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The number 10

What is so special about the number 10? Since we first learned to count on our fingers, ten feels like a special number. It's where the British Prime Minister lives, 10 Downing Street. It's how many seconds it takes to declare a knockout in boxing. It's the percentage of people that are lefthanded. It's also our tenth issue of Insight magazine.

Here in our tenth issue, we feel like we're still going strong, landing on desks twice a year and discussing medical devices from top to bottom. Five years ago we launched *Insight* to share ideas, thoughts and advice, while also sparking discussion or

even a moment of inspiration. We've really enjoyed creating Insight. We had a look back in the archives, recall some of our most popular articles, such as Intelligent inhalers, Living life with type 1 diabetes and 'the one with the x-ray specs' from issue eight.

In this issue, you'll see articles from a few familiar faces, as well as some new ones. Topics range from the first moon landing to reusable rockets and how they relate to medical devices. Once again we look to the future of healthcare with advances in lung disease diagnosis and sharing what good design means for medical

devices. David Harris explains why it's so difficult to get things moving in an inhaler, while Stella Wooder and guest author, Richard Huckle examine the difference in taking a medical device or medicinal product to market - and the pitfalls to avoid. And if that wasn't enough, we've thrown a top ten list in there too. Enjoy.



Dan Flicos, CEO



Martin Bontoft

Head of Design Research

"Meaningful user-centred innovation is tremendously powerful for organisations. It doesn't assume new and expensive technologies, but just aims to help designers and engineers give people what they want."



Richard Huckle

Senior Consultant (Regulatory Affairs) Richard is the Senior Consultant for Regulatory Affairs at Pope Woodhead & Associates.



Vicky Shipton

Head of Marketing Vicky heads up Team's marketing department and is responsible for ensuring *Insight* magazine is the best it

can possibly be.

"No matter what people tell you, words and ideas can change the world." **Robin Williams**



David Harris

Head of Respiratory Drug Delivery David applies solid aerosol science and fluid dynamics to improve the efficacy of inhaler technology.







Stella Wooder

Head of Project Management

"Working with colleagues to develop and deliver innovative, pragmatic and robust medical devices which improve people's quality of life remains a highlight for me!"



Craig McGarrell

Industrial Designer

Craig is a passionate designer, striving to create simple solutions to complex design problems.





Ben Wicks

Head of MedTech

Ben has a background in microbiology, immunology and virology, as well as 18 years' experience in science, engineering and commercialisation of medical devices and diagnostics.



Musk and his team ignored them and set about designing and building rockets which could be launched, returned to Earth and reused. On December 22nd 2015, SpaceX launched one of its Falcon 9 rockets from Cape Canaveral. The rocket delivered eleven satellites into orbit, but uniquely, the first stage of the rocket was safely returned to a nearby launch pad where it landed vertically¹. They've since repeatedly landed several rocket stages on their autonomous drone ship out in the Atlantic. If you haven't watched a clip of one of the rockets landing, then go and watch it now - it's ace!

There are many things that I admire about what SpaceX has achieved, but what stands out most was the realisation that cost reduction was key to unlocking greater access to space, so SpaceX made this their goal from the outset. \rightarrow

Point-of-care diagnostics

The medical device industry has been talking about Point-of-Care (PoC) diagnostics changing the delivery of healthcare for more than two decades now, but PoC diagnostics products haven't really delivered on their potential. Very few of us have had a panel of blood tests done in real time by our primary care physician. Blood glucose meters and pregnancy test strips are big business and some PoC diagnostic products have found various niches, but the vast majority of blood tests are still sent off to a central lab for testing.

Cost is the single biggest barrier to more widespread adoption. Problems with accuracy, precision and usability have gradually been ironed out, but cost remains the overwhelming obstacle limiting greater uptake and integration of PoC products into mainstream healthcare.

PoC diagnostics will only begin making a significant impact on healthcare delivery if and when new products are launched at a radically lower cost - along with the necessary accuracy, precision, reliability, usability and connectivity. You've got to have the full package. Fall short on any one of these and you can join the long line of companies that almost made it.

How much cost reduction is required?

Lots of quantitative analysis has been done but personally I think that end user costs need to be more than halved in order to allow PoC tests to deliver on their full potential. This is a huge challenge. Such a big reduction in cost is unlikely to come just by making incremental cost savings. It will require companies to think differently from the outset. Just like SpaceX, cost-of-goods targets must be central to the overall development strategy.

One of the problems with the PoC diagnostics industry is that clever assay technologies have normally been the starting point for new businesses. Few companies, if any, have considered cost first and used their economic model to inform their technology selection. However, unless leaders are willing, like Elon Musk, to face harsh commercial realities then they will struggle to make transformative leaps forward.

