Institution: The University of Manchester

Unit of Assessment: 3 (Allied Health Professions, Dentistry, Nursing and Pharmacy)

Title of case study: Smart inhaler improves adherence to treatment for children with asthma

Period when the underpinning research was undertaken: June 2012 - December 2020

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
Tariq Aslam	Professor of Ophthalmology and Interface Technologies Reader in Ophthalmology Senior Lecturer in Ophthalmology Honorary Senior Lecturer	2019 - present 2016 - 2019 2013 - 2016 2010 - 2013
Clare Murray	Clinical Senior Lecturer	2007 - present
David Henson	Emeritus Professor of Optometry Professor of Optometry and Vision Science	2017 - present 2004 - 2016
Ian Murray	Professor of Optometry and Vision Science Senior Lecturer	2016 - present 2004 - 2016

Period when the claimed impact occurred: 2016 - 2020

Is this case study continued from a case study submitted in 2014? N

1. Summary of the impact

Asthma is the commonest childhood disease, affecting around 1,000,000 children in the UK and 100,000,000 worldwide. Treatment is delivered with inhaler devices, but adherence is often poor. Our research at the University of Manchester on sound analysis and gamification has transformed treatment acceptability by developing an inhaler mask with an audible whistle sound to indicate good technique. This whistle sound activates cartoons on a mobile device specifically designed to encourage compliance. The technology has led to a spinout company, Clin-e-cal, and been used by over 100,000 children worldwide. Studies demonstrate it reduces problems in medication delivery.

2. Underpinning research

Children with asthma are often anxious about treatment and have poor adherence with their medication, leading to serious health consequences. The aim of this project was to counter this major health issue by producing an affordable system which would improve breathing technique and adherence with treatment for children with asthma symptoms.

In early studies, Aslam developed expertise in computerised image processing including transformation and analysis of image data with highly sensitive and specific expert system algorithms. These algorithms have been able to extract clinically relevant information from ophthalmic images taken using multiple imaging modalities [1, 2]. The same techniques acquired in ophthalmology were used for this respiratory project to analyse and extract clinically useful information from the sound of correct inhaler use to detect correct inhalations.

Aslam studied gamification techniques with Henson to facilitate the complex tasks of measuring peripheral visual fields in children [3] and with Murray to develop automated and accurate central vision testing using games on tablet computers [4, 5]. Principles from these ophthalmology projects, to encourage children to interact with vision tests via games, were translated to encourage children to interact with inhaler medication.

Aslam used the above experience to design a system for masks and spacers such that the sounds of correct inhalation could be detected and activate multi-stage cartoon animations / games on a screen – these would reduce anxiety and encourage specific and correct breathing patterns in children. In collaboration with Murray, Aslam designed and conducted a study to measure the impact of the device on children's acceptance of spacer treatment using questionnaires given to children and parents [6]. Both parents and children responded positively to the device in this initial feasibility study: 13/14 children said it helped them take their medication and 13/14 parents felt that the device helped their children use their spacer and made them calmer. Children responded positively, citing the system as something that was fun rather than stressful.

This system provided the framework for a final version named Rafi-tone ('Respiratory Aid for Inhalers'). Rafi-tone consists of a mask that emits a whistle when the child is breathing correctly, serving as a simple, reliable and reassuring indicator to children and parents. Detection of the whistle sound by a mobile application can drive a cartoon game, designed to encourage the correct form of breathing - the system essentially involves children in an onscreen, fun, animated game, which rewards them for correct inhaler use.

3. References to the research

1. **Aslam TM**, Shakir S, Wong J, Au L, Ashworth J. Use of iris recognition camera technology for the quantification of corneal opacification in mucopolysaccharidoses. *Br J Ophthalmol* 2012;96(12):1466-8. doi: 10.1136/bjophthalmol-2011-300996

   First demonstration of use of analysis of iris recognition camera images for objective assessment of eye disease.

