Making the UK the best place to do respiratory research and innovation

Foreword

Despite our academic achievements, respiratory outcomes in the UK have not improved in the last 15 years and respiratory diseases remain the third leading cause of death, affecting 1 in 5 people and costing the UK £11 billion each year.

Respiratory disease is the third biggest killer in the UK, yet research funding is not sufficient in order to change that. Respiratory R&D needs an increase of £100 million per year to bring public funding in line with the proportionate impact of respiratory disease on the nation's health (2% to 6% of health research spend; from £47m to £150m).

Respiratory disease can be a catalyst for the UK to cement its place as a global life sciences leader and make the UK the best place to do respiratory research and innovation by joining up our unique data assets.

Mission: Reduce respiratory morbidity and mortality by 20% in 5 years

By tackling the greatest challenges in respiratory disease on four fronts – prevention, diagnosis, treatment, and self-management – we believe we can save and improve millions of lives. Realising the ambition set out in the Life Sciences Vision will require both funding to cement the talent pipeline, and a long-term commitment to strengthening the infrastructure to bring respiratory research and innovation into the 21st century, both of which are key to attracting large-scale industry investment. This paper sets out phased efforts to build towards virtual 'centres of excellence' in the four key areas that deliver on long-term goals.

Building a platform for respiratory research and innovation

Challenge

- Respiratory diseases are poorly understood, and existing data is poorly connected, which reduces our ability to stratify risk and inform population health management.
- Respiratory-specific biomarkers (e.g., lung function, blood eosinophil levels, exhaled nitric oxide levels) are not routinely measured in UK primary or secondary care.
- This lack of data undermines our capacity to perform research to understand the long-term progression of disease – decline of lung function - and generate new hypotheses for diagnosis, treatment, management and prevention. Failing to take advantage of the NHS' datasets limits our appeal for R&D investment by industry.

GOAL: Make the UK the best place to do respiratory research and innovation by joining up our unique datasets and including respiratory biomarkers in large scale cohort studies.

Opportunity

- **Establish new, linked data platforms, world-leading in size, scale and breadth,** to bring together existing NHS and novel datasets alongside real-world evidence, to drive inward investment into UK respiratory R&D and grow our national data infrastructure and workforce.

- Include the **collection of respiratory biomarker samples** in a suitably representative sized cohort of patient within Our Future Health, to understand disease progression and its causes, and the links between respiratory disease and other conditions.
- Develop and iterate HDR UK's BREATHE Hub – to make better use of the data currently available, and to lay the foundation for building a **respiratory data ecosystem** with multiple integrated data sources - driving new understanding of the causes, long-term progression and unequal burden of respiratory diseases and informing how to treat and cure them.
- Drive **unprecedented understanding of the progression of respiratory diseases** by creating a new respiratory cohort, where lung function is measured from its peak in early adulthood onwards to track and treat decline over time, alongside other blood and breath biomarkers, imaging, quality of life etc.

Phase 1: 2022-24 Funding to enable the inclusion of existing respiratory biomarkers in Our Future Health to enable better understanding of longitudinal progression of lung function decline and its impacts on other conditions. Potential for industry support for a sub-cohort of potential diagnostic biomarkers.

Phase 2: 2022-25 Funding for HDR UK's BREATHE Hub, an advanced data capacity platform to enable greater use of both NHS and real-world data in respiratory research and innovation and to underpin Learning Health Systems.

Phase 3: 2024-30 Funding a new £10m/year cohort to track respiratory-specific biomarkers across the lifetime and generate new hypotheses for the causes, management, and treatment of respiratory disease. Measuring lung function from peak, i.e. driving license age, over a lifetime to provide a more complete picture of disease onset and progression, and opportunities for prevention.

National Diagnostics Centre for Respiratory Disease

Challenge

- Respiratory diagnosis is complex, slow, inaccurate and relies on invasive and/or aerosol-generating tests, which are prohibited in our post-Covid world because of disease transmission risk. Most diagnoses rely on clinical judgement rather than objective tests.
- Millions of people are thought to have undiagnosed COPD, and asthma is routinely mis-diagnosed. Use of respiratory diagnostics, especially spirometry, were effectively shut down during the pandemic – due to the potential role in spreading Covid – which greatly affected diagnosis rates. In 2020 there was a 51% reduction in COPD diagnosis compared to 2019.
- Other life-threatening conditions, such as Idiopathic Pulmonary Fibrosis, are diagnosed late and with poor prognosis.
- The lack of early-stage diagnostic capability contributes to a lack of development of early-stage treatment options, by limiting the target population available for trials.

GOAL: Develop objective tests and, where relevant identify new biomarkers, that can accurately differentiate between respiratory diseases and can be measured remotely through partnering with health technology companies.

