



CONNECTED INHALERS MAKING A REAL IMPACT ON RESPIRATORY OUTCOMES

Adherium was founded in 2001 (as Nexus6) to develop solutions to help manage asthma better. Now, in 2016, Adherium's Smartinhaler™ platform represents one of the world's largest ranges of sophisticated adherence devices for prescription asthma and COPD medicines, with a robust peer-reviewed evidence base. In this article, Garth Sutherland, CEO of Adherium, describes the problem of chronic non-adherence in asthma and COPD, how Adherium's Smartinhaler™ solutions have proved themselves in the clinic, and why now is the time to move to real-world scale.

The costs of health care and the burden of disease continue to rise, seemingly without limit, putting both healthcare delivery and healthcare payment under extreme pressure.

Driven by escalating need, the opportunities for innovation are escalating in tandem. Digital health is hitting its stride, with record-breaking market values, record-breaking levels of investment and matching levels of hype. A 2015 report¹ valued the

global digital health market at US\$55 billion in 2014, while an April 2016² report highlighted a record \$1.8 billion funding into digital health in Q1 2016 alone. This covers many different categories, from financial (insurance) to consumer (wellness, like Fitbit) to analytical (big data) to clinical (from electronic records to decision support).

A source of much frustration in health care has been the inability to maximise the solutions already available, with non-adherence to medications identified as a massive problem. In the US, the overall cost of suboptimal medicine use including non-adherence, under-treatment, administration errors and under-diagnosis, is estimated to be approximately \$213 billion annually, or 8% of annual healthcare expenditure (Figure 1).³

Chronic diseases are considered especially problematic for adherence, but also promising targets for improvement given the right interventions, hence many digital and mobile health companies are targeting chronic diseases like diabetes, asthma and COPD.

"Treatment non-adherence is a critical issue in addressing population health from both economic and quality of life perspectives."

THE CONSEQUENCES OF POOR ADHERENCE IN ASTHMA AND COPD

There are two main types of medications used to treat asthma and COPD. The first, commonly-called "relievers" or "rescue" medications, are used to provide near immediate relief from symptoms. The second, referred to as "preventers" or "maintenance" medications, are taken regularly (daily) to control the disease and minimise flare-ups or exacerbations.

Poor medication adherence is common in COPD and asthma, with only approximately 50-55% of US patients taking their medication as prescribed (Figure 2).⁴

The WHO assessed preventer medication adherence could be as low as 28% in developed countries.⁵ WHO states that this

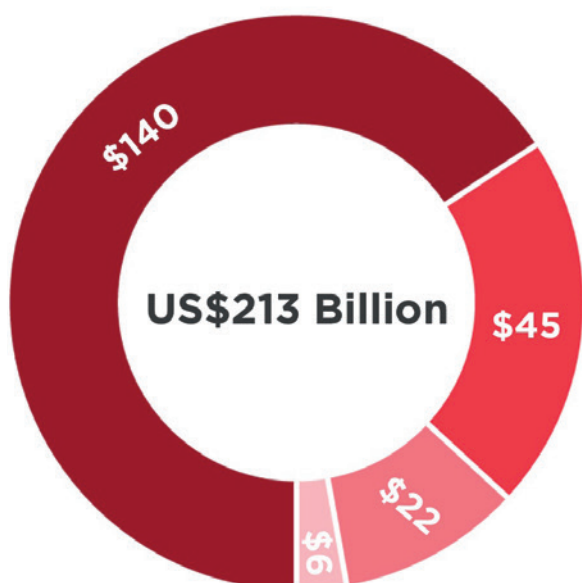


Garth Sutherland
Founder, Group Chief Executive
Officer & Chief Technology Officer
E: info@adherium.com
T: +64 9 307 2771

Adherium Ltd
Level 2
204 Quay Street
Auckland 1010
New Zealand

www.adherium.com

Avoidable Costs (US\$ Billion)



Healthcare System Utilisation

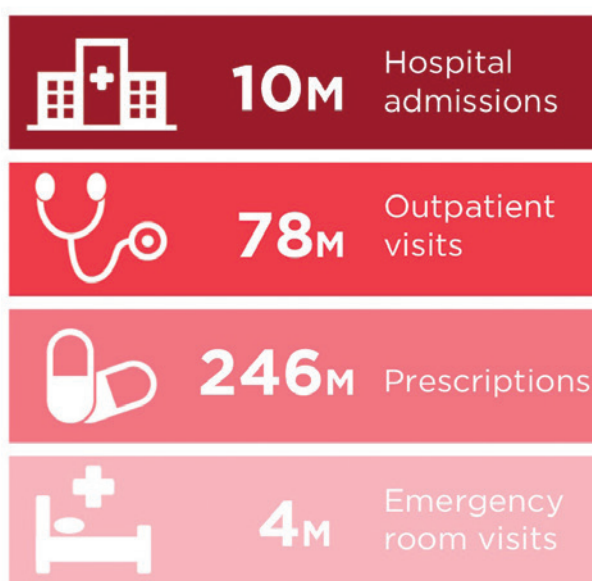


Figure 1: Avoidable costs of suboptimal medicine.³



Figure 2: In the US, only 50-55% of asthma and COPD patients take their medication as prescribed.⁴

“results in poor asthma control which has clinical consequences, such as increased hospitalisation and emergency department visits, resulting in unnecessary high costs of health care.”

