The Future of Respiratory Drug Delivery Devices

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INTRODUCTION

Globally, around 300 million asthma and COPD sufferers depend on complex medical devices to deliver their medication effectively. However, respiratory drug delivery is not easy – delivery of the correct dose, so that it is effectively distributed into the lungs, requires the user to synchronise release of the drug from the device, actuation, with inhaling the drug. The exact technique depends on the type of device but data shows that up to 94% of users do not use their inhalers properly and some 60% do not always take their medication.

This failure to medicate correctly can have serious consequences. In the UK, for example, a child is admitted to hospital every 20 minutes because of an asthma attack. More troublingly, a UK review concluded that two-thirds of the 1,200 asthma deaths in the UK each year could be avoided with simple routine care. At the same time, there is also compelling data to show that increasing medication adherence can reduce hospital admissions by as much as 60%.

Pharmaceutical companies recognise that making inhaler devices as intuitive and user-friendly as possible is important for increasing adherence, and to develop such devices, have been partnering with device companies, like Bespak, for decades. As a result, advances such as Metered Dose Inhalers (MDI), integrated dose counters, and Dry Powder Inhalers (DPI) have become commonplace. In the last 10 years, the emergence of rapid prototyping, which enables intricate mechanical designs to be created, refined and implemented, has helped accelerate the introduction of innovation in delivery devices to the market.

We are now seeing a shift in innovation towards “smart” or “connected” devices. There are already a number of Bluetooth-enabled inhaler devices on the market (see page 7) that can connect to a smartphone, but it is unclear how readily these will be adopted by patients.

With further development of the devices, and additional work on how to enable patient access, could connected devices be the “Holy Grail” for respiratory drug delivery? We’ve sought the views of both patients and the pharma industry to understand where people see potential for smart inhalers and to identify some of the hurdles that connectivity will need to overcome to realise its full potential.
There are a range of approaches to developing and delivering connected devices for patients, but the underlying principles are that drug delivery through an inhaler can be monitored, tracked and recorded, and that this information can be remotely communicated.

This will initially be to a patient’s mobile or computer, but also via a network to a platform that doctors, nurses or carers can access.

**A VISION FOR CONNECTED DEVICES**

**POTENTIAL BENEFITS**

- **Patients:**
  - Empowerment leading to increased self-awareness and better disease management
  - Education of disease state and progression
  - Better awareness and identification of early onset symptoms enabling patients to intervene

- **Healthcare provider:**
  - Reduced emergency admissions
  - Cost saving due to a lower number of hospital bed days and complexities due to exacerbations and co-morbidities
  - Enhancing disease understanding with real-world data for more intelligent disease management

- **Pharmaceutical company:**
  - Understanding of longer term patient data for more intelligent disease management
  - Data to underpin future research and usage guidelines and inform development of the next generation of therapeutics
  - Brand loyalty due to the system offering a more holistic approach

The flow of data with connected devices
WHERE ARE WE NOW?

Connected or ‘smart’ inhalers fall into two broad categories; either integrated or add-on. The first meaning a standalone inhaler device that comes with integrated electronics and connectivity, the second, a device which combines with an existing inhaler to create a connected device. Both approaches have benefits, but one of the biggest for add-on devices is the flexibility to use it with multiple inhalers over time, meaning a reduced cost over the lifetime of patient treatment.

One example of an add-on is available for use with Symbicort inhalers. Not all asthma patients will need connectivity so an available add-on device can be provided only to those that need it. To date trials with these device and inhaler combinations are showing an increase in adherence to medication and a reduced need for courses of steroid medication.

In theory, this is a cost effective approach and shows some real benefit, however anecdotal evidence suggests that people throw away devices with the connected add-on still attached and forget to transfer them to the new device. Is it that we need to better convey the benefits of the smart inhaler to the patient so that they value the device? Or simply give clearer instructions and education?

Integrated devices are often more costly and therefore may show real benefits in niche applications such as cystic fibrosis, where engagement with young adults in relation to adherence is difficult. The cost-benefit of implementing an integrated device needs to be assessed on a case-by-case basis to ensure it is justified.

We need to understand, as an industry, which patients will benefit from connected devices, and then better understand the experience from their perspective. We may discover that not all patients will see a benefit, and for those that do, the benefits will be perceived differently between individuals.

