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RESPIRATORY DISEASES: UK MARKET

TRENDS, INSIGHTS & OPPORTUNITIES

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Medtech Navigator

The Medtech Navigator, part-funded by the European Regional Development Fund (ERDF), is a three-year programme, delivered by Health Enterprise East Ltd., to facilitate knowledge exchange between the medtech industry, many of whom are small and medium sized enterprises (SMEs), the NHS, and academia. The programme seeks to enable companies to identify potential market opportunities in a variety of specific disease areas and apply for Innovation Grant funding through the programme, thereby engaging SMEs in new R&D projects that are both customer-focussed and collaborative in nature. This will allow the creation of partnerships between clinicians, academics and industry to develop novel medical technologies which will improve healthcare and quality of life for patients and the healthcare market of the future.

Health Enterprise East Ltd.

At Health Enterprise East believe in improving healthcare through technology and innovation.

We work with the NHS, medical technology industry and government organisations to help turn innovative ideas into products and services that will benefit patients.

Our experienced team offers clients a diverse range of business and innovation management services. Our strengths include IP management, technology commercialisation, health economics and strategic market access advice.

Based in Cambridge, we work with over 25 NHS organisations nationally and medtech companies globally. Our aim is to help our clients address the challenges faced along the product development pathway, connecting them with relevant healthcare experts and funding opportunities.

Report Summary

This report contains information relevant to those developing innovations in respiratory disease. An assessment of the industry landscape is given by analysing the market size and an overview of the larger companies active in the market is provided. We take a closer look at what UK based medtech companies are developing in the respiratory disease area with a particular focus on the needs of the NHS and how these needs might be addressed. We analyse the innovations that have been funded over the last 5 years by UK based funding bodies such as Innovate UK, SBRI and NIHR i4i. Finally, we review the patent landscape and summarise what the top 5 companies are in each area of interest.

www.medtechnavigator.co.uk

Contents

1. Background

Respiratory disease affects approximately 20% of the population and is the third biggest cause of death in England (after cancer and cardiovascular disease). Lung cancer, pneumonia and chronic obstructive pulmonary disease (COPD) are the biggest causes of death [1].

Hospital admissions due to respiratory diseases have increased sharply over the past seven years at three times the rate of all other admissions[1]. Most respiratory admissions are non-elective and admissions can double during the winter. Respiratory disease therefore remains an important priority in the management of the winter pressures faced by the NHS.

According to NHS England, incidence and mortality rates from respiratory disease are heightened in areas of social deprivation and within disadvantaged groups, the gap is widening and leading to poorer health outcomes. The most deprived communities in the UK have more smokers, greater exposure to air pollution, inferior housing conditions and increased exposure to occupational hazards, all of which are expected to contribute to the increased incidence and mortality rates.

1.1 The NHS Long Term Plan

The NHS Long Term Plan presents the NHS's priorities for care quality and outcomes improvement for the decade ahead. Chapter Three of the plan identifies respiratory disease as a clinical priority. The plan explains how lung conditions, including lung cancer, are estimated to cost wider society around £9.9 billion each year.

The Long Term Plan sets out a series of expectations and aims centered around how the NHS can better detect, diagnose and treat respiratory problems earlier[1]. The NHS aims to:

- Promote early and accurate diagnosis of respiratory diseases, by supporting staff training in respiratory testing e.g. spirometry testing.
- Grow lung rehabilitation services across the country ensuring treatments are completed in a good quality system.
- Review and improve the way medication is prescribed and promoting correct inhaler use.
- Improve the response to Pneumonia and thus help to relieve the winter pressures on the NHS.
- Improve existing services and create new services which promote self-management of conditions and personalised care.

Delivery of the Long Term Plan

To deliver the Long Term Plan the NHS has partnered with various organisations and groups. The national respiratory programme has set out to develop ways to improve outcomes for people with respiratory disease and meet the Long Term Plan ambitions. Key partners for delivering this national programme of work are the British Lung Foundation (BLF), British Thoracic Society, Asthma UK, Primary Care Respiratory Society (PCRS), NHS RightCare, Getting It Right First Time (GIRFT) other arm's length bodies and voluntary sector organisations. The NHS is also working alongside The Taskforce for Lung Health to prevent more people from developing lung disease in the future and to improve the care of people currently living with lung disease.

A new partnership has recently been formed between Asthma UK and the BLF. On 1 January 2020, Asthma UK and the BLF officially merged together to combine their efforts in supporting people living with asthma and other lung diseases. Both the BLF and Asthma UK will retain their individual identities.

2. The Number of Patients Affected by Respiratory Disease

European Union

Chronic respiratory diseases, for example asthma and COPD, affect over 60 million people and are responsible for more than 150,000 deaths in the European Union (EU) per annuum[2]. The economic burden of these chronic respiratory diseases is high in the EU. In 2013 the total yearly cost of care and productivity losses equated to €33.9 billion for asthma and €48.4 billion for COPD[2].

United Kingdom

The Global Burden of Disease study demonstrates that the top five causes of early death in England are: heart disease and stroke, cancer, respiratory conditions, dementias, and self-harm[3].

It is estimated that 12.7 million people in the UK are living with respiratory disease. Surveys of the general UK population have approximated that 1 in 5 have a history of asthma, COPD or another longstanding respiratory illness. Half of these, around 6.5 million people, are reported to have taken medicines prescribed for lung disease in the last 12 months. Evaluations based on general practice records indicate that approximately 8 million people have been diagnosed with asthma, 1.2 million with COPD, and over 150,000 with interstitial lung diseases (pulmonary fibrosis or sarcoidosis). Numbers have been found to be generally equivalent for males and females. Approximately 86,000 people in the UK have ever been diagnosed with lung cancer, and over 5,000 (heavily weighted toward males) have ever been diagnosed with mesothelioma[4].