Performance and usability

Whilst cost is critical, it isn't good enough just to be cheap. A successful PoC diagnostic product needs also to address accuracy, precision, reliability, usability and connectivity. Test accuracy and precision is a non-negotiable threshold which must be met by any diagnostic system. Without adequate assay performance you simply don't have a product, so we won't discuss performance here.

Usability, from a risk perspective, has come under greater scrutiny from regulators over the last ten years. The subject of risk-based usability or human factors has been described eloquently in other *Insight* articles and Team has been at the forefront of this field for almost two decades, so I won't dwell on it here, except to say that usability has to be 'baked in'. Usability and human factors considerations can't be bolted on to the end of a diagnostic system development programme any more.

Connectivity

Data connectivity is currently a hot topic in medical devices generally, particularly in the context of PoC diagnostics. There's no point in doing tests rapidly and near the patient if you can't quickly share and act on the results. This isn't a new observation.

Twenty years ago in 1996 Parvin et al. commented that "numerous questions persist regarding POCT. For example, management of patients' data (billing, entry into medical records and medical information systems) is not automatic or always straightforward."²

Getting data connectivity right will be pivotal if PoC diagnostics are going to deliver on their full potential.

I don't think that inadequate connectivity has greatly limited PoC adoption up until now, but I do believe that in order to gain widespread adoption, (assuming costs are reduced), successful products will require connectivity to be extremely well implemented. Healthcare IT systems are gradually becoming more integrated so any PoC technology must slot easily into this ecosystem. Sadly healthcare IT systems have historically been poorly implemented; hence the process of slotting in a new product has been painful, clunky and slow.

The reasons why healthcare IT systems have been so poor are many, and one major challenge is that you can't develop new technology on a trial-and-error basis. Just like air traffic control, healthcare is too safety-critical to just 'suck it and see'. You can't simply try something out and hope that the test results or sensitive patient data won't get corrupted, lost or disclosed. This has handicapped the medical industry. Consumer electronics and home computing have evolved quickly because they could rapidly undergo many iterative development loops and nobody died when the technology fell over. Think back to word processing in the 1980s, when hardware and software could be anything from bad to completely awful. Essays got lost, documents got corrupted and transferring files between computers, programmes or operating systems was a complete lottery. But, gradually over time, the world improved things like Lotus Notes and WordPerfect thankfully disappeared, Apple and Microsoft started talking to each other, e-mail became ubiquitous, cloud storage appeared and, thanks to a huge amount of development trial and error, we now have the ability to share documents quickly, easily and reliably. To get round this problem and build really good connected health infrastructure the medical industry is working extra hard, using the latest development tools and applying lessons from the consumer world wherever possible. I expect it to take another three to four years for health informatics systems to be refined and widely adopted within the diagnostics world, but the train is now moving and it isn't going to stop.



"Some of the current crop of PoC diagnostics start-ups will inevitably fade away"

The future

The agile, smart companies who recognise the need to consider cost from the outset, and who can bring together all the other interlinked aspects of PoC systems such as usability and connectivity, will survive and thrive. Organisations without the necessary vision, decision-making ability or perspective will struggle.

At this stage it isn't clear who the winners and losers will be. Some of the current crop of PoC diagnostics start-ups will inevitably fade away. A handful of the most forward thinking, agile and decisive companies will make a success of it. They may not accomplish the stratospheric market penetration in healthcare that the likes of Amazon and Google have achieved in the consumer world, but we shouldn't be surprised to see new players taking significant market share, because they've thought about cost from the outset and also delivered on assay performance, usability and connectivity. ENDS

References

- 1. You should watch the launch video on the SpaceX website, it's absolutely brilliant.
- 2. Impact of point-of-care testing on patients' length of stay in a large emergency department – Clinical Chemistry 42:5 711-717 (1996)

Sometimes you just have to be there

The benefits of spending more time with patients and device users







Of course, if it's a moon landing there are some practical reasons why you can't be there and, back in 1969, even watching it on a TV was a challenge. Nevertheless, there are some things that simply demand your presence, when you feel privileged to share, where your wonder is amplified by the wonder of those around you. I have felt that same privilege and wonder spending time with people using medical devices: watching that daily, small victory of an injection; understanding why a mother's non-adherence was a necessary consequence of the care of her baby; and how the debilitating effects of COPD was robbing a father of his role and his masculinity.

I don't know about you, but I design because I care. I believe - and, as time goes on, I think I have more evidence to back this up - anything that makes me care more, helps me to design better.