A VISION FOR CONNECTED DEVICES

The near-future – an engaged patient experience

Gemma is an 11-year-old asthma sufferer. Her doctor has prescribed her a preventative treatment that she is required to take daily. Gemma is typical of most pre-teens – not wanting to be defined by her condition, and with a rebellious streak. As a result, she is always leaving her inhaler in the wrong place and missing allotted times for a dose.

But her latest inhaler has caught her attention. It was printed using the family’s 3D printer after she selected, from a variety of designs, the one with her favourite You-Tuber featured on the side. The core components and the doses arrived by post and simply slot into the frame.

Snapchat pings up reminders, in among her chats with friends, and the inhaler can always be located. Her phone rings if she leaves the house without it.

The interactive app on her phone that links to the inhaler takes her through the steps of correct usage. It also tracks how well she achieves against optimal breathing patterns.

The results are compared with the friends she has made across the globe, who share their problems and frustrations with managing their asthma. It also links through to her avatar in her favourite game, opening up new worlds if she tracks above a certain level.

6 months later, Gemma is still tracking well and has not had an asthma attack since the new inhaler arrived. Having got bored of her favourite game, she has now switched her progress points to Netflix credits for the latest films. This helps maintain her continued engagement with her condition and her treatment.
Adding electronics into an inhaler has the potential to cause issues that may not initially be apparent. For most connected MDI devices the electronics are incorporated down the sheath of the device, which is the most obvious location. However, such a solution has the potential to impact on the resulting drug spray which can lead to a change in the amount of drug delivered to the desired area of the lung. This could be problematic with the risk being the patient not receiving the full dose of their medication, and/or the pharmaceutical company having to completely revalidate the device. Therefore, having access to the right expertise is of vital importance in the successful design and development of these systems.

The app with which a patient monitors their progress has a significant impact on the likelihood of adhering to their recommended regime. Central to thinking about this is asking how can we expect to increase patient adherence and compliance with connected devices when inhaler abuse of standard devices is so well documented? Fundamentally, the patient will need to understand the benefits or have some sort of incentive to encourage them to use their smart inhaler correctly.

As an industry, we will need to not only make drug delivery devices easy-to-use, convenient and fit-for-purpose, but also be tuned in to patients’ lifestyles and habits. Should we start tailoring the design to the user, not just in terms of patient group, but also the demographic target population? For example, in designing connected devices for children with asthma, incorporating a suitable reward system based on correct usage of their device so that is seems to be more fun and engaging, rather than being viewed as a chore.

We reference this potential in ‘The near-future – an engaged patient experience’ scenario, and believe this is a crucial element for success.
We recently surveyed chronic COPD patients to understand their most pressing concerns about their condition and how they believed connectivity might help address them. Almost half (48%) of participants were worried about the worsening of their condition and 24% were worried about being admitted to hospital. Interestingly, only 43% of participants wanted their inhaler to actively help them in managing their condition better, whilst 63% were of the opinion that connectivity would help in preventing worsening of their respiratory conditions.

The question is then how? How could connectivity help in preventing worsening of COPD patients’ respiratory conditions? 48% of those surveyed felt connectivity would have the most benefit if it could help in predicting exacerbations. Therefore, can we develop smart devices so that they monitor patients in a more integrated way, collecting data on their activity, symptoms, and external factors such as the environmental conditions like air quality? The aim would be to detect any patterns and try to understand the potential triggers for that individual patient, so that we can predict when an exacerbation is likely to occur.

We also surveyed a cross section of representatives from industry who are focused on drug delivery by the lung. The highest proportion (45%) believe compliance with the required drug regime is the key issue that patients face, whilst next most important was the patients’ ability to use the right breathing technique for successful dose delivery by the lung (33%).

To overcome these key issues, industry respondents believed that better patient education and smart delivery devices were key changes needed in respiratory drug delivery. Specifically, 67% of industry participants felt that connectivity could help with compliance of treatment regimes, whilst 33% of respondents hoped connectivity could help in preventing acute episodes.

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Even though there was a recognition that smart inhalers could help prevent worsening of their respiratory conditions, 59% of the chronic COPD patients surveyed said they would not want a connected device. If such devices are to be successfully introduced into large patient populations, it will be essential to understand why this is the case, and to identify what can be done to overcome these concerns.