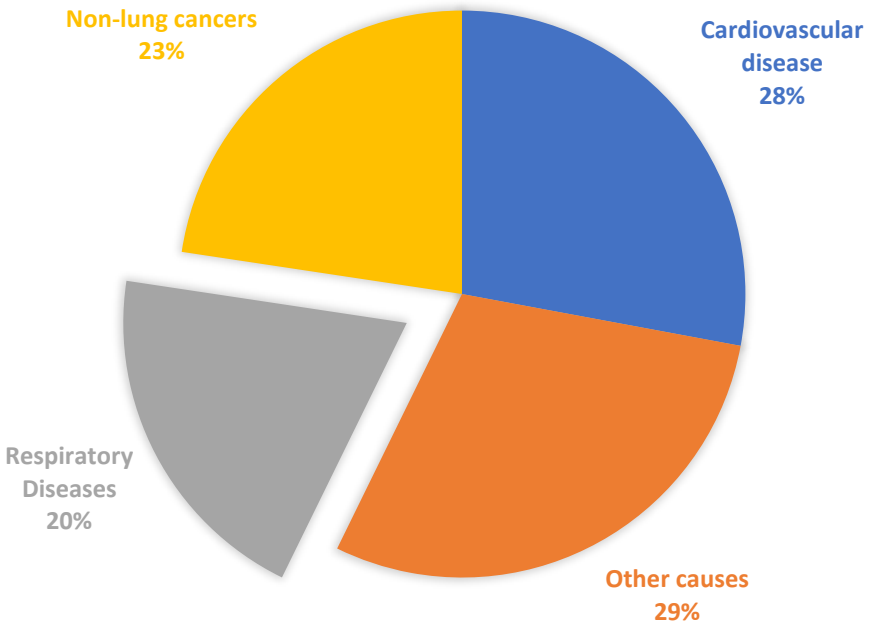

Figure 1 Statistics from British Lung Foundation[4]

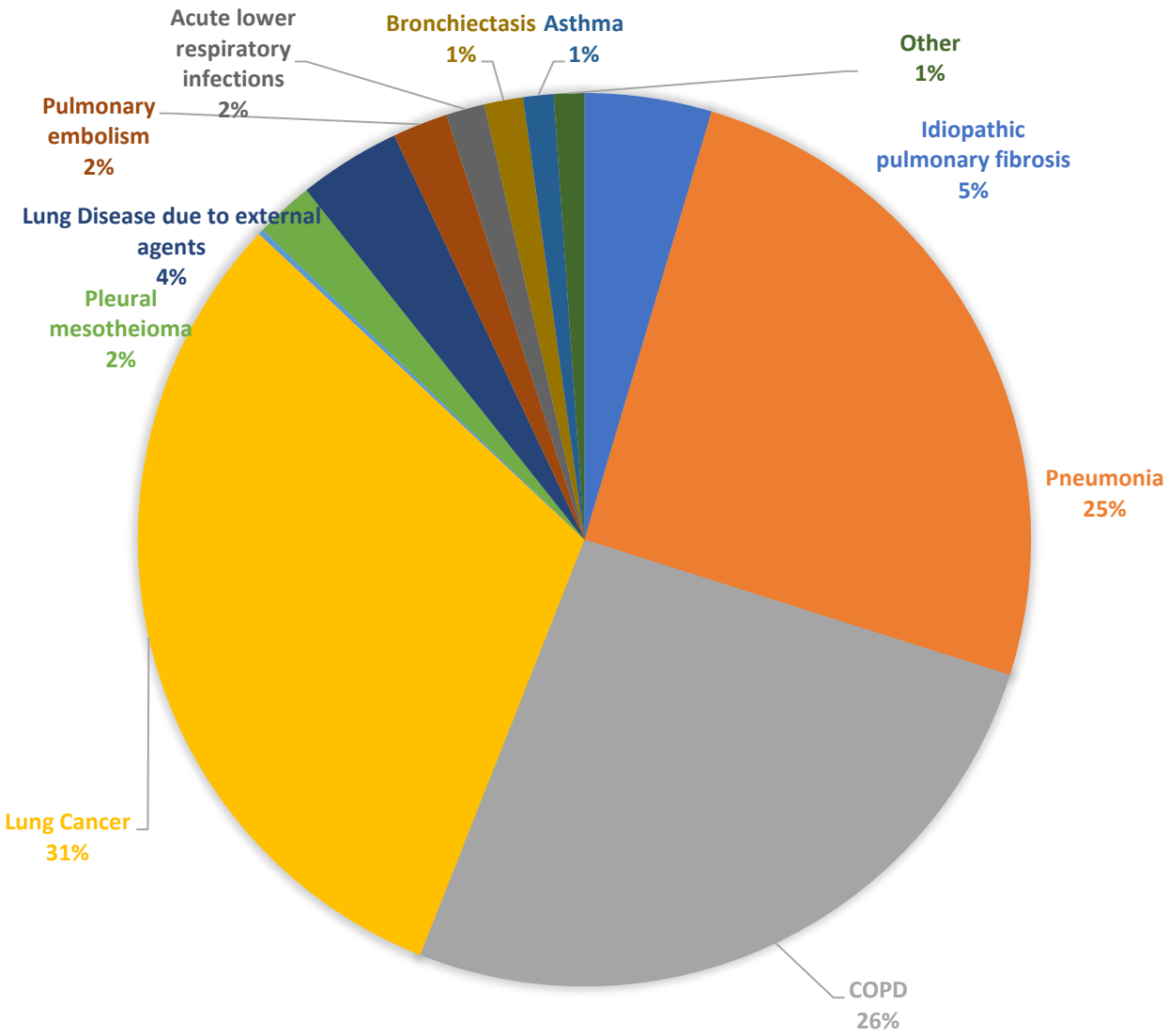

Figure 2 Statistics from British Lung Foundation[4]

3. Market Size

All lung conditions (including lung cancer) directly cost the NHS £11 billion per year[5]. The yearly economic burden of asthma and COPD on the NHS is approximated at £3 billion and £1.9 billion respectively[5].

The global respiratory care devices market was valued at $12.9bn in 2015, and is poised to reach £21.3bn by 2022, registering an estimated CAGR 7.4% during that period. Respiratory care devices are those used for diagnosis, monitoring and treatment of respiratory diseases.

3.1 Medical Devices and Respiratory Disease

Current treatments available for many respiratory diseases rely heavily on the use of medical devices, such as inhalers and nebulizers, to deliver medication to the lungs. Other examples of medical devices in use for respiratory disease are the therapeutic gas delivery devices which are used when a patient is unable to get enough oxygen by inhalation alone. Other general devices that are more often used in a home setting include humidifiers, dehumidifiers and oxygen concentrators.

There are many contributing factors which are affecting the respiratory disease medical device market, increases in air pollution have been combined with the high incidence of asthma, COPD and lung cancer globally. Changing lifestyle, increasing obesity and habits such as overeating and smoking are also playing a major role in the growth of respiratory diseases worldwide. It is therefore likely that the market for respiratory disease devices will continue to grow with incidence rates[6].

