

Respiratory research in the UK: investing for the next 10 years

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In July 2021, the UK Office of Life Sciences (OLS)¹ published a Life Sciences Vision for the UK highlighting key areas for action. The report specifically flagged reducing morbidity and mortality from respiratory disease as one of the seven healthcare mission priorities. In addition, the report emphasised more generally the need to support underpinning infrastructure to enable better use of health data and genomic data and increasing the efficiency of clinical research delivery to improve healthcare.

The importance of a flourishing respiratory disease research community in the UK has also been brought into sharp focus by the COVID-19 pandemic. The UK has achieved international acclaim for its ability to deliver definitive therapeutic trials in COVID-19 and has also made major investments into research on long COVID-19 through UKRI and NIHR which will further inform clinical practice. There remains however a key question: how well prepared is the respiratory research community to deliver on the OLS vision?

Some further insights on the state of UK respiratory research can be gained from two recent consultation exercises. The first of these was designed to identify priority areas for attention and took place between 2017 and late 2019 by a group brought together under the informal auspices of the UK Respiratory Research Collaborative (UKRRC). It included two multidisciplinary open sessions held at the winter British Thoracic Society meeting and meetings with key stakeholders including major respiratory charities and a range of opinion leaders. Unfortunately, the pandemic intervened before this work was completed, but nevertheless it provided valuable stakeholder insights. A further high-level round table meeting with government convened by Asthma+Lung UK reinforced the need for a new approach.

In this article, we summarise the main messages which came out of the consultations undertaken by UKRRC and Asthma+Lung UK and review the changes brought about

by the pandemic. We identify key areas on which, as a specialty, we should focus to ensure the UK is positioned to address the challenge thrown down by the OLS vision and make suggestions on how to address this challenge.

DISEASE BURDEN

Any prioritisation of the respiratory research agenda requires accurate data on underlying disease burden. The British Lung Foundation (now Asthma+Lung UK) has in the past supported work to provide estimates of disease burden but accurate data based on surveys of the general population are now quite dated. The Health Survey for England 2010 and Scottish Health Surveys 2008–2010 found that approximately one in five people in the UK (~12.7 million) reported a history of asthma, chronic obstructive pulmonary disease (COPD) or another respiratory illness. Half of these reported taking prescribed medication for lung disease in the last year. In keeping with these estimates, general practice records suggest that in 2012, about 8 million people in the UK had been diagnosed with asthma, 1.2 million with COPD and over 0.4 million with other forms of lung disease. COPD remains the second largest cause of emergency hospital admission and costs the NHS £1.9 billion per year. The UK also has in general worse lung disease outcomes than the rest of Europe (especially asthma mortality, asthma prevalence, COPD prevalence and lung cancer rates). To put this in context, estimates are also available from the Global Burden of Disease Study, which for 2017 suggested that worldwide around 550 million people have chronic respiratory disease, an increase of 40% since 1990.²

In 2011–2012, lung diseases accounted for 20% of all deaths in the UK, 8% of all hospital admissions and 10% of all inpatient bed-days.

Since January 2020, the COVID-19 pandemic has increased the relative importance of respiratory disease as a cause of morbidity and mortality in the UK. As of April 2022, there have been 21.8 million cases of COVID-19, resulting in 823 000 hospital admissions and 171 000 individuals have died within 28 days of COVID-19 infection.³ Current ONS data for the UK suggest around 1.3 million people are currently suffering from symptoms of long COVID-19. Estimates also suggest COVID-19-related

lung fibrosis may result in a doubling of the number of patients suffering from interstitial lung disease, although this needs to be confirmed. In addition, the pandemic has markedly altered access to clinical pathways for those with conditions other than COVID-19, resulting in a large rise in the numbers on waiting lists and delayed presentations of patients with other respiratory diseases.

Changes in environmental exposures will also in the long term alter disease burden. While reduced smoking rates and generally improved air quality are obviously to be welcomed, much remains to be done, particularly in understanding the consequences of changing patterns of exposures driven by air quality at the indoor and outdoor interface and the potential effects of a move to carbon net zero. Increasing use of vaping products may have longer-term effects on respiratory health. The numbers of people who are obese is also increasing. There are changes due to influence of socioeconomic and other inequalities in driving risk of developing lung diseases and altering the ease of access to healthcare pathways. These are also issues highlighted in the OLS report.

CHANGES IN HEALTHCARE DELIVERY AND RESEARCH MODELS

Healthcare delivery models were changing in the UK before the pandemic, but these changes have been accelerated by COVID-19. Increasingly healthcare is delivered in the community or remotely rather than in teaching hospital settings. Larger numbers of patients now have significant comorbidities which require a more personalised approach to healthcare. The way in which clinical trials are delivered is also changing, with increasing use of 'real life' trials assessing interventions in the context of usual healthcare rather than the traditional randomised placebo controlled clinical trial setting and more trials adopting a Bayesian design, the RECOVERY (randomised evaluation of COVID-19 therapy) trial⁴ being a classic example. Access to healthcare data for research remains a challenge, but the enhanced access to clinical data for COVID-19-related research emphasises the way in which research studies can be 'fast tracked' to provide results as rapidly as possible. Multidisciplinary team approaches to disease are increasingly important. All of these changes need to be factored in when revisiting research delivery models.