So, what's a good way to care more? Can I really be talking about AAMI Technical Information Report 51? Well, yes indeed I am, and although the authors don't couch it in this way, if you follow their "Guidance for contextual inquiry" you will care more.

They talk about "a deeper understanding ... providing insight ... evidence". Of course, all of those things are important.

These, and other great things, are the products of spending time with patients and device users, but you will also care more.

TIR51 makes it all sound so technical and complicated when, in essence, it is little more than what designers of my generation used to call "familiarisation" or "observation": spending time with people doing the things, or using the products, of interest. Trying not to get in the way too much, shrugging off the embarrassment of asking 'stupid' questions, taking away as many quotes and photos as possible and the sense of what's going on.

There is more to it than that, of course; you can't just rock up at someone's house or lurk around in clinics. It does have to be carefully arranged, and we have to pay attention to the necessary preparations and permissions, but none of that has to get in the way of simply 'being there'. I have done this type of research with clients present and in situations of great intimacy and importance for the participant. We have sat through tears and anger, family dinners and blazing rows; memorably, I've even had to help out once during surgery.

What do you need to do this? TIR51 talks about notebooks, cameras, video recorders, etc – all the usual tools one might imagine. These are the practical steps – and there are others, of course, all well documented in TIR51 – but the key step, for you and for me, is to be humble.

We have to bring some humility and openness to this type of research. As professionals, we may have deep expertise in some aspect of the disease, drug or device, but the patients' experience of their disease and how they cope with it is unique and potentially vast. You may see them for an hour, they spent nearly 9,000 hours last year coping with it. You have to acknowledge that whatever people do just is. Whether they do it "correctly" or "perversely", it just is.

"We have to bring some humility and openness to this type of research"

No, they don't always read the instructions; yes, they will pay undue attention to the neighbour with no medical gualifications; maybe they'll breathe out first, maybe they won't. One of the difficulties of contextual inquiry - a very personal challenge - is to stop yourself from intervening and correcting something you know to be wrong. There are good reasons not to, not least that I have no medical training, and there have to be exceptions for real harm, but part of the value of this work is the gritty reality, the quirks and mistaken beliefs. (Having said all that, I often find myself reminding people that their doctor is always there for advice on technique.)

The key aim of this type of research is to draw out their hard-won experience and expertise.

AAMI TIR51:2014 "Human Factors Engineering – Guidance for contextual inquiry"

Contextual inquiry has its origins in the growth of usability or human computer interaction methods during the 1980s and 90s. It sits in the phenomenological school of qualitative design and it seeks to explain how people experience things and events. It is similar to ethnography in that it deals with the lived experiences of people, but it has a much narrower focus, specifically on the user, product or task of interest.

It has very little theoretical underpinning so people new to the technique can rapidly gain valuable insights and data, which can vary in scope from observed problems and work-arounds, through to new ways of conceptualising tasks or desired outcomes.

Basically, people are watched within the actual context of a product's use – in the precise location, at the same times, with the usual resources, demands and management oversight. The session is normally recorded and key moments or artefacts are photographed. With each session, the researcher will refine their area of interest, keeping a broad view but also focusing attention on key tasks and asking questions about specific areas of doubt. In this way the research becomes a collaborative endeavour in which the user prompts the questions as well as providing the answers.

The analysis is usually discursive, simple story-telling; researchers (often with the subjects present) will share what they have seen, important observations will be noted and patterns or themes will be identified.

There is massive value in seeing the reality, unearthing the problems and taking them seriously in design. The empathy – the caring that arises – inspires as well as informs; it brings teams together with a shared goal. And I have to admit to a certain mischievous pleasure: when you've taken a client to see just how their product is used in truth, and you've faced them with the sheer improbability of that truth, you'll never go back to the pedestrian ways of doing design. ENDS

Top 10 medical heroes

By Vicky Shipton



With our 10th issue of Insight, we thought it would be a good idea to provide a little insight into the people at Team. We love to find solutions to medical challenges but who inspires us? Whose developments have made the biggest impact on medicine and people? Here are the results of our (less than scientific) internal poll: \rightarrow



Hippocrates

He is known as the 'Father of Western Medicine'. He promoted the idea that the gods didn't cause illnesses.



Jenner invented the first vaccine small pox. He is known as the 'Father of Immunology'.



John Snow

(Not the Game of Thrones character!) John Snow was a physician and a leader in the adoption of anaesthesia and medical hygiene.

1850s Florence <u>Nightingale</u>

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She provided care for those injured during the Crimean War. Through her passion and determination, nursing became a profession for women.



Louis Pasteur

He was initially mocked for his ideas when first presented, but Pasteur proved there were micro-organisms in the air and not that the air itself was growing (spontaneous generation). Within one year, 1865, beer, wine and milk were all pasteurised.