According to Market Watch, the global respiratory disease devices market is split according to product type and end-user. According to product type, the market has been segmented into the inhaler, nebulizer, humidifier and dehumidifier, respiratory mask, oxygen concentrator, and other consumables and accessories. The inhaler is expected to have a major market share during the forecast period of 2019-2023, with a significant growth rate. By end-user, the market has been divided into hospitals & clinics, and homecare. Homecare is expected to have a considerable market share due to high usage of inhaler by the patient on a regular basis.

It is predicted that North America and Europe will retain a sizeable portion of the market share because of the higher per capita health expenditure, in addition to the well-developed healthcare infrastructure in these regions. The Asia-Pacific region is expected to be the fastest growing region during the forecast period with China, India, and Japan all predicted to be lucrative in the Asia-Pacific region. This is based on these regions having ever increasing levels of air pollution and are therefore expected to have the largest increase in incidence of respiratory diseases[6].

Some of the major stakeholders in the worldwide medical device market for respiratory disease are 3M Co., AstraZeneca PLC, Becton Dickinson & Co., Boehringer Ingelheim International GmbH, Chiesi Farmaceutici SPA, Cipla Inc., DeVilbiss Healthcare LLC, GlaxoSmithKline PLC, Koninklijke Philips NV, Mylan NV, Novartis AG, Smith Medical, Inc., and Teva Pharmaceuticals Industries Ltd[6].

3.2 The COPD Market

As the level of air pollution rises across the world, coupled with lifestyle changes, such as less regular exercise and increase in BMI, it is expected that COPD levels will rise accordingly. COPD is an often under diagnosed condition and approximately 50% of sufferers are unaware of their diagnosis[7]. Innovative solutions are sought to try to improve diagnostic rates, reduce the burden of exacerbations and prevent admission to hospital, thus enabling patients to self-manage their conditions proactively in their own homes[8]. Over the next five years, it is predicted more imaging technologies, such as Computed Tomography (CT), will be developed to better diagnose patients during this period of growth. This is predicted to be coupled with an expansion of technically advanced devices, for example pulse oximeters, for more effective management of COPD in outpatients[9]. The area of mobile health (mHealth) has rapidly grown in recent years but approaches specific to COPD have failed to show sustained improvement in COPD outcomes. Therefore, more innovative solutions that incorporate smartphone and internet based technologies, are usable by the target elderly COPD population, and are integrated into self-management, diagnosis, monitoring and education tools are required[8].

There are roughly 6 million COPD sufferers in the UK which greatly impacts upon health care provision and society. Nearly £4 billion is lost each year from reduced productivity as 24 million working days are lost due to COPD. The human cost is also concerning, with approximately 23,000 deaths due to COPD each year working out at around one death every 20 minutes. A large proportion of costs associated with COPD go towards the management of patients as inpatients suffering from acute exacerbations of their condition.

3.3 Self Care

The market for self care in all respiratory diseases is expected to increase in the UK. As we advance into a more connected world, people with a variety of health conditions have taken it upon themselves to take control of their conditions in conjunction with expert advice and peer support in the community and online. The King's Fund has coined the term 'shared responsibility for health' and according to the Long Term Plan, over the next five years the NHS will increase support for people to manage their own health[10]. Asthma and respiratory conditions will be amongst the first priorities for the NHS along with diabetes prevention and management, maternity and parenting support, and online therapies for common mental health problems[1].

4. Top 10 Companies in Respiratory Disease by Area

4.1 Respiratory Disease Diagnostics

The respiratory diagnostics market is dominated by established players and the market can split according to the following diagnostic tests[11]:

- Mechanical Tests e.g. Pulmonary Function Tests
- Imaging Tests e.g. X-Ray, Computed Tomography, Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET)
- Traditional Diagnostic Tests e.g. Immunodiagnostics, Biochemical Characterization, Microscopy
- Molecular Diagnostic Tests e.g. DNA Sequencing & Next-Generation Sequencing (NGS) and Microarrays

The major companies with diagnostic products on the market for respiratory disease are listed below[11]. These companies were identified by assessing the extent of their products and services provided for the respiratory disease diagnostic market. Strategy, analyst insights and recent developments were also assessed to form the Top 10 list.

1. Philips Healthcare
2. Becton, Dickinson & Company
3. Abbott Laboratories
4. Thermo Fisher Scientific Inc.
5. Biomérieux
6. Alere Inc.
7. Bio-Rad Laboratories, Inc.
8. Cosmed
9. Seegene Inc.
10. Sdi Diagnostics

4.2 Respiratory Disease Care Devices

The market for care devices in use for respiratory disease can be split into the following categories[12].

- Therapeutic e.g. Ventilator, Mask, PAP Device, Inhaler and Nebulizer
- Monitoring e.g. Pulse Oximeter and Capnograph
- Diagnostics
- Consumables

Large names that dominate this market and are listed below[12]. These companies were identified as major players in the respiratory disease care device market using a combination of indictors. More general information, such as a business overview and the products on offer,

was collected and analysed, along with a more detailed look at recent developments and SWOT analyses.

1. Philips Healthcare
2. Resmed, Inc.
3. Medtronic PLC
4. Masimo Corporation
5. Fisher and Paykel Healthcare Co., Ltd.
6. Getinge AB
7. Air Liquide
8. Drägerwerk AG & Co. KGaA
9. Hamilton Medical AG
10. Invacare Corporation

5. An Overview of Products Already on the Market

5.1 Medical Devices: Inhalers

Given the relatively high morbidity, mortality, and economic burden, the major objective in the treatment of respiratory diseases is to optimise disease control, whilst retaining low levels of flare-ups and maintaining severe exacerbations as a rarity. Oral, injectable, and inhaled products are readily available on market.

Drug delivery by inhalation is a preferred method of delivery as high drug concentrations can be reached locally within the lungs, with reduced risk of side effects[13]. Yet, this method of drug delivery is greatly impacted by patient inhaler use and can therefore be less effective than other more conventional routes of drug delivery. As such, there are numerous inhalers already on the market and these can generally be split into two groups: pressurised metered dose inhalers (pMDI) and dry powder inhalers (DPI)[14]. Within and between these categories the inhalers differ in effectiveness of drug delivery and ease of use.