Opportunity

- Use the UK's existing capabilities to **lead the world market** in developing globally saleable diagnostic assets. The potential market for respiratory diagnostics is huge – it is estimated that 20% of people in the UK (for example) will have respiratory symptoms at some point in their lives.
  - o Set a **grand challenge for the development of new pandemic-proof diagnostic tools**, spurring inward investment to develop new products that utilise key technologies outlined in the Innovation Strategy (such as Artificial Intelligence) and sensing technologies to detect changes in breath/speech/sleep/cough to diagnose conditions.
  - - **Trial tools in the new Community Diagnostic Hubs and** in-home spirometry pilots using remote devices to identify and monitor respiratory conditions, reducing the NHS diagnostic backlog and paving the way for market access and broader uptake within the NHS and elsewhere.
  - o **Capitalise on the transformation of public attitudes to at-home diagnosis** by COVID (cf lateral flow tests), creating tools that allow detection of respiratory infections to significantly reduce exacerbations and the winter NHS burden, as well as the number of sick days lost nationally. Tests for other strains of respiratory viruses could be brought to market in 3 years, and wider at home testing programmes could be implemented in higher risk seasons.
  - o Better utilise CT imaging in **NHS Targeted Lung Health Checks** to allow the detection of new markers for early COPD[i]. Use AI to identify 'normal' scans to minimise human resource and save millions of pounds

Phase 1: 2022-25 Co-funding with industry to better utilise the opportunity and the data created by Targeted Lung Health Checks, using these data to increase our ability to identify and treat COPD and other respiratory conditions earlier. The screening programme also presents an opportunity to recruit for in-depth -omics trials and other research activities. There is potential for a Sector Deal with industry partners.

Phase 2: 2022-24 Themed call funding £10m/year from NIHR/i4i and Innovate UK to pump-prime the UK diagnostics base, to build on insights from our unified data sources (including lung health checks, BREATHE and real-world data) and enabling SMEs to develop novel respiratory diagnostics.

Building on the Targeted Lung Health Checks, a £10m/year partnership with industry to fund regional pilots of risk stratification of patient records, to identify patients for Lung Health Checks who would not currently qualify (under 50, non-smoker) to pick up other respiratory conditions and maximise recruitment, with testing via community diagnostics hubs.

Phase 3: 2022-30 Public-private investment for a new £20m/year National Diagnostics Centre for Respiratory Disease – based in the North of the UK where respiratory outcomes are poorest – to drive the identification of new biomarkers and development of new objective tests, attracting investment focused on Artificial Intelligence for health and expansion of Northern based -omics capabilities. Possible partnership between EPSRC, MRC and industry.

Centre for Experimental Lung Medicine

Challenge

- The respiratory pipeline has stalled, with few new drugs in the past 20 years that can modify disease trajectory for the majority of people with respiratory disease. High costs and risks prevent private investment.

- Lack of efficacy is now the most common cause of drug attrition, and this is a particular problem in respiratory as preclinical animal models are so poorly predictive of the human condition.
- Meanwhile, the drugs available are ineffective in huge proportions of the clinical population, for example up to 50% of people with asthma respond poorly to steroids, the standard and commonly prescribed treatment.

GOAL: Accelerate the development of new therapeutic target product profiles and make the UK the best place for large-scale digital clinical trials.

Opportunity

- Build a Northern science base, founded on cornerstone technologies, that make the UK attractive for the long-term and would be applicable to study other conditions.
  - Leverage data from our unified data sources, including Our Future Health, BREATHE and a new cohort, applying technologies such as **artificial intelligence and quantum computing** to identify new treatable traits and drug targets, paving the way for the development and testing of new treatments by industry through UK-based clinical trials.
  - Increased **recruitment of new patients** from geographical areas with the worst respiratory outcomes through the Targeted Lung Health Check.
  - De-risk industry investment with an emphasis on **new, digital platform trial designs** and discovering new classes of respiratory drugs that can transform respiratory outcomes.

Phase 1: 2022-24 Facilitate and maximise recruitment to respiratory trials by linking with the Targeted Lung Health Check, whilst providing clarity on patient-centred endpoints by working alongside MHRA and NICE.

Phase 2: 2022-24 NIHR/MRC/EPSRC Themed calls of £10m/year focused on innovative trial design for respiratory therapeutics and interdisciplinary collaboration for the implementation of new technologies that can support drug target identification.

Phase 3: 2022-30 Funding for a new £20m/year Centre for Experimental Lung Medicine – modelled on the Experimental Cancer Medicine Centres (ECMC) – headquartered outside the Golden Triangle, capitalising on and increasing our capacity in key technologies including artificial intelligence, quantum computing and **regenerative medicine** to identify novel drug targets. Partnerships could extend beyond pharma, including Nvidia (Cambridge-1), Microsoft Quantum, Chan Zuckerberg Initiative (Human Lung Cell Atlas), Benevolent.AI and Healx

Centre for Digital Management of Respiratory Disease

Challenge

- The UK has one of the worst asthma death rates in Europe, but two thirds are preventable through better treatment adherence and self-management.
- Patients are not currently being equipped with the tools they need to understand their condition, remain adherent to their treatments and develop other healthy behaviours.
- The majority of existing digital tools for self-management are not fit for purpose and current NHS infrastructure does not support, encourage or enable the development of consumer (patient)-focused products that could be transformative.