Treatment non-adherence is a critical issue in addressing population health from both economic and quality-of-life perspectives, with patients facing potentially life threatening risks if they are not supported in their medication adherence by the broader health system.

Adherium is a global leader in the design

“What is new and a cause for hope is the wave of miniaturised, connected and consumerised technology that has washed over all aspects of modern life especially in the last decade.”

and development of evidence-based digital health solutions that address suboptimal medication use and remote patient management. Adherium’s smart health solutions use connected devices, software and data to improve the quality of care – and quality of life – for those with asthma, COPD and other chronic diseases.

DIGITAL AND MOBILE HEALTH SOLUTIONS FOR CHRONIC DISEASE

Adherence has long been recognised as a cause of unachieved outcomes, and therefore is an opportunity to address. Over the decades, waves of resources and solutions have been thrown at the problem of chronic non-adherence, to little effect.

What is new and a cause for hope is the wave of miniaturised, connected and consumerised technology that has washed over all aspects of modern life especially in the last decade. This has enabled different solutions for tackling adherence (and other problems) that not only have clinically proven effectiveness but, critically, hold the promise of effective scalability in real-world use. Helping people with asthma or COPD to control their condition better is one of the areas where a critical mass of experience and evidence has been accumulated, and is now tipping from research, development and pilot/small-scale use towards large-scale execution in the real world.

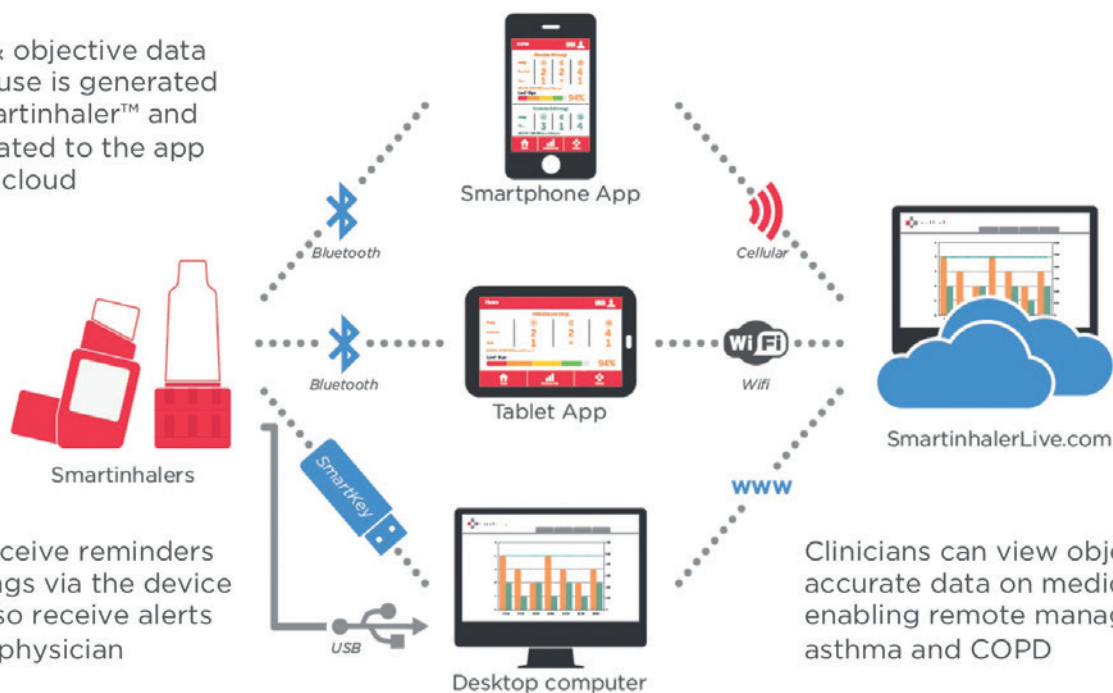
Advanced digital/mobile health interventions comprise multiple parts:

- Sensors and inputs for tracking and measurement, gathering accurate objective data.
- Communication between sensors and devices, software, patients, clinicians and other stakeholders (whether using smartphones, tablets, desktop computers or other).
- Feedback and advice to the patient from their inhaler or smartphone. For adherence, this is the primary intervention channel.
- Feedback and advice to healthcare professionals (HCPs) and other stakeholders. This channel provides for HCP-mediated interventions.