A Snapshot of Products on Market Across Europe

Product	Organisation	Unmet clinical need
XeThru X2M200 Respiration Sensor	Novelda AS	Non-invasive respiration sensor. A single sensor detects body movement, presence, distance, respiration frequency, and provides breathing pattern tracking.
Vivo 60	Breas Medical AB	A life-support ventilator intended for paediatric (>5 kg) and adult patients requiring highly secure and comfortable ventilation in the hospital or at home.
A range of smart inhalers	Adherium Ltd	Smart inhalers used to track medication usage.
Sophie	Schiller AG	Specialist ventilator for neonatal and paediatric patients

6. SMEs Active in the Area of Respiratory Disease

In addition to the larger companies which appear in the top 10 lists, the UK also has a thriving collection of SMEs working in the respiratory disease area. We have provided an overview of the types of innovations these companies are developing with a focus on digital and smart inhalers. This is not intended to be an exhaustive or comprehensive list but a snapshot of how others are addressing the unmet needs of respiratory disease.

6.1 Digital Innovation in Respiratory Disease

We are spending an increasing amount of time on our phones and other smart devices, yet many asthma patients do not have a digital personal asthma action plan. Having such a plan makes an individual four times less likely to be admitted to hospital. Unfortunately, for too many patients these potentially lifesaving plans are still in paper form. This is a good example of the requirement for digital solutions within the healthcare setting. Basic patient information gathering for respiratory diseases such as COPD and asthma is still being collected at face-to-face review appointments with little standardised coding thus hampering data sharing[15]. Given that these inefficiencies are combined with a over-burdened general practice, it can be argued that this ineffective system may be why many patients with respiratory diseases often miss review appointments.

Services in other health areas, such as diabetes and mental health, are vastly improving due to new digital tools, however, digital innovation in respiratory care has sadly lagged behind. Asthma in particular has struggled due to the difficulties in managing an episodic condition combined with multiple triggers and a complex treatment pathway. Despite the wealth of evidence that self-management is effective in asthma, more work is needed due to the sheer number of asthma patients (5.4 million) in the UK. Digital solutions are needed that can perform cost-effectively at this large scale[15].

Digital solutions are being developed and are aimed at tackling some of the key challenges in respiratory disease. The main areas for digital technologies are:

• Increasing adherence to medicines.

• Helping patients self-manage dynamically to reduce their risk of an adverse event with solutions personalised to an individual's triggers.

• Equipping healthcare professionals with the tools to identify those people at higher risk of an adverse event.

6.2 Smart Inhalers for Adherence Monitoring

Asthma is a great example of how innovation can improve health outcomes as the invention of pressurised metered-dose inhalers has led to a swift improvement in patient outcomes[16]. Given the rise in smartphone usage across all demographics in the UK, it is unsurprising that numerous Bluetooth connected smart inhalers have been designed for the treatment of those with respiratory diseases such as asthma. Such inhalers are equipped to collect and send data on medication use and to alert users on when to use them. In addition, these features make remote monitoring more readily available and can aid in regular consultations with healthcare professionals[17].

Examples of Innovative Smart Inhalers

Propeller Health

Based in USA

https://www.propellerhealth.com/

Propeller Health have developed a small sensor which sits atop of both reliever and preventor inhalers. It aims to track symptoms and adherence with its time and place monitoring features. Reminders to use a preventor inhaler can also be set up by the patient or responsible carer.

CareTRx

Based in USA

The CareTRx sensor fits on metered dose inhalers for chronic respiratory disease management. The sensor is combined with a data analytics platform and an accessible user interface to help asthma and COPD patients manage their condition. CareTRx have been acquired by Teva Pharmaceutical Industries Ltd - an Israeli American company.

Cohero Health

Based in USA

https://coherohealth.com/

Cohero Health have developed sensors that track adherence for both types of inhaler. They have developed both adult and child friendly apps which can link to Cohero's wireless mobile spirometer aiming for better big picture monitoring of a patient's respiratory condition.

CapMedic

Based in USA

https://www.capmedicinhaler.com/

The innovative sensor records how an inhaler is being used and then educates the individual on any improvements to technique via the app.

Adherium

Based in New Zealand

https://www.adherium.com/

AstraZeneca partnered with Adherium Limited to produce the Hailie™ solution formally known as the Smartinhaler. The smart attachments connect to a range of inhalers and are designed to increase medication adherence.

A Medtech Innovation Briefing report published on 11 January 2017 outlined the costs to benefits of using the Smartinhaler within the NHS. It listed Cohero Health, CareTRx, and Propeller Health amongst the CE marked competition of the device. The report indicated that smart inhalers would be classed as an additional cost to care as they do not negate the need for a personalised asthma plan and scheduled review appointments – the current standard of care. The overall opinion was that the concept of a smart inhaler is not necessarily novel due to the number of devices on market. It was agreed that the impact upon patients would be high if improved adherence could be evidenced. This could lead to improved control and reduced symptoms therefore potentially reduce the number of hospital visits and need for escalation of treatment [18].

6.3 Digitally Enabled Methods for Condition Management and Symptom Prevention

Technology-enabled respiratory disease management is at the forefront of the latest innovative technology. The aim of this digital solution is to promote self-management whilst maintaining vital healthcare professional-led management and input. Emphasis is also placed on educating individuals whilst facilitating shared decision making between professional and patient.

Patient led respiratory disease management opportunities:

- Improving adherence to prescribed medications will help patients control symptoms and risk. An example of this would be an improvement in inhaler technique.
- Education in trigger avoidance. An example of this would be location specific alerts to triggers such as cold air alerts for COPD patients and pollen for asthma sufferers.
- Technologies that enable better monitoring of symptoms such as apps with a diary like function.
- Providing timely advice that is easily accessible in emergency situations.

Professionally led respiratory disease management opportunities:

- Tech enabled risk stratification tools to predict who is most at risk and therefore requires closer monitoring and possible intervention.
- Electronic prescription monitoring and medicines monitoring to reduce the risk of over prescribing.

Opportunities in respiratory disease for shared decision-making support:

- Improving the efficiency of review appointments for patients with chronic respiratory conditions.
- Personal, electronic action plans that patients can refer to.

6.4 Support for Respiratory Disease Management: Healthcare Apps

There has been a large surge in the number of health care apps, also referred to as mHealth available to download with over 100,000 apps listed in the mHealth sections of both Apple and Android's app stores.

The NHS has its own approved library of apps which it only recommends once stringent assessments have been made in order to safeguard patients[19]. The assessment is comprehensive and can be a little tricky to navigate therefore some of the key components are listed below:

- Clinical safety
- Data protection
- Security
- Usability and accessibility
- Interoperability
- Technical stability

Further information on the assessment criteria can be found on the NHS Apps Library Website.

There are currently four apps listed on the NHS Apps Library specific to respiratory disease[19].

The **Digital Health Passport** is an app designed to help young people with asthma take control of their condition.