2. Balaskas K, Nourrit V, Dinsdale M, **Henson DB**, **Aslam T**. Differences in spectral absorption properties between active neovascular macular degeneration and mild age-related maculopathy *Br J Ophthalmol* 2013;97(5):558-560. doi: 10.1136/bjophthalmol-2012-302305

   This publication in one of the highest profile journals for the field provides a novel application of imaging.

3. **Aslam TM**, Tahir HJ, Parry NRA, **Murray IJ**, Kwak K, Heyes R, Salleh MM, Czanner G, Ashworth J. Automated Measurement of Visual Acuity in Pediatric Ophthalmic Patients Using Principles of Game Design and Tablet Computers. *American Journal of Ophthalmology* 2016;170:223-227 doi: 10.1016/j.ajo.2016.08.013

4. **Aslam TM**, Parry NR, **Murray IJ**, Salleh M, Dal Col, C, Mirza N, Gzanner G, Tahir H. Development and testing of an automated computer tablet-based method for self-testing of high and low contrast near visual acuity in ophthalmic patients. Graefes *Arch Clin Exp Ophthalmol* 2016;254(5):891-899. doi: 10.1007/s00417-016-3293-2

   This paper and the preceding one were the first to demonstrate game-based, reliable and accurate vision testing in paediatric and adult patients.

5. Wang Y, Ali Z, Subraman S, Biswas S, Fenerty C, **Henson DB, Aslam T**. Normal Threshold Size of Stimuli in Children Using a Game-Based Visual Field Test. *Ophthalmology and Therapy* 2017;6:115-122. doi: 10.1007/s40123-016-0071-5

This paper is part of a series charting development of a system which has become the first internationally to demonstrate reliability and validity of using games to assess visual fields in children.

6. **Aslam TM**, Shakir S, **Murray C**. Feasibility Study of Interactive Game Technologies to Improve Experience with Inhaler Spacer Devices in Young Children. *Pulm Ther* 2016; 2:189-197. doi: 10.1007/s41030-016-0023-1

This was our first paper demonstrating the potential of our technology to transform children's perceptions about their inhaler therapy.

4. Details of the impact

Context

Asthma is a life-threatening disease requiring drug-delivery into the lungs via devices known as inhalers. Younger children can find taking the inhaler difficult and so it is often attached to one end of a cylindrical chamber, or spacer, and then pressed to release the drug into this spacer. A mask on the other end of the spacer allows the child to breathe in the drug more easily from the chamber through several breaths. However, this technique is associated with poor adherence and reduced drug delivery to the lungs. Treatments are missed or given with poor technique, which is exacerbated by children being distressed. Poor adherence with spacers in children is a major health and socio-economic problem, with an estimated 14% of all children globally experiencing symptoms, and levels of adherence to treatment reported to be as low as 28%.

Pathway to impact – new technology

The Rafi-tone system, developed in 2016, uses a mask designed to produce a specific whistle which provides an auditory cue when breathing is correct. Software provides entertaining visual encouragement to a child when this is heard (Figure 1) and logs correct treatment in a digital calendar. The mask whistle improves carer and children's confidence that the drug has been inhaled, and the additional app is used by educators to train carers and children in whistle spacer use, especially if there are known compliance issues.

Figure 1. Illustration of the mask, spacer and inhaler, with mask whistle activating the Rafi-tone games.

Aslam's research is novel in providing an accessible system, combining animation type games to motivate treatment compliance and providing reassurance to parents/ carers that optimum treatment has been given.

Reach and significance of the impact

a) Clinical impact on asthmatic children worldwide

The mask and associated app make inhaler use more fun, transforming perceptions and improving adherence and breathing technique in children.

An independent, international randomised controlled trial of 371 children was conducted, comparing app use with standard verbal instructions [A]. The trial found that lung functions of children using the app were significantly ($p<0.001$) improved. The percentage of patients improved according to an asthma control test was higher in the app group compared to the verbal instruction group. Compliance also improved subjectively and objectively.

