantage of the current support in the UK for diagnostics industry (see box). In addition, each NHS commissioning group should have a dedicated clinician or manager to deal with stakeholder issues related to diagnostic innovation (**Recommendation 2**).

2. Poor prioritisation of needs, and subsequent adoption

Failure to identify ‘what is the clinical need’ at the early stages of diagnostic development is a major problem. We recommend more effective and more meaningful collaboration between industry, academia, clinical care providers and funders (**Recommendation 3**) and better evidence for efficient and effective ways for eliciting clinical needs (**Recommendation 4**).

3. Need for evidence of clinical and cost effectiveness

Developers of diagnostic technology need a ‘diagnostic toolkit’ that clearly sets out the evidence requirements for effective adoption of new technologies across Europe (**Recommendation 5**). Included in this are levels of evidence that take into account how to incorporate evidence from different contexts and settings and how to develop cost effective models that take into account the various clinical pathways. At a national level, government bodies regulating market access should incentivise industry to collect the required evidence (**Recommendation 6**).

4. Reimbursement based on fee-for-service, rather than on value

Even where there is clear evidence of clinical and cost effectiveness, and even where a diagnostic has been recommended by NICE, adoption can still be slow and patchy. Adoption of new tests can be very difficult in the NHS: money is distributed over different budgets, Trusts and commissioning groups are relatively independent, and there can be a resistance to change.

Strengthening links between stakeholders

NIHR Diagnostic Evidence Cooperatives (DEC):

four Diagnostic Evidence Cooperatives that aim to stimulate collaborations between different stakeholders in diagnostic testing. For example, the aim of the Oxford NIHR DEC is to improve the implementation of in vitro diagnostics in primary care settings. The DEC will develop collaborations between primary care front-line clinicians, laboratory services, diagnostic test researchers, the diagnostics industry, NICE diagnostics programme, and other relevant NHS groups.

Academic Health Science Networks (AHSN):

which aim to improve health-care through faster identification, adoption and spread of proven innovations, including through collaboration with industry.

Technology Strategy Board: is the UK’s innovation agency with a goal is to accelerate economic growth by stimulating and supporting business-led innovation. Working with multiple stakeholders, its Stratified Medicine programme recognises the need to address the challenges of adoption of new diagnostics if the UK is to maximise its potential.

NIHR Biomedical Research Centres (BRCs):

drive progress on innovation and translational research in biomedicine into NHS practice.

NIHR CLAHRC: NIHR CLAHRCs are an alliance of academic and healthcare organisations working to develop and promote a more efficient, accelerated and sustainable uptake of clinically innovative and cost effective research interventions into patient care.

So, improving the strategies to support the implementation of ‘proven’ diagnostics needs to be better in the UK. There are already a number of mechanisms within the NHS to support the adoption of novel technologies that improve patient outcomes and/or enable beneficial service redesign.

These include innovation tariffs within the payment by result system.

NICE already uses many strategies to support implementation of NICE guidance, support products include commissioning guides, costing spread-sheets, generic business cases for capital purchases, pod-casts and a range of bespoke tools tailored on a case-by-case basis. Implementation support activities at NICE were augmented in April 2013 by the transfer of the former National Technology Adoption Centre to NICE. Now known as the Health Technology Adoption Programme, activities include detailed adoption and site demonstrator projects which detail the 'real life' impact on care pathways and cash flows as well as identifying and mitigating the key barriers to adoption.

Another key initiative to support adoption of NICE recommended technologies is the NICE Implementation Collaborative, established in response to a recommendation in the NHS Innovation Health and Wealth report. This is a partnership between the NHS, the life sciences industry, healthcare professional bodies, key health organisations and the public, who have committed to work with each other and other organisations to understand and analyse the barriers that exist to the implementation of NICE recommendations.

5. Silo budgeting and silo management

Many of the diagnostics services, e.g. laboratory medicine and radiology are organised, funded and managed as independent budget silos, and in some countries are expected to generate a profit for the organisation. A consequence of this is that when a new test becomes available the key problem for adoption is the funding of the test, with little thought being given to the impact of the test on other parts of the service which may become redundant, e.g. other tests, clinic visits, hospital admissions etc. Therefore it is key to develop more robust methods and experience in the detailed economic tools that can be used to define the test characteristics that could make it cost effective (**Recommendation 7**), map out the care pathways, (**Recommendation 8**), and develop in some cases generic models that can be used to model evidence across multiple different settings and scenarios (**Recommendation 9**).

6. Opaque decision-making processes around innovation initiatives

In contrast to new pharmaceuticals, where there is an accepted process for adoption in the NHS once clinical and

Diagnostics at NICE: The NICE diagnostics assessment programme is a specialist programme to undertake complex assessments.

The methodology includes cost effectiveness analysis, requiring the quantitative determination of outcome benefits, measured in Quality Adjusted Life Years (QALY). The detailed evaluation process and advisory committee structure, which includes specialist members recruited for each topic, makes it suitable for tackling disruptive technologies. NICE also evaluates diagnostics in the context of clinical guidelines where cost effectiveness methodology is also applied.

A quicker and simpler cost consequences approach to evaluation is applied in the NICE medical technologies evaluation programme. This is suitable for products where the value proposition is cost savings.

NICE has recently launched a new work stream – Medtech innovation Briefings (MIBs). These are quality-assured summaries of the available evidence on medical device and diagnostic topics. They do not include recommendations and the technologies included in MIBs should not be considered as NICE-approved. MIBs are intended to support local decision-making where a formal evaluation by NICE may not be needed or appropriate at that stage.

cost effectiveness have been demonstrated, there is no similar process for new diagnostics. This risks stifling not only innovation in healthcare delivery, but also impairing the UK's attractiveness for diagnostic industry research and development. Several of this report's recommendations take advantage of further developing the strong industry, research, and governmental support for the diagnostics industry in the UK. In particular, developing and delivering an effective evidence base for diagnostics should be seen as a marker of quality for adoption of diagnostics not only in the UK, but globally.

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