My mhealth: **myAsthma** helps patients to manage their asthma, improve upon inhaler technique, understand the treatment being offered and track medication and general wellbeing.

My mhealth: **myCOPD** helps COPD patients to better manage their condition. Similar to the myAsthma app by the same company, this app is also used to improve inhaler technique, improve breathing, reduce exacerbations and to track medication.

Rafi-Tone is an app specifically for children to aid with their breathing.

6.5 Near Market Products in Respiratory Disease

The Innovation Agency Exchange provides an online forum accessible across the healthcare sector to share innovations and challenges, and collaborate on ideas, projects and products to improve patient care. Under the area of respiratory disease there are 19 products/projects listed and of these 17 are listed as a proven innovation, 2 are listed as under evaluation with potential for adoption and none are listed as innovation in development[20]. Those with a strong respiratory component are listed below.

- **Patient Monitor** by message dynamics provides virtual consultations allowing clinicians to regularly monitor patients with long-term conditions such as chronic respiratory disease and aims to prevent avoidable admissions. In COPD the savings are predicted to be circa £1,500 per annum, per patient.
- **The COPD and heart failure services** by Inhealthcare gathers patient readings including blood pressure, oxygen, temperature, weight, heart rate and C02.
- **FebriDx** by Prospects Diagnostics Ltd is a rapid 'Point of care ' diagnostic test to reliably differentiate bacterial from viral infection in acute respiratory infection.
- NHS England has implemented a series of **respiratory programmes** such as programmes for stopping smoking, management of breathlessness in COPD and implementing optimal inpatient care.
- **Respirasense** by PMD solutions, is a continuous motion-tolerant respiratory rate monitor aiming to detect patient deterioration faster than with conventional respiratory rate monitoring.
- **Active+** is an evidence-based exercise class, supported by self-care technology, education and training, in a peer-to-peer supported programme developed by Aseptika Ltd and partners.
- The **PneuX** Pneumonia Prevention System by KLIPS UK, prevents hospital-acquired pneumonia by using a tracheal tube with a highly engineered silicone cuff and tracheal seal monitor to prevent leakage into the lungs.
- **EDGE** is a software system for the management of COPD, developed by Oxford University Hospital and with support from the Department of Health.

As most of those listed above are already market ready, aiming to be adopted the NHS, we have also identified innovations that are earlier on in the development pathway below. The market ready innovations will already have had significant investment to get them this far. It is therefore worth assessing the funding streams available to propel forward innovations in the area of respiratory disease in the UK.

6.6 Funding for MedTech Innovation

Funding is a key component of any SME's success in developing a medical device. Medical devices can take longer to get to market than other non-medical products due to the need for clinical studies, ethical approval and CE marking, to name a few. Innovate UK, NIHR i4i and NHS England's SBRI Healthcare programme are reliable and reputable sources of funding for UK medtech devices, however only the innovations of the highest calibre are funded. Innovate UK and SBRI Healthcare fund SMEs, whereas the NIHR funds academic, NHS and/or SME partnerships. We have provided an overview of the funding bodies below. These funding rounds are very competitive, therefore, to help illustrate what areas these funds are investing in, we have also included a series of tables indicating which respiratory disease products and companies have been supported over the past few years. These tables can be found in the Appendix.

Innovate UK

Innovate UK is part of UK Research and Innovation, a non-departmental public body funded by a grant-in-aid from the UK government. Innovate UK aim to drive productivity and economic growth by supporting businesses to develop and realise the potential of new ideas, including those from the UK's world-class research base[21].

NIHR i4i

The NIHR Invention for Innovation (i4i) Programme supports the preclinical and clinical development of medical devices in areas of existing or emerging patient need. The aim of the i4i programme is to de-risk early stage projects that have a strong potential for commercialisation and acceptance for use in the NHS, making them attractive to follow-on funders and investors. i4i funds collaborative research projects that have demonstrated proof-of-principle and have a clear pathway towards adoption and commercialisation[22].

SBRI Healthcare

The Small Business Research Initiatives scheme (SBRI) aims to find solutions for identified healthcare problems. Since 2008 the NHS has backed the SBRI programme, supporting over 150 companies to develop innovative technologies that match the needs of the health service[23]. A handful of these are now selling into global markets and delivering innovation to the healthcare community. Previous SBRI Healthcare competitions have called for technological and innovative solutions to both COPD and Cancer (including lunch cancer) as well as more general calls such as improving medicines adherence and the 'GP of the Future'.

6.7 Four Medtech Companies to Watch

The UK has some of the most exciting respiratory disease technology companies in Europe. Here are four companies worth watching out for in the next couple of years.

Aseptika Limited (Activ8rlives)

Asthma+me is a self-care solution for children aged 6-12 years with moderate-to-severe asthma treated as out-patients.

Over one million children in UK have a

sthma, 10% require secondary or tertiary care. Research shows that less than 50% of children take medications regularly as prescribed. Asthma deaths in children are rare but have increased, with poor adherence found to be a preventable cause in 34%. Barriers to medication adherence can be addressed by providing education, reminders and incentives.

The Asthma+me solution has the potential to support self-management asthma at scale, support healthcare digital transformation, risk stratify on need and personalised-care approach, reducing emergency admissions and improving patient safety and quality-of-life.

An initial feasibility trial showed a significant increase in confidence to self-care and parent's knowledge about maintaining asthma control and what to do in the event of an asthma attack.

Asthma+me is a CE-marked (Class 1) medical device, is on the market in the UK, undergoing a randomised clinical trial and health economics evaluation within the NHS in preparation for submission to NICE.

http://www.activ8rlives.com/

Cambridge Respiratory Innovations Limited (CRiL)

CRiL is focused on becoming the #1 supplier of respiratory health and outcomes data to the patient, clinician and healthcare provider. It aims to transform the diagnosis and management of respiratory conditions by monitoring the changes in waveform shape of CO_2 in normal tidal

breathing - a previously difficult-to-measure respiratory biomarker.

As a result of funding from NHS England's SBRI Healthcare programme, CRiL now has a market-ready version of its monitor undergoing final tests for CE-marking. This device, the N-Tidal C™, will be used to continue CRiL's own clinical studies. It will also be used for the first time in pharmaceutical clinical trials, providing a rich respiratory dataset to assess lung function. N-Tidal will transform the diagnosis and monitoring of these respiratory conditions.