An independent post-marketing survey of 6-10 weeks' use of the mask and app was conducted on 112 asthmatics (aged 1-11) and their parents. Survey results showed that use of doctor/hospital services reduced from 16/6 at baseline to 4/1 respectively at follow-up [B]. All of the 10 independent healthcare practitioners surveyed stated that their patients were better controlled using the Rafi-tone system [B]. This evidence implies significant benefit to children who have used the system. There have been over 112,000 international mask sales since its inception in 2016. App use is steadily rising, with over 4,000 maintained downloads, currently 250 per month (as at July 2020). The mask and app are available in the UK, France, Norway, Sweden and Australia.

A GP practice pharmacist stated that she "*had the most amazing experience*" with the Rafi-tone system and that this technology was a "*game changer*" for her practice and patients [C]. Other quotes from health carers have included "*Great idea. Easy to use and good distraction for children—makes inhaler delivery so much easier*" [D]. Example quotes from parents have included "*Good distraction and improved technique. New to inhalers so made him less scared*"; "*Yes, it has definitely helped in breathing technique. T was previously taking shallow breaths but with the game managed to focus on deeper breaths and concentrated on playing the game.*"; "*…helps to direct the child's attention and focus on breathing. Enjoyable activity. No bad points - a really good idea. A good way to introduce inhalers*" [D].

b) Economic impact of Clin-e-cal, a new technology company

Clin-e-cal, an innovative digital health company, arose entirely from the research for Rafi-tone. Founded by Aslam through a partnership with doctors, researchers and hospital teams, it has been established now for six years [E]. Clin-e-cal's collaboration with Clement Clarke International directly led to the whistle that activates the Rafi-tone app. The app successfully qualified for the prestigious NHS apps store [F]. The mask is produced by Clement Clarke and is available via prescription [G], meaning that it is readily available.

Clin-e-cal has two full-time members of staff, a board of six members and robust and increasing income streams of approximately currently GBP20,000 per month. The company has attracted GBP250,000 external venture capital funding, allowing expansion and diversification.

In summary, research studies, testimonials and sales indicate that the easily accessible Rafi-tone technology has transformed clinical care for tens of thousands of children internationally, improving adherence and addressing the serious morbidity associated with asthma and viral induced wheeze.

5. Sources to corroborate the impact

A. Impact of Advanced Patient Counseling Using a Training Device and Smartphone Application on Asthma Control. Haitham Saeed, Mohamed E A Abdelrahim, Hoda Rabea and Heba F Salem. Respiratory Care 2020; 65 (3) 326-332. doi: 10.4187/respcare.06903.
   Independent clinical trial which found a significant improvement in lung function of children using the app.

B. Salford CCG RAFI TONE / Able spacer innovation survey, 2019.
This survey was designed and carried out by an independent research group, Accelerate Associates. Results were reported at The International Society for Aerosols in Medicine (ISAM) 2019, as abstract N-123: Implications For Paediatric Asthma Care From Gamification Of Inhaler Spacer Technique, Toor S, Crawford E, Aslam T, Sanders M. This post-marketing survey was of 112 asthmatic children and their parents. Parents using the app reported a reduction in need for appointments and >50% parents were sure the app+Spacer helped their child. All 10 healthcare practitioners questioned stated that the patients in the survey were better controlled. The proportion of patients experiencing asthma symptoms also decreased.

C. E-mail from a pharmacist in independent practice describing the impact of Rafi-tone technology (25 September 2019).
The pharmacist expresses the impact it had on an example difficult child and her opinions on how it will have broader impact for other patients.

D. Feasibility Study of Interactive Game Technologies to Improve Experience with Inhaler Spacer Devices in Young Children. Aslam, T.M., Shakir, S. & Murray, C. Pulm Ther 2016; 2: 189-197. doi 10.1007/s41030-016-0023-1.
This study demonstrates the positive impact on children who used first iterations of this technology.

E. Companies house page
Lists Aslam as a Director and company documents (e.g. share issues/accounts) that evidence investment.

F. NHS Digital web page www.nhs.uk/apps-library/rafi-tone/ (featured in respiratory section)
Demonstrates that the app is approved by the NHS.

G. NHS drug Tariff listing of A2A Spacer small mask
Demonstrates that the mask is available on prescription.