6 1860s Joseph Lister

Inspired by Pasteur's work, Joseph Lister promoted the idea of sterile surgery. His methods included washing hands before surgery.



Sigmund Freud

In 1900, Freud published 'The Interpretation of Dreams'. In 1910, he founded the International Psychoanalytical Association with Carl Jung.

Marie Curie

She was a prize winner in physics for her studies in radiation. She won a second Nobel Prize in Chemistry in 1911 for her work on the discovery of radium and polonium and work in radioactivity.



Alexander Fleming

He said, "When I woke up just after dawn on September 28, 1928, I certainly didn't plan to revolutionise all medicine by discovering the world's first antibiotic, or bacteria killer...but, I suppose that was exactly what I did."





These ten influential people have helped to inspire millions of people to further health and medicine around the world. But for Team there are some more personal reasons behind who inspires us. Ben Wicks is first up in explaining who inspires him.

"Dad, wouldn't it be amazing if we could travel back in time and see what life was like here 200 years ago?"

My daughter loves history – she's studying the history of medicine so it's a frequent topic of conversation. One such recent conversation got us onto the subject of whether we'd be scared going back in time to the 1800s. On reflection, we both agreed that the absence of healthcare would be a genuine worry. She was worried about surgical procedures being done without general anaesthetic, while I was adamant that I'd be taking some antibiotics with me on any journey back through time.

So when I was asked who I considered to be the most important scientists in medicine I immediately focused on anaesthesiology and microbiology.

This led me first to John Snow, considered the founding father of epidemiology because he realised cholera was spread by contaminated water supplies in London, and not by bad smells, which was considered the most likely culprit by some at the time. But as well as studying epidemiology, John Snow was also a pioneer in the understanding of respiration and delivering anaesthetics. Snow was a really smart bloke from an uneducated background who found his way into medicine and turned out to be a great all-rounder and a thoroughly decent man.

Despite a terrible lack of scientific rigour in medicine at the time, Snow looked at the facts, did first-hand research, read about emerging science and tried to understand biology and physiology. Few people realise that he did some outstanding work on improving the resuscitation and care of new-born babies which saved countless lives. Next on my list is Joseph Lister who continued to develop the understanding that microorganisms caused infectious disease. Lister pioneered the use of antiseptics in surgery and wound care earning him the reputation as the "Father of modern surgery".

Lister was another good scientist who read up on Louis Pasteur's work (who really should be in anyone's Top 10) and used evidence-based medicine to guide his work.

Lastly, I've gone for the man who first discovered penicillin – Alexander Fleming. It wasn't the first antibiotic ever discovered (some chemical antibiotics had been developed in the 1920s) but it did pave the way for modern antibiotics which, in my opinion, have had the greatest and most tangibly astonishing impact on healthcare. Estimates vary but it's widely accepted that antibiotics have added more than 15 years to life expectancy. probably twice that which a cure for all cancers would add. We take antibiotics for granted but they are incredibly important. Fleming's patient, and initially overlooked. scientific endeavours have helped extend and protect the lives of billions of people.

I'm grateful for the work of each of these individuals and the countless others – often unrecognised – who have developed our amazing understanding of human health and disease. I love living in an age where we understand so much about science and I feel privileged to play even a very small part in trying to improve the health and wellbeing of mankind. But if I am ever offered the chance to travel back in time I will definitely take some antiseptic wipes with me! Andy Fry, one of Team's founders, shares his reasons for his choice of a medical hero. As someone who has spent years helping to make injecting insulin a better experience, Andy's choice was simple – the people who discovered insulin.

1891 – 1941 Frederick Grant Banting KBE MC FRS FRSC

The discovery of insulin at Toronto General Hospital by Frederick Banting counts as one of the greatest medical achievements of the 20th century. After a few years of research and testing, on January 23, 1922, a 14 year old boy, Leonard Thompson, terminally ill from type 1 diabetes, was given an injection of insulin extracted and refined from a beef pancreas. Literally overnight, the boy began to recover from what had been an inevitable, painful and distressing death.

The 1923 Nobel Prize for Medicine was awarded to Banting, then aged 32. He shared the honour with Professor JJR Macleod, who provided lab facilities for the insulin research. Banting shared his half of the prize with Charles Best, the trainee doctor who assisted Banting throughout the research.

The WHO estimate some 422 million people were suffering from diabetes in 2014. Although insulin is now produced by combinatorial chemistry, no longer from animal organs, it remains the principal drug used in the management of what was, until 94 years ago, a dreaded and fatal disease.

As one commentator put it; 'With insulin, the stone was rolled away, and diabetes became a matter of life, not death.' Fred Banting was the one who rolled away the stone.