Some indication of the underlying reasons may come from the subsequent responses which showed that 58% of COPD patients were concerned about the security of connected systems and 27% were concerned that systems would stop working connected systems and 27% were concerned about the security of connected devices. This raises questions of who should own the data, who should have access, what data should be collected, and how it should be used? When we asked industry representatives who should own and have access to the data, 56% said the patient and 22% said the pharmaceutical company.

Clearly, if the pharmaceutical company were to own the data, then patient consent over what data is collected and used by the pharmaceutical company would be strictly regulated. This topic is nevertheless a sensitive one and such requirements do not necessarily allay patient concern. Health data is fundamental to the promise of connected devices in terms of patient benefit, and we intend to explore this area further in a future article.

The key barrier is integrating connectivity into drug delivery devices at a reasonable price

Senior Manager, Pharmaceutical

Whilst many benefits to the patient have been identified, large scale uptake of connected devices will depend on financial benefits for all stakeholders. When asked who should bear the added cost of connected devices, industry participants were split, with 34% for health insurer, 23% for health care provider and 22% for the pharmaceutical company.

The investment model for connected devices is unlikely to be a ‘one size fits all’ approach. The model will depend on the indication, patient demographic to be addressed, geographic location, and the social and economic benefits generated. Device developers are driving forward the message that connected devices have benefits from a holistic perspective and are improvements over existing devices, however the financial case tends to be less well-articulated.

The cost effectiveness of introducing a device for a large patient population, such as asthma, may seem difficult to justify. However, taking a holistic view of the healthcare system, as the device developers are doing, there are early indications that the cost savings from reduced hospital admissions could significantly help offset the upfront investment.

Interestingly, one smart device provider is trialling a direct-to-consumer monthly subscription option in a focused market, ahead of launching into larger markets. The rationale is that the parents of children with asthma will be willing to invest in encouraging and monitoring their child’s inhaler usage as a way of proactively safeguarding their health.

The strongest cases for cost effectiveness, however, may be niche patient populations where high cost drugs are prescribed, or underserved patient groups could benefit in terms of adherence and empowerment in managing their disease. Looking outside of drug delivery by the lung, an app for Parkinson’s disease that looks at patient symptoms to determine medication regimes has shown major benefits to that patient population. As with Asthma and COPD, for Parkinson’s disease nonadherence is also linked to poor quality of life, increased hospital admissions and premature mortality. For Parkinson’s, the cost-benefit ratio is strongly in favour of encouraging further uptake of the app.

Another factor limiting these devices, and tipping the cost-benefit ratio in the wrong direction, is that they are run on batteries, which drives heat to core components and may affect device function. Batteries also introduce a challenge of environmental recovery and disposal strategies that comply with environmental legislation.

This leads to the obvious questions: who will ask for devices to be returned to what location for the correct recycling and disposal? If unresolved, such questions could hold back the potential that connected devices can bring to the industry.

At the same time, pharmaceutical companies have recognised the benefits of such technologies, and many are now exploring the potential through pilot studies and country-by-country launches related to the leading products in their COPD portfolios. They can see the long-term benefits that this approach can bring to pipeline development by gaining insights into the patient and disease condition that were previously difficult to capture.

Patients and pharmaceutical companies will benefit the most from connectivity

Senior Engineer, R&D
CONCLUSION

Reviewing the current status of the arrival of smart connected respiratory devices to the market, there has already been excellent progress – connected devices are available, patients are engaging with the technology, and improved adherence has been achieved.

Beyond the first generation of smart devices, with standard Bluetooth chip and Wi-Fi connectivity, we are on the brink of further exciting advances. Innovative systems will follow that help us understand people’s environments in relation to their disease state, that are not battery dependant, and that give the carer peace of mind without overburdening them.

The move towards such systems will be a game changer in the industry and will allow patients to have a greater understanding of their disease and will help the wider industry to determine where future research and education is needed. It will also drive empowerment in niche indications where patients need a greater level of engagement.

There are still many technological, economic and social challenges that will need to be overcome, as we have discussed above. But smart connected devices offer the patient and industry many exciting opportunities that are now proving themselves in clinical settings. We are all eagerly anticipating the next developments in this fast-moving and dynamic space.

Device manufacturers must partner with each other to deliver smart devices for the best market outcome

Business Development, R&D

References