THE UK CAPACITY TO DELIVER RESPIRATORY RESEARCH

The UK is fortunate that in the past over a prolonged period researchers based in UK institutions have led the way in international research in respiratory diseases. In England,

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Box 1 Eight key actions

1. Rationalise and extend core datasets on respiratory disease incidence, prevalence and outcomes to provide centralised open access to data which is regularly updated to facilitate research and healthcare delivery.
2. Establish a monitoring observatory to examine risk factors for respiratory disease and model predicted changes in disease patterns.
3. Prioritise case finding initiatives for undiagnosed respiratory diseases, including a universal lung healthcare check.
4. Establish a task force to increase access to effective therapy for respiratory diseases with a particular emphasis on 'hard to reach' groups.
5. Create UK virtual centres of excellence for different respiratory diseases to facilitate delivery of clinical research studies, with a remit to work across the healthcare sector to improve efficiency through effective collaboration.
6. Set up working groups to subphenotype and redefine respiratory diseases and to make recommendations on research into future therapeutic approaches.
7. Establish a task and finish group to explore barriers which prevent trainees following careers in respiratory research and to identify incentives to increase future capacity.
8. Establish a cross-sector UK strategic group to provide leadership and oversight of the respiratory research portfolio, to monitor progress on key actions and delivery of the OLS Vision.

investment through NIHR into Biomedical Research Centres and clinical trial networks such as that provided by the Respiratory Translational Research Collaboration and primary care networks provide some infrastructure support. However, the level of investment lags behind other specialty areas with less than 2% of the health research spend directly supporting respiratory disease research (excluding cancer), in contrast with data from the 2018 CRC report showing that respiratory disease accounts for 6% of disability-adjusted life years in the UK.⁵ Public Health England data also show large differences in disease burden at regional and national levels resulting in substantial healthcare inequalities which remain to be tackled.

There are concerns about declining numbers of academics expressing a desire to

follow a career in respiratory research and a reduction in clinical academic posts in the specialty. The 2017 UK-wide survey of clinical and health research fellowships reveals only 3% of fellowships were awarded in respiratory medicine compared, for example, with 23% in cancer. Respiratory medicine also suffers from a relative lack of charity funding, and while the recent merger of the BLF and Asthma UK into a single charity should help enhance strategic support from the Association of Medical Research Charities (AMRC) and the rest of the third sector, the overall level of funding available is much less than for other areas such as cancer and cardiovascular disease. While there remains a thriving SME sector in the UK, several large pharma companies have closed or relocated their UK respiratory research laboratories abroad, further reducing infrastructure.

A UK PLAN FOR RESPIRATORY RESEARCH

In our view, now is the time for a radical overhaul of the way we deliver respiratory research in the UK to address the changing patterns of disease and healthcare delivery. We strongly believe research needs to be firmly embedded in routine clinical practice across the whole NHS to address this challenge.

ADDRESSING RESPIRATORY MORBIDITY AND MORTALITY

To fully address respiratory morbidity and mortality, we need better access to contemporary cross-sectional data on respiratory health in the UK which is regularly updated. One part of the solution could be to repeat the Health Survey for England 2010 respiratory component in the near future but ongoing monitoring of disease incidence and prevalence is needed, for example, to define the longer-term impact of COVID-19 on disease burden. Therefore, we should maximise the opportunities provided by integrating health data across the entire NHS, industry and academia through collaborative working with Health Data Research UK and NHS Digital to ensure we maximise benefit from relevant healthcare datasets. This should incorporate existing and new respiratory cohorts. The new 'Our future Health' programme is a further opportunity. We believe including spirometry on 1 million people enrolled in the Our Future Health programme and identifying a subcohort (~5000–10 000) within this programme in whom we could measure respiratory biomarkers sequentially over 10 years to understand early markers of disease and identify new therapeutic targets would be of value.

However, these measures alone will not identify all those at risk of developing lung disease. We suggest everyone in the UK should have a lung health check at the age of 25 years and then regularly (perhaps every 5 years) to identify those with lung disease and treat it early (by targeted smoking cessation, occupational intervention and early management of new respiratory disease).

To predict future trends in disease, we will need to accurately quantify the contribution of outdoor and indoor air pollution and other environmental factors as well as socioeconomic factors, obesity and multimorbidity to respiratory disease burden in the UK. This will allow us to develop better predictive models to estimate the effect of altering environmental and other exposures on respiratory health. To improve access to healthcare, we need better case-finding of both common and rarer lung diseases, particularly in primary care, to ensure early diagnosis and treatment, which highlights the need for better diagnostics.