What is amazing is how many lives all of these people have made better. A simple thought – make things better - and one we try to achieve at Team. ENDS "it's extremely difficult to achieve a meaningful simulation of aerosol behaviour within a dry powder inhaler"

Why is it so difficult to create a dry powder aerosol?

A particle's perspective

By David Harris



The real issue with respirable particles is that in order to be respirable, they have to be really, really small - about a fiftieth of the diameter of a human hair, and this small size presents many challenges in terms of understanding their behaviour both within an inhaler airway and on their journey into the lungs. Respirable particles typically have an aerodynamic diameter of 1 to 5 µm depending upon which region of the lung they are targeting. "Classical" (read "predictable") mechanics begins to run out for particles below 2 µm – they become more subject to effects such as Brownian motion (diffusion), electrostatic and other less predictable influencing factors. Because of these factors it becomes much more difficult to understand and control a particle's likely behaviour.

Another effect of reducing particle size is that the surface-area-to-volume ratio of the material increases. Electrostatics will have a much greater effect on smaller sized particles because of this - and consequently smaller particles will acquire a higher specific charge (charge-to-mass ratio) through contact electrification (triboelectrification) simply due to the higher chance of contact (higher surface area) per unit of mass. And just to complicate things further, in low humidity environments any electrostatic effects are exacerbated due to an increase in surface resistivity through lack of relatively conductive moisture.

Even with the most powerful computers available today, it's extremely difficult to achieve a meaningful simulation of aerosol behaviour within a dry powder inhaler (DPI), simply because the underlying physics is not well understood. In contrast, and with sufficient computing power, the lift and drag coefficients of a passenger aircraft could be predicted to within a few percent, in order to optimise the efficiency of the aircraft design.

To add to all this complexity, respirable API (active pharmaceutical ingredient) particles are usually blended with much larger, inert "carrier" particles of lactose. The physics behind this carrier fraction is on a very different scale to that of the respirable particles – typically the lactose particles are around 10,000 times the mass of the much smaller respirable particles. And almost all blends are at least 95% lactose (w/w), so it's actually the carrier fraction that dominates the overall behaviour during the transition through the airway of the DPI.

It's worth noting that the close range adhesive forces that are responsible for holding agglomerates of particles together (Van der Waals, electrostatic and capillary) generally decay with the inverse-square of the separation distance $(1/r^2)$. This means that the respirable particles that are attached directly to the surface of the carrier particles have a very strong force of attachment and consequently they are very difficult to separate. Those that are attached via other respirable particles, e.g. in a dendritic structure, are held with a much weaker, net adhesive force, and therefore far more likely to become aerosolised when the inhaler is used.

How much energy is required to separate a drug particle from a carrier?

We know that increasing the separation energy increases the chance of separating (detaching) micronised budesonide API from a typical commercial-grade lactose. But how does this compare to the quantity of energy that is available from an inspiratory manoeuvre?

In 2010, a group of us studied the lung characteristics of 90 healthy individuals (ranging from 4 years old to over 50) and found that the quantity of inspiratory energy available was related monotonically to the individual's height, and independent of age or gender. Even the shortest subjects in this study consistently achieved approximately 3 J of inspiratory energy – which is several orders of magnitude higher than the quantity required to separate 90% of budesonide particles from lactose.

If so much energy is available, why are DPIs inefficient?

One particular challenge with carrier based formulations is that the API particles are a tiny proportion of the blend, and in a well-mixed and homogenous formulation are evenly attached to the carrier particle's surface. When the user inhales and the airflow through the airway of the inhaler entrains the formulation, the API particles do not experience any aerodynamic drag force as the vast majority are effectively shielded in the boundary layer around the carrier fraction.

The physics associated with a single lactose carrier particle as it travels through an inhaler airway is hugely complicated. And it transpires that there is a huge body of scientific research underway looking at a similar scenario of particle interaction – the physics of sandstorms.

How do sandstorms reach such huge altitudes?

Sand particles are much larger and heavier than respirable particles, and really not particularly airborne. But sandstorms can reach altitudes of two miles, and travel across entire continents! Only recently has research demonstrated a plausible explanation to these phenomena...

It's all about momentum exchange. For example, if you drop a large bouncy ball with a much smaller second one on top of it, when they hit the ground, the smaller ball will fly off much higher than the height at which they were dropped from. This effect underpins the way in which sandstorms gain altitude – the countless particle-particle impacts result in the smaller ones bouncing higher and higher, and collectively the entire sandstorm can reach huge altitudes.

Although there is much similarity in the underlying science, it appears that these two similar but separate research areas have never "collided."