To work, all of this has to be accurate, secure and safe. Furthermore, it must have a low user burden, have good usability and deliver a good overall user experience, for patients and for all other stakeholders involved in delivering or executing such solutions.

Adherium’s Smartinhaler™ platform is designed to help patients adhere to their preventer medications and allow clinicians to monitor and manage patients’ therapy remotely (including adherence) to improve patient outcomes. The platform comprises a medical device (from the Smartinhaler™ range), specifically designed for each type of inhaler required, and the SmartinhalerLive™ platform, which comprises the wireless communication, mobile and desktop apps, and cloud-based software (Figure 3).

Accurate & objective data on inhaler use is generated by the Smartinhaler™ and communicated to the app and to the cloud



Patients receive reminders and warnings via the device and can also receive alerts from their physician

Clinicians can view objective and accurate data on medication use enabling remote management of asthma and COPD

Patients, Parents & Caregivers can track their own performance using the company's proprietary app or via client company apps

Figure 3: How the Adherium Smartinhaler™ platform operates.

CLINICAL OUTCOMES FROM DIGITAL INTERVENTION

Adherium's Smartinhaler™ platform features one of the world's largest ranges of sophisticated adherence devices for prescription asthma and COPD medicines, with the most robust peer-reviewed evidence base (Figure 4).

A total of 27 clinical studies on Adherium Smartinhaler™ have been published in peer-reviewed journal articles, and over 48 publications reference Smartinhaler™

"Given the accumulating weight of experience and of clinical proof, the critical step in this field is going to market at scale."

technology. Right now, more than 60 clinical programmes are running in over 30 countries using Smartinhaler™.

Adherium's Smartinhaler™ has been proven to change patient behaviour, increasing the use of preventive inhaled

medications, over and above changes generated through training from physicians and behavioural psychology techniques. Use of the Adherium system has been clinically proven to improve adherence by up to 180% and has been shown to reduce use of rescue medications and to reduce occurrence of severe exacerbations.

For example:

- Interim data from a 12-month study in children⁶ has demonstrated that use of the Smartinhaler™ substantially increases adherence and significantly reduces the number of oral steroid courses required over the period. The interim data shows at 12 months a 144% increase in adherence in the Smartinhaler™ group *versus* control arm, a 37% reduction in the number of oral steroid courses required in the 12 months from 2.7 to 1.7 and increased lung function as measured by FEV1 (mean forced expiratory volume in 1 second % predicted), 87% in the control arm *versus* 100% with Smartinhaler™.
- A six-month study in 220 school-aged children who presented to the emergency department with an asthma exacerbation⁷ showed that adherence to

preventer medication increased by 180% in the group receiving reminders from Smartinhaler™. Use of rescue/reliever medication was reduced by 45%. Parent-reported exacerbations occurred in 7% of children in the Smartinhaler™ group at the two-month mark compared to 26% in the control group.

- Another six-month study with Smartinhaler™, in primary care with 143 patients aged 14 to 65⁸ demonstrated an increase in adherence to preventer medication by 59% and a reduction in severe exacerbations by 61% (11% of patients in the Smartinhaler™ group *versus* 28% in the control group) (Figure 5).

MAKING THE TRANSITION FROM STUDIES AND PROGRAMMES TO REAL-WORLD SCALE-UP

Given the accumulating weight of experience and of clinical proof, the critical step in this field is going to market at scale. In July 2015, AstraZeneca and Adherium entered into a ten-year commercial product development and supply agreement. Adherium will supply innovative new devices and sensors that AstraZeneca will incorporate within



Figure 4: The Adherium product range.

global patient support programmes for patients with COPD and asthma.

AstraZeneca had already successfully used Adherium technology in clinical evaluations and clinical trials, and piloted its use in programmes to support patients in the management of their conditions. This partnership validates the commercial importance of the Adherium technology in the global digital health market.

Bringing a workable and meaningful solution to the market is critical. With Adherium's "track and remind" solution, which has been robustly demonstrated and proven to have clinical impact, there is a proven intervention that is simple enough to be implemented and scaled. There will

be many developments coming down the line, from incremental (miniaturisation, internalisation or integration, battery life etc) to additive (insight and intervention algorithms developed from big data), but there is also a lot to be both gained and learned from implementing the current solution.

As pharma and health technology companies implement and scale their digital health products, services and supporting infrastructure, they will have to adapt to take on new capabilities and organisation structures. While this may be difficult (change always is), they will be better placed to execute subsequent incremental innovations within their adapted organisations and business models.