We need new and better therapies for the many respiratory diseases where outcomes remain poor. To address this, we should fully embrace systems and multiomic approaches for respiratory disease and enhance support for the underpinning laboratory-based research which this requires. We also need to develop new technologies to monitor and support patients more effectively. This should all be done with strengthened public and patient input into cocreation of new 'products', be they pharmaceuticals, devices, interventions or new care pathways.

ADDRESSING CAPACITY AND INFRASTRUCTURE

In order to ensure the ability to continue to deliver existing research programmes in the basic and clinical sciences relevant to respiratory disease and to support new programmes of research, the UK urgently needs to address declines in academic and industry infrastructure. We should rapidly develop new national collaborative physical or virtual research centres of excellence and networks concentrating on multidisciplinary approaches to answer key respiratory research priorities.

We need to continue to develop strong collaborative links between academia and industry. As discussed in the OLS Vision, we must increase the global attractiveness of the UK for industrial collaborative respiratory research and innovation and mitigate any effects of Brexit. We must ensure the UK continues to contribute to and leads international collaborative research and innovation programmes through Horizon Europe and other international collaborations. We also have a moral obligation to continue to

support global health research on the causes and impact of respiratory diseases which has been impacted by the recent reduction in support for the UK international aid budget.

One consequence of the pandemic has been the 'fast tracking' of regulatory approvals for COVID-19-related research, including simpler processes to access health-care data. However, as we emerge from the pandemic, there is a major risk we will revert to the pre-pandemic approaches to research approvals, which would be a real missed opportunity for change. We should look to adopt the benefits to research of accelerated and simpler research governance processes more widely, beyond just COVID-19 research.

Finally, to make sure we can deliver on these objectives, we must remove barriers for trainees wishing to enter clinical research. We need to determine what are the main barriers that are preventing medical and allied professional trainees from pursuing research careers and put in place actions to mitigate these. We should set minimum targets for numbers of research trainees in the different professional groups to ensure critical mass is maintained and monitor trainee numbers accordingly. To help achieve this, we need to improve flexibility of training for both medical doctors and allied health professionals and improve mentoring for all trainees interested in research at early stages in their training.

REDEFINING RESPIRATORY DISEASES

Given the high burden of chronic respiratory disease, we need to improve our ability to identify subphenotypes of diseases and tailor patient-specific interventions at those most likely to benefit. This has been achieved to some extent, for example, with therapies targeting Th2-driven severe asthma, use of CFTR modifiers in cystic fibrosis and precision medicine approaches to lung cancer chemotherapy, but there remains much to be done in many other respiratory diseases. We should also prioritise interventions designed to reduce exposure to environmental causes to those at highest risk of respiratory disease throughout the life course to reduce future disease burden: this requires better predictive models of individual risk.

BETTER SERVICE DELIVERY

We need to promote more research to define the most efficient service delivery models to deal with the increasing workload in both primary and secondary care due to respiratory diseases in an ageing population and identify models of delivery to ensure the 'hard to reach' groups in our communities have access to healthcare

and research opportunities. A key element will be promoting patient activation and engagement through better support for self-management and ensuring that digital self-management programmes and products are designed around the needs and behaviours of all patients.

The creation of the Integrated Care Systems (ICSs) in England and an increased emphasis on care across the primary and secondary care divide in the devolved nations provides an opportunity to improve co-ordination of care pathways for disease across the health service. It is encouraging that research is a key deliverable in the ICS performance framework. However, many ICSs have little experience of research so joint working with academic partners will be critical.

We will also need to address in more detail the interplay between respiratory symptoms and multimorbidity/frailty using a person-focused rather than organ-focused approach, including research on the roles of mental health, obesity and deconditioning as causes of breathlessness. These approaches should also help deal with the impact of long COVID-19 on the population.

DELIVERING THE OLS VISION

Delivering on the healthcare mission objective in the OLS Vision for Life Sciences needs a 10-year strategic plan with relevant milestones and monitoring embedded. While it is essential to maximise use of existing resource, it is unlikely that everything could be achieved without significant additional investment. We should argue for prioritisation of funding schemes such as those supported by UKRI and Innovate UK to support the OLS priorities listed above. Delivering the vision will also need significant investment from industry so we can develop the new drugs, diagnostics, therapeutic devices and technologies to transform health outcomes in partnership. Finally, overarching co-ordination will be essential. There is currently no single structure to ensure this happens effectively and we need to create one. To facilitate this, we believe it is time to bring together current major funders of respiratory research, including NIHR, the research councils, industry and AMRC members to develop the framework to maximise the respiratory research community's ability to deliver on the OLS vision. This will require integrated actions across the healthcare communities, to avoid research happening in disconnected silos: key tasks are highlighted in [box 1](#).

The OLS Vision provides a challenge for the respiratory community with which we must engage. Both the health of our

population and the future international standing of our respiratory research will depend largely on how we address this vision over the next few years.

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