So how do inhalers actually work?

Let's face it – we've been working on them collectively for six decades, and the market leading device is about 25% efficient – even this seems like an amazing achievement given how hard it is to separate closely bound particles. So what can be done to improve this?

It's about maximising the chance of deagglomeration... CFD and other techniques enable accurate simulation of high efficiency swirl chambers, so that powerful mathematical models can then be constructed from the CFD data to allow interpolation of the design space. Proxies for deagglomeration efficiency can be estimated for different airway geometries so that their performance can be optimised.

What can we learn from a particle's path through an inhaler?

The forces effecting the particles are difficult to control. We know that close-range adhesive forces by their very nature are extremely difficult to overcome using airflow or impact alone. Rather annoyingly, there is plenty of energy available – it's just a bit tricky to transfer it to the particles. We need to explore all the possibilities that these particles present. By increasing the chance of impact we increase the chance of detachment. Unfortunately deagglomeration is too often the path less travelled by particles. ENDS Team Consulting Insight Issue 10

r Safety after aunch

How post-market surveillance in medicines compares with monitoring in medical devices

By Stella Wooder & Richard Huckle



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The path to market launch for both medicinal products (aka medicines, drugs or pharmaceutical products) and medical devices is lengthy and stringent – and rightly so, as we need to ensure that the risks of the medical products (i.e. medicinal product, device, or combination product) to patients are minimised. But what happens once the medical product is approved for use in the "real world"; is there an appropriate "safety net" to protect patients?

Once a medical device is in the market, it may be used by untrained or inexperienced users for example, or a drug may be prescribed to a patient with additional or even undiagnosed health complications. There is growing emphasis on post-market surveillance (PMS) – monitoring the safety of a medicinal product or medical device in real world use – as part of the pharmacovigilance process.

In this article we look at the approach to PMS in Europe, for medicinal products versus medical devices. \rightarrow

Safety in numbers

Like the practice of medicine itself, the premise of all medicines and medical devices is that they should "do no harm". However, we recognise the need for new therapy options – drug and device - to progress disease management and make life better for patients. The trick is to get the balance right: innovation to provide improved healthcare, but without throwing patient safety to the wind.

The journey towards a safe medicine or medical device begins early. In the development stage, pharmaceutical and medical device manufacturers face the challenge of ensuring stringent regulatory processes are followed for assessing the risk of a product. But, despite the prevailing standards and regulations for assuring effectiveness and safety, there remains a level of risk attached to drugs and devices approved for market release.

Take the case of a drug in development, the de facto approach to testing efficacy and safety is the clinical trial, but the number of subjects recruited into a clinical trial is usually small relative to the total patient population. The patient cohort is usually picked with specific criteria in mind, representative of the indication that the drug needs to address, but without complicating comorbidities. Special groups are usually excluded, for example pregnant women, children, or those with renal or hepatic disorders. The clinical testing period is often short compared to the relevant course of therapy – this is particularly the case with drugs addressing chronic conditions such as rheumatoid arthritis, diabetes and asthma. The limitations on the data obtainable in clinical trials could potentially result in a limited - or distorted - picture of safety (and also efficacy). Once a drug is released onto the market for use by a patient group which includes those not represented in clinical trials, the safety picture may change. The use of medicines over longer time periods by a wider population can lead to adverse effects not seen in the clinical trial population. High-profile examples in which this was the case include Vioxx (an osteoarthritic/acute pain medication) and Avandia (an anti-diabetic), which both remained in the market for some time before a pattern of safety problems was detected.

Safety problems are by no means limited to drugs; they can also occur in medical devices, as in the recent well-publicised case concerning silicone breast implants. It took a UK report (June 2012) to expose faulty implants manufactured by French company Poly Implant Prostheses (PIP), which had double the rupture rate of other implants.

So how do manufacturers get important medicines and devices into market in a timely fashion whilst protecting patients and supporting prescribers in clinical settings? The answer is essentially, "safety in numbers"; legislative effort is required to demonstrate continued safe use of a medical product by gathering clinically relevant data – specifically, real-world post-authorisation monitoring information. The routes taken by drug and medical device manufacturers are different, but the end result should be the same: safer healthcare delivery.

Post-market surveillance of medicinal products

Routine (mandatory) risk minimisation applies to all medicines. This requires all medicines to have the following combination of elements:

- The Summary of Product Characteristics (or SmPC) – essential information for a healthcare professional on how to use the medicine, including when the medicine should not be used and special warnings and precautions for use.
- Patient Information leaflet (or PIL).
- Packaging labelling.
- Pack size and design.
- Legal (prescription) status of drug.