GOAL: Drive health innovation and attract commercial investment by partnering with the NHS to enable the testing and implementation of disease management optimisation solutions.

Opportunity

- Encourage tech SMEs, Innovate UK, EPSRC and others to create and market cutting-edge, transferrable tools that facilitate better health and disease management and support a digitally enabled National Health Service.
  - Incentivise CCGs, AHSNs, the national respiratory networks and wider NHS to **test, trial, and optimise self-management support tools** to improve outcomes nationally.
  - Work in partnership with innovators - from established tech giants such as Google, Microsoft, Amazon and Apple, to local and national SMEs with a respiratory interest – to make the UK **the 'silicon valley' of respiratory health** tech development and attracting in billions in investment.
  - Enable integration of real-world evidence into the BREATHE hub for further research, with further opportunities for **sensor, algorithm and digital biomarker development**.

Phase 1: 2022-24 NHS funding to support pilot programmes for digital respiratory management within CCGs with the worst outcomes, including remote pulmonary rehabilitation and self-management support tools. Partners selected in collaboration with the national respiratory board and supported by regional Academic Health Science Networks to implement new technologies.

Phase 2: 2022-24 i4i/Innovate UK/EPSRC themed call £10m/year, in collaboration with BREATHE real world data hub, to pump prime the development of online tools that allow people to better manage and track their symptoms. Focussing on smart, data-enabled tools which are founded on both patient unmet needs, and real-world data analysis. This would include physical devices with novel sensing technologies, algorithm development, and user-facing applications which utilise and integrate data effectively.

Phase 3: 2022-30 A new £20m/year Centre for Digital Management of Respiratory Disease, which leverages the insights from BREATHE's real-world data hub to create the Learning Health Systems of the future – developing technology enabled care pathways which utilise data in the most effective ways and assist shared decision making. The Centre would differentiate itself through contextualising real-world data with patient insights and behaviour, de-risking the development of new products and informing the decisions of procurers and regulators – NHS, NICE and MHRA. Possible partnerships with health operations of Google, Microsoft, Apple.

Centre for Prevention of Respiratory Disease

Challenge

- Respiratory disease is an area of huge inequality, more heavily impacting the poorest communities both in the UK and globally
- Respiratory viruses are a [major cause of asthma and COPD exacerbations](#) with considerable impact on winter admissions.
- Air pollution contributes to around 36,000 early deaths. Long-term exposure to $PM_{2.5}$ and NO_2 is associated with increased incidence of COPD. However, our understanding of these mechanisms remains poor, undermining the development of therapeutics.

- Moreover, there is an increasing body of evidence on the intergenerational effects of air pollution on lung function.

GOAL: Reduce emergency admissions by 20% in the 20 worst affected areas through targeting underlying causes of respiratory morbidity and mortality.

Opportunity

- Applying the same speed and ingenuity to vaccines to seasonal respiratory viruses as seen during the Covid-19 pandemic, and targeting the use of vaccines for those most vulnerable, could have a dramatic effect on quality of life and reduce admissions. A significant opportunity exists for the development of **next-generation of inhaled mRNA vaccines** that can enable simpler storage conditions, and provide more robust mucosal protection.
- Epidemiological studies to further understand key factors which would best contribute to a rapid reduction in morbidity and mortality. **Using Big Data modelling and AI to design novel interventions** that reduce admissions
- Understanding the mechanisms that cause respiratory disease including the **microbiome and air pollution**

Phase 1: 2022-24

Funding for trial of novel vaccines for major respiratory viruses as a public health measure to reduce admissions. Potential to drive the creation of infrastructure that contributes to pandemic preparedness. Drive immediate value from Vaccine Manufacturing and Innovation Centre. Potential public funding from Innovate UK/BEIS via VMIC. [Industry funding could build on efforts from Moderna](#).

Phase 1: 2022-24

Through local pilots of citizen science schemes using high quality personal air pollution monitors, build our capacity to capture real-time air pollution levels to create a better picture of hyper-local levels and to allow for the implementation of effective alert systems. Potential industry partnerships with clean energy suppliers, electric car and transport manufacturers. Potential public funding from EPSRC, NERC, OHID, and UKHSA.

Phase 2: 2024-26

£10m NHS AI Lab/NIHR funding to use AI technologies to better establish existing disease burdens, future prevalence and burden, and to model and identify new prevention strategies. Emphasis on primary prevention in children.

Phase 3: 2022-30 A new £20m/year Centre for Prevention of Respiratory Disease. Unprecedented basic science funding to understand the mechanisms that cause exacerbations as a result of air pollution, and seek to better understand the lung microbiome. Potential to catalyse -omics technologies and lung-on-a-chip platforms.

[i] George R. Washko, Grace Parraga
European Respiratory Journal 2018 52: 1801570; DOI: 10.1183/13993003.01570-2018