Early independent health economics research indicates that N-Tidal will save the NHS up to £67 million per year in the treatment of moderate-to-severe COPD and £21 million per year in the treatment of moderate-to-severe asthma.

https://www.criltd.co.uk/

N-Tidal™
Breathtaking Technology

My mHealth

My mHealth are leaders in the development of web app mobile self-management platforms across a range of long-term conditions for patients in clinic, remotely and at population level. The company creates engaging, interactive, evidence based digital platforms for patients that can be used on almost any device. From smart phones to smart TVs, the user experiences a unique, customised, and personalised experience.

My mHealth developed a web-based COPD self-management programme "myCOPD" which provides the necessary information, education, support and communications to give patients greater control over their disease. From perfecting inhaler technique using videos, receiving best practice advice from world experts, and a complete online pulmonary rehabilitation course, myCOPD aims to deliver world class COPD care.

Using myCOPD, patients have more control over their symptoms which can reduce the number of visits to a GP or hospital and improve their condition. There is an expert patient community online where knowledge and advice are shared. In many cases the technology has transformed people's lives. Many sufferers who were housebound have seen a big improvement in their quality of life.

MyCOPD, (which has been shown to correct 98% of inhaler errors) is part of NHS England's NHS Innovation Accelerator (NIA) program and the first app approved for the Innovation Technology Tariff (ITT) enabling providers to purchase the app for free for a set period.

https://mymhealth.com/

Owlstone Medical

Owlstone Medical has developed a breathalyzer for disease. Founded originally as a spin-out from the Engineering Department at Cambridge University to commercialise the miniature chemical detection system that co-founder Andrew Koehl had developed during his PhD, Owlstone Medical was formed to focus on non-invasive diagnostics for cancer, inflammatory disease and infectious disease. The company's Breath Biopsy platform is being used as part of the LuCID (lung cancer indicator detection) project applies this technology to the detection of lung cancer by measuring chemicals in patients' breath.

Every year, there are around 45,000 new cases of lung cancer in the UK. When diagnosed at Stage I, 35% of patients will live at least a further five years, while for those diagnosed at Stage IV, the five-year survival rate is close to zero. However, at present just 15% of new cases are diagnosed at Stage I. By increasing this to 25% of cases, LuCID aims to save 3,200 lives every year. LuCID promises the twin benefits of a more pleasant clinical experience and improved health outcomes. Current lung cancer screening techniques, such as chest x-ray, CT-scan and bronchoscopy, are not without risks, and bronchoscopy in particular is a highly invasive medical procedure, involving a tube being fed through the nose or mouth, down the windpipe and into the lungs. By contrast, a breath test is a straightforward, minimally-invasive procedure that can be quickly and easily carried out.

https://www.owlstonemedical.com/

7. Ongoing Clinical Trials in Respiratory Disease

The NIHR Clinical Trials database was searched for trials currently recruiting patients for investigations into respiratory disease. The total number of trials recruiting patients in the area of asthma was 51, 70 trials were recruiting patients with CODP and there were 119 active recruiting studies for Lung Cancer[24]. An overview of these trials can be seen in Figure 3.

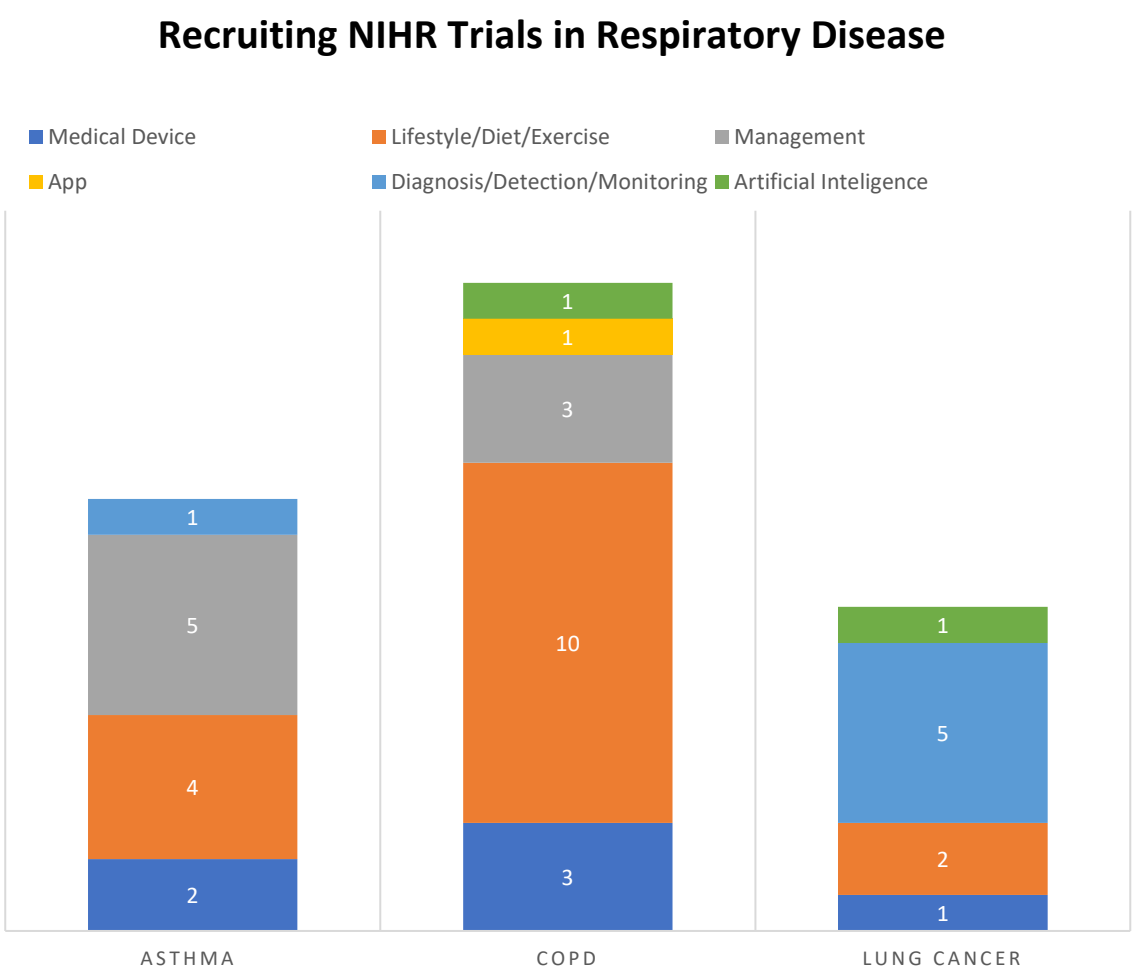

Figure 3 Overview of trials being conducted in respiratory split into type of innovation (excluding drug and drug delivery trials). Data adapted from NIHR Clinical Trials Database accessed 24th January 2020.