Additional Risk Minimisation Measures (aRMMs) are used to reduce the occurrence of known risks associated with medicines¹. Subject to additional monitoring are any medicines:

- Authorised on or after 1 January 2011 that contain a new active substance.
- That are characterised as a biological medicine such as a vaccine or large protein biological substances.

- Which require further studies i.e. which need to provide data on long term use of the medicine.
- Which have been given conditional approval under exceptional circumstances, for example, if the product is designed to treat very rare indications where evidence is likely to be difficult to collect, or it would be contrary to acceptable principles of medical ethics to collect such evidence.

Medical Device (Directive 2007/47/EC)

Any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of:

- Diagnosis, prevention, monitoring, treatment or alleviation of disease.
- Diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap.
- Investigation, replacement or modification of the anatomy or of a physiological process.
- Control of conception.

and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted by such means.

Medicinal Product (Directive 65/65/EEC)

Any substance or combination of substances presented for treating or preventing disease in human beings or animals. Any substance or combination of substances which may be administered to human beings or animals with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions in human beings or in animals is likewise considered a medicinal product.



What do arMMs consist of in practice?

This varies from medicine to medicine, and will depend on the identified and potential risks that have been revealed in clinical trials and other research stages and which must be documented in the medicine's risk management plan. An aRMM can be as straightforward as active communications to healthcare professionals (colloquially known as "Dear Doctor" letters"). However, some drugs warrant more complex or onerous aRMMs.

One example is Otsuka Pharmaceutical's Jinarc[®] (tolvaptan), a pharmaceutical therapy available in Europe which is able to target autosomal dominant polycystic kidney disease (ADPKD) in patients. A chronic and progressive genetic disease, ADPKD causes a proliferation of cysts and growths in the kidneys and results in complications that include chronic and acute pain, hypertension and kidney failure, requiring dialysis or renal transplant. The disease is thought to affect between 3-4 people in every 10,000 – around 205,000 people in Europe².

Additional monitoring that Otsuka as market authorisation holder has to carry out includes ensuring that all healthcare professionals who are expected to prescribe Jinarc have access to an educational package (a summary of product characteristics and training material) aimed at highlighting the potential risk of liver toxicity and providing guidance on managing this risk.

The importance of pregnancy prevention prior to initiation of, and during treatment with, Jinarc is also included in the education of healthcare professionals. The aRMMs for Jinarc also include an information pack for patients/ carers, containing not only the PIL, but educational material and a patient alert card. These information elements emphasise the risks associated with taking Jinarc and appropriate advice should the symptoms occur.

Another requirement of Otsuka, as the marketing authority, is that it conducts a non-interventional post-authorisation safety study (PASS) to investigate the risks of liver toxicity, basal cell carcinoma and glaucoma associated with use of Jinarc, and to capture information on pregnancy outcomes in Jinarc patients, and also patterns of drug use - in particular off-label use and use in patients over 50 years old – and adverse drug reactions associated with long term use of the drug.³ Measuring the effectiveness of aRMMs is also necessary, to establish whether each of the "special" risk minimisation interventions has been effective or not, and if not why not and what corrective actions are necessary.4 ightarrow "The use of medicines over longer time periods by a wider population can lead to adverse effects not seen in the clinical trial population."

Post-market surveillance of medical devices

Medical devices bring their own safety challenges, including: technical complexity, operator misinterpretation, and device variability or inconsistency. In Europe, their route to market is also significantly different to that of medicinal products. Devices are certified – "CE marked" - for market use by private, Notified Bodies (NBs) operating on a commercial basis. The work of NBs is overseen by the Competent Authority (CA) in each EU member state. NBs certify a device according to European Commission directives which specify standards for manufacturing, expected performance, safety profiles and labelling and responsibilities for adverse event reporting⁵. However, it is the CAs who have primary responsibility for PS. Although NBs may provide guidance for a PS during their review of a medical device, European Commission directives do not provide authority for CAs or NBs to insist on post-approval studies. There is no clear evidence that PS studies or the set-up of device-use registries⁶; there is no requirement to formally publicise conducted PS studies, or the compilation of a registry, making it difficult to assess how much post market authorisation activity goes on in practice.7

After complications, such as with PIP breast implants and some metalon-metal hip replacements, the EU Commission urged member states to tighten controls and improve surveillance of medical devices in the market. It achieved this in part with the MEDDEV guidance documents⁸, and the journey of bringing the regulations up-to-date had already begun in 2012. Today's technology and science have outpaced the existing EU legislation drafted in the 1990s, as in contrast to most devices in the 1970s, newer products - ranging from permanent implants to home-use diagnostic devices - can potentially pose greater risks to patients. Other factors driving the revision of the legislation include:



EU Member States' interpretation and implementation of the current rules is variable between member countries, which may result in different levels of patient and public health protection in the EU.