They will also be best placed to unlock additive innovation, for example by being first to have the high-quality, huge data sets needed to move into big data insights and analytics, and to move to new models with risk and gain sharing, and payment by outcomes. The stakes are raised when moving to scale but so too are the opportunities and rewards.

REFERENCES

1. <https://www.psmarketresearch.com/press-release/global-digital-health-market>
2. <http://www.startuphealth.com/content/insights-2016q1>
3. *Avoidable costs in US Healthcare: The \$200 Billion Opportunity from Using Medicines More Responsibly (June 2013) IMS Health pages 1 and 3.*
4. <http://www.statista.com/statistics/258142/drug-doses-us-patients-take-as-prescribed-by-condition/>
5. World Health Organization. *Adherence to long term therapies: Evidence for action.* 2003. P13.
6. Morton R, European Respiratory Society International Congress, September 2015. Oral Presentation and Abstract number: OA4772 http://erj.ersjournals.com/content/46/suppl_59/OA4772.
7. Chan AHY et al, "The effect of an electronic monitoring device with audiovisual reminder function on adherence to inhaled corticosteroids and school attendance in children with asthma: a randomised controlled trial." *Lancet Respir Med*, 2015, Mar, 3, 3, 210-219.
8. Foster JM et al, "Inhaler reminders improve adherence with controller treatment in primary care patients with asthma." *J Allergy Clin Immunol*. 2014, Dec, 134, 6, 1260-1268.

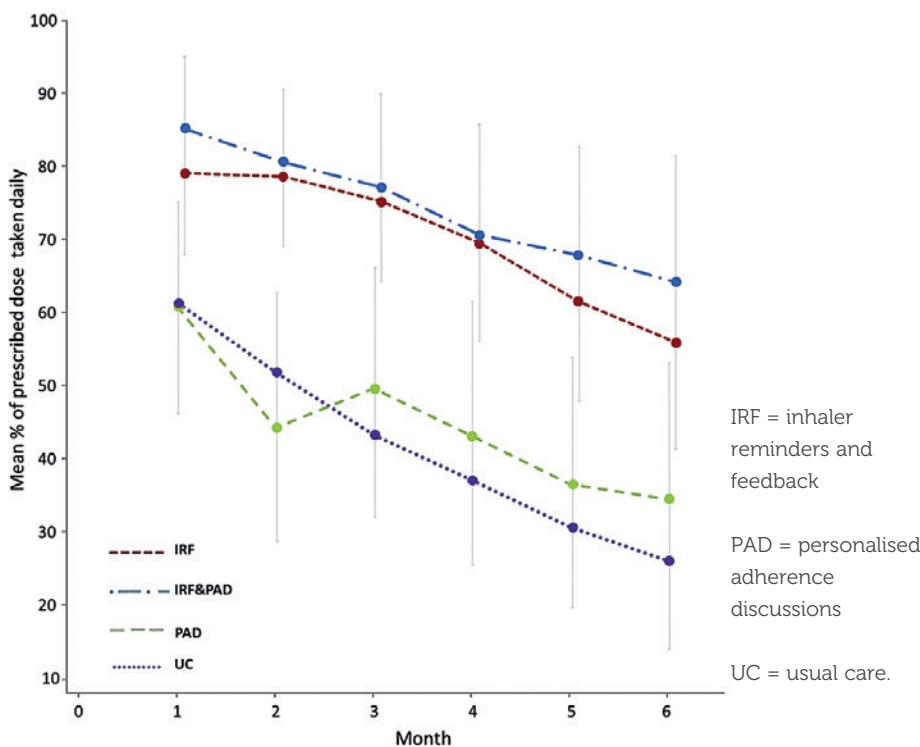


Figure 5: The adherence advantage of Adherium Smartinhaler™ is maintained over time.⁸ (Source: Foster et al, "Inhaler reminders improve adherence with controller treatment in primary care patients with asthma". *J Allergy Clin Immunol*, 2014, Vol 134(6), pp 1260-1268. Copyright © 2014 Elsevier. Reproduced with kind permission.)



Adherium's SmartInhaler™ is proven to:

- Increase medication adherence by 180%, and reduce rescue medication use by 45% in children with asthma¹.
- Increase medication adherence by 59%, and reduce the risk of severe exacerbations by 61% in adults with asthma².

¹ Chan, Amy HY, et al. "The effect of an electronic monitoring device with audiovisual reminder function on adherence to inhaled corticosteroids and school attendance in children with asthma: a randomised controlled trial." *The Lancet Respiratory Medicine* 3.3 (2015): 210-219.

² Foster, Juliet M., et al. "Inhaler reminders improve adherence with controller treatment in primary care patients with asthma." *Journal of Allergy and Clinical Immunology* 134.6 (2014): 1260-1268.