8. A Review of the Patent Landscape

8.1 Patent Classifications

The Cooperative Patent Classification (CPC) system is a common, internationally compatible classification system for patent publications and is the result of a partnership between the European Patent Office (EPO) and the United States Patent and Trademark Office (USPTO). There are numerous medical classes, the A61B class covers diagnosis; surgery; identification and the A61M class covers devices for introducing media into, or onto, the body (includes inhalers). A patent database was searched to identify the most common patent classes for medical devices in the area of respiratory disease between 2017-2019. The results can be seen in Table 1. By far the largest area was devices that diagnose and evaluate respiratory diseases.

Table 1: Top medical areas where IP is being filed in the respiratory disease area.

	CPC Category	**CPC Code**	**Number of records**	**Description of Area**
1	A61B	5/00	307	Measuring for diagnostic purposes
2	A61B	5/08	185	Measuring devices for evaluating the respiratory organs
3	A61M	16/00	104	Devices for influencing the respiratory system of patients by gas treatment, e.g. mouth-to-mouth respiration; Tracheal tubes
4	A61B	18/14	89	Probes or electrodes therefore
5	A61B	5/1455	80	Using optical sensors, e.g. spectral photometrical oximeters
6	A61B	5/0205	77	Simultaneously evaluating both cardiovascular conditions and different types of body conditions, e.g. heart and respiratory condition
7	A61B	18/00	72	Surgical instruments, devices or methods for transferring non-mechanical forms of energy to or from the body

8	A61B	17/00	67	Instruments for performing medical examinations of the interior of cavities or tubes of the body by visual or photographical inspection for surgical purposes
9	A61B	5/087	66	Measuring breath flow
10	A61M	15/00	59	Inhalators

8.2 Companies Active in Filing Patents in Respiratory Disease

The same patent database was searched to establish which companies were most active in filing patents in the A61B and A61M subclasses for respiratory disease over the past 2 years, between 2017-2019.

The top 5 applicants filing patents in the area of respiratory disease over the last 2 years:

1. Koninklijke Philips
2. Resmed Inc.
3. BTG PLC.
4. Boston Scientific Corp.
5. Coviden PLC.

1. Koninklijke Philips

Phillips filed 103 patents and are focussed on monitoring devices making use of digital technology. Methods for processing data and methods for determining respiration were frequently mentioned.

2. Resmed Inc.

Resmed filed 36 patents and their focus is on respiratory therapy with both apparatus and method claims. This means there are claims for the tools that are used and the way in which they are used.

3. BTG PLC.

BTG filed 36 patents and their focus is on lung capacity/volume reductions, COPD was mentioned in numerous patents.

4. Boston Scientific Corp.

Boston Scientific Corp took a more traditional approach of filing patents for medical devices and filed 30 patents in the 2-year period. Many titles described systems and methods for treating various respiratory diseases. Key words and phrases picked out were lung volume reduction; wound closure; bronchial valves; denervation and devices for treatment of occluded lumens.

5. Coviden PLC.

Coviden filed 30 patents in a similar area to Boston Scientific, lung volume was mentioned along with lung denervation. Other key phases were apnoea analysis and navigational bronchoscopy.

8.3 Patent Search by Clinical Area

A search was also carried out for specific areas of respiratory disease using a 5-year date range of 2014-2019. Coviden PLC (a subsidiary of Medtronic) appeared in all 3 searches for asthma, COPD and lung cancer. Koninklijke Philips, Nuvaira Inc and Boston Scientific Corp appeared in 2 out of the 3 lists for the top 5 companies. The number of patents filed in the 5-year period is provided in brackets next to the company name.

Top 5 Applicants in Asthma

1. Koninklijke Philips (111)
2. Nuvaira Inc. (104)
3. Boston Scientific Corp. (83)
4. Coviden PLC. (60)
5. Regeneron Pharmaceuticals PLC (44)

Top 5 Applicants in COPD

1. Nuvaira Inc. (89)
2. BTG PLC (62)
3. Coviden PLC. (54)
4. Boston Scientific Corp. (49)
5. Resmed Inc (43)

Top 5 Applicants in Lung Cancer

1. Coviden PLC. (219)
2. Koninklijke Philips (140)
3. Immunnomedics Inc. (95)
4. University of Texas (87)
5. Waters Corp (84)

9. Conclusions

There are several challenges that lie ahead for the NHS as it copes with ever increasing cases of respiratory disease. Given the complexity and range of respiratory disease we have separated the conclusions into cancer and other respiratory diseases, such as COPD and asthma, due to their differing clinical pathways within the NHS.

Lung Cancer

For lung cancer a major aim for the UK is to narrow the survival gap and move closer to the best performing countries in Europe. To do this, challenges in diagnosing and treating cancer must be addressed. The key ambitions in the NHS as detailed in the Long Term Plan for cancer are that by 2028, 55,000 more people each year will survive their cancer for five years or more; and by 2028, 75% of people with cancer will be diagnosed at an early stage (stage one or two)[1]. The NHS Cancer Programme is responsible for delivering on the Long Term Plan and its priorities include earlier and faster diagnosis, together with increased screening. To address these aims, innovations in new screening services need to be expanded to detect cancer earlier in asymptomatic patients. However, increased levels of screening, need to be coupled together with the requirement for earlier and faster diagnostics to prevent further increasing pressures on diagnostic capacity of the NHS.

Other Respiratory Diseases

Several challenges in diagnosis, treatment and prevention of respiratory disease have been identified in this report. To address these needs, innovations need to optimise care and address specified blocks in the clinical pathway.

There has been a push for new digital solutions and improved mHealth. However, the main priority should be to implement the basics first – paper-free action plans, basic risk stratification and data sharing are needed. It is also clear there is a clinical need for more self-management of such conditions and mHealth applications can go a fair way to achieving this. The ability for patients to self-manage their conditions is also dependent on strict adherence to medications, it is estimated that between a third and a half of prescribed and dispensed medicines, such as inhalers, are not used as recommended. Non-adherence and underuse represent a loss to patients, the healthcare system and society at large, as it is a lost opportunity for health improvement and a waste of valuable resources for healthcare systems. Smart inhalers are a good example of how innovators are addressing the desire for patients to self-manage whilst maintaining the oversight of a clinician. This ability to record and share data may also help to relieve pressures on primary care as the data can acted upon at review appointments thus making these appointments less cumbersome and will hopefully go on to improve patient attendance.

Recurrent Themes

The recurrent themes to this report lead us to conclude innovations are needed to help alleviate some of the pressures faced by the NHS. These solutions should be easily integrated into the existing system and provide value to both patients and clinicians.

10. Appendix

Table 1: Innovate UK funded companies 2018-2019 specialising in respiratory disease.

Award Call	Company	Project	Award
Feb 2019 Innovate UK Smart Grants	Cambridge Respiratory Innovations Limited	Intelligent inhaler proof-of-concept (INTELLIHALER)	£345,309
ICURe Follow on Funding 2019: Round 3	ImmuONE	The Inhalation Challenge	£202,110
SME Support to Evaluate Innovative Medical Technologies 2019: Round 4	Cambridge Respiratory Innovations Limited	Clinical effectiveness of N-Tidal C in monitoring Chronic Obstructive Pulmonary Disease in the community (MONITOR)	£119,272
Biomedical Catalyst 2018 Round 2 Late Stage	Acurable Limited	A wearable technology for diagnosing sleep apnoea in children	£820,925
Biomedical Catalyst 2018 Round 2 Late Stage	Snoozeal Limited	Connected and intelligent device for personalised diagnostic, treatment and management of sleep breathing disorders. SnooZeal-Connect	£261,547
Digital Health Technology Catalyst Round 3 2018: Collaborative R&D	Aseptika Limited	Asthma+me SMART: Development of an AI-supported clinical decision support system for children with moderate-to severe asthma treated in specialist paediatric clinics.	£243,915
Investment Accelerator 2018: Innovation in Precision Medicine	Breatheox	Personalised asthma care at home	£464,696
Open Grant Funding Competition 2018: Round 3	PFL Healthcare Limited Brahms	Breathing Resistance Assessment via Home Monitoring of Sleep	£155,189

Table 2: NIHR i4i funded projects specialising in respiratory disease.

Award Title: i4i Awards in Respiratory Disease	**Contracting Organisation**
Novel multielement rf coil for MR imaging of hyperpolarised helium and xenon	Renishaw PLC
Development of a novel rapid intravascular PO2 sensor	University of Oxford
Development of a miniaturized, low-cost, optical eNO sensor for asthma monitoring	Swansea University
A unique non-invasive device to measure cardiopulmonary function; - from Invention to Evaluation.	University of Oxford
Bringing a fast intra-arterial oxygen sensor to readiness for commercialisation and future patient trials.	University of Oxford
N-Tidal B personal respiratory monitor: an MHRA-notified non-interventional clinical and health economic study with asthma patients to generate the evidence for award of a Class IIB license.	Cambridge Respiratory Innovations Limited
The Inspired Sinewave Technique: a novel technology for the diagnosis and assessment of Chronic-Obstructive Pulmonary Disease	University of Oxford
Design and optimisation of a Saliva-based Point-Of-Care bioSensor for non-invasive monitoring of COPD exacerbations: COPD-SPOC sensor	University Hospitals of North Midlands NHS Trust
Breath Analysis in Intensive Care: Proof of Concept for Non-Invasive Diagnosis of Ventilator Associated Pneumonia	The University of Manchester
A Smart Saliva-based Point-Of-Care biosensor for interactive management of Chronic Obstructive Pulmonary Disease: COPD-SPOC monitor	University Hospitals of North Midlands NHS Trust
IDEAL: Artificial Intelligence and Big Data for Early Lung Cancer Diagnosis	Oxford University Hospitals NHS Foundation Trust

A Personalised Early Warning Decision Support System with novel Saliva Bio-Profiling to Predict and Prevent Acute Exacerbations of Chronic Obstructive Pulmonary Disease - 'Predict&Prevent AECOPD'	University Hospitals of North Midlands NHS Trust
GO2-digital (New Generation Oxygen Supplies with Digital Patient Interface)	Luxfer Gas Cylinders Limited
A novel endotracheal tube to reduce incidence of post-intubation stenosis and ventilator associated pneumonia in children and adults requiring artificial ventilation.	Nottingham University Hospitals NHS Trust
Improving Primary Ciliary Dyskinesia diagnosis using artificial intelligence.	Royal Brompton and Harefield NHS Foundation Trust

Table 3: A summary of SBRI Healthcare funded projects specialising in respiratory disease.

Award Call	Company	Project	Award
Improving outcomes of patients with COPD through better long term and self-management of the disease (2013)	Aseptika	BuddyWOTCH. A wrist wearable Class IIb medical monitor for patients with severe respiratory and cardiovascular disease.	£1,099,344
Improving outcomes of patients with COPD through better long term and self-management of the disease (2013)	Cambridge Respiratory Innovations Ltd	An inexpensive COPD home health device specifically targeted at personal monitoring and treatment management.	£1,099,107
Improving outcomes of patients with COPD through better long term and self-management of the disease (2013)	Glyconics	Fourier-Transforming infrared spectroscopy (FTIR) for the analysis of sputum in patients with COPD.	£98,941
Improving outcomes of patients with COPD through better long term and self-management of the disease (2013)	My mHealth	myCOPD is an IT patient self-management, and patient management system for COPD.	£1,059,107
Improving outcomes of patients with COPD through better long term and self-management of the disease (2013)	Team Consulting	High performance and low cost capsule inhaler for the treatment of COPD.	£98,930
Improving Diagnosis and Treatment Management of Cancer (2013)	Owlstone	Non-invasive Screening Device for Early Stage Lung Cancer.	£1,094,772
Improving medicines adherence (2014)	Cambridge Respiratory Innovations Ltd	A personal asthma management device.	£100,000
Improving medicines adherence (2014)	Selective Antibodies	A rapid patient-side, dip stick testing system for TB drug adherence monitoring, allowing both patient and health care-worker.	£100,000
General Practice of the Future (2016)	Cambridge Respiratory Innovations Ltd	A low cost self-care asthma monitor using its innovative N-Tidal technology.	£1,099,939
General Practice of the Future (2016)	Applied Nanodetectors	A diagnostic breath test for viral and bacterial respiratory infections.	£99,886

Cancer: Screening, Earlier Diagnosis & Faster Diagnosis (2017)	Aidence BV	Lung cancer screening pathway powered by Artificial Intelligence.	£100,000
Cancer: Screening, Earlier Diagnosis & Faster Diagnosis (2017)	Oncimmune Limited	EarlyCDT-Lung+ for Cancer Risk Stratification of Indeterminate Pulmonary Nodules.	£94,000

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