The ability to trace a medical device to the supplier, ensuring a quicker response to safety concerns, particularly if a product recall is required.



Transparency

Providing healthcare professionals and patients with information on how medical devices have been assessed for their fitness to be in the market and what clinical evidence there is to show they are safe and effective. The aim is to extend the existing Eudamed⁹ database of device issues and to make nonconfidential information publicly available. Critically, there will be reinforcement of rules and data for the continuous post-market assessment of medical devices. Post-market clinical follow-up may be performed on a device following marketing approval, which is intended to answer specific questions relating to clinical safety or performance (residual risks) of a device when used in accordance with its approved labelling. This can be viewed as equivalent to the post-authorisation safety study (PASS) for a drug. A post-authorisation safety PASS is carried out after it has been authorised, to obtain further information on its safety, or to measure the effectiveness of any implemented risk-management measures.

Comparing apples with pears?

Drug regulation is a much older discipline than device regulation, and any legislation on device regulation came into being only in the 1990s. Yet in the past decade, the number and complexity of medical devices has exploded. In contrast to most devices in the 1970s, these newer products pose substantially greater risks, even life-threatening, to patients. For example, many new medical devices are permanently implanted in a patient's body and can be moved or changed, if at all, only with great risk to the patient. ENDS





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Curators ofour

Styled for life. Built for health.

by Craig McGarrell



personal exhibition

In all parts of life we surround ourselves with carefully curated objects. Things we deem valuable which speak to who we are as people. They become part of our own personal exhibition, showcasing to the world who we are as an individual, from the way we dress, the cars we drive, to the phones we use and the furniture we fill our homes with. Those of us living with a health condition often rely on devices and objects which we do not get to choose, and can often contradict our curated identity. \rightarrow

Living with a health condition can be an unpredictable and unpleasant experience, and with the addition of a medical aid thrust into our lives it can add further interruption to our lifestyle. becoming a constant reminder of our health. These aids can act as a badge or a beacon which shout to onlookers "look at me, I am ill, my body is less able than yours". A badge which can easily create a negative stereotype. The nerdy kid with an asthma inhaler. The weak and elderly with mobility aids.

Because of these negative connotations, you'd be forgiven if you become selfconscious - compromising your lifestyle around your aid, or worse, choosing to neglect your aid and health for your lifestyle. Scenarios such as "will I be ridiculed by my classmates if I have to use it during class?" or "I rarely go on beach holidays any more because I don't feel good in a bikini with my insulin pump on show", highlight how important the relationship between a device and your personal identity can be.

The irony here is that these devices are enabling objects - tools designed to improve your quality of life, yet through their experience and existing connotations they become surrounded by negativity, frustration and neglect. So why should they project a negative image? Why can't they be seen in a positive light, something which feels familiar, fitting comfortably amongst your carefully curated environment? To me, it's all about how we design the objects to fit into your lifestyle.



Exhibit A – The elusive benefit



"The benefits of influencing the way someone feels about their therapy is much harder to quantify, especially through design"

In our industry, millions of dollars and man-hours go into creating devices which are safe and effective in the hands of users - but when it comes to meeting the emotional needs of the individuals who interact with these objects on a daily basis, are we giving them fair consideration? The benefits of influencing the way someone feels about their therapy is much harder to quantify especially through design when compared to factors such as technical robustness or pure usability. Yet as elusive as they may be, the benefits are there and consumer health is a great place to look for inspiration - particularly in relation to engagement, an aspect that can help us tackle the ongoing issues of compliance and adherence.

Fitbit and Apple Watch may be the obvious poster boys, but I'd like to draw your attention to Sabi and Withings. These health related companies take a design driven approach into your lifestyle, by focusing on an experience beyond the considerations of simply working.

Sabi have examined and improved upon some of the pitfalls of longstanding traditions surrounding health aids, to produce inclusively designed alternatives which appeal to a much broader range of consumers. Their products include a cohesive assistive bathroom range including an easy to install attractive grab rail – void of stigma and a pill management system which removes fiddly interaction for an aesthetically pleasing alternative. They have created intuitive, easy to use products that wouldn't look out of place in the hands of the most fashion conscious consumers.

Withings create smarter products for healthy living, reinventing ritualistic scenarios and everyday objects we already use, such as the wristwatch, weighing scales or a thermometer, products which also monitor your lifestyle and activity to learn more about your health.

Designed in an elegant non-clinical manner, honest to their purpose and aesthetically sensitive to their environment, they take a fresh look at the image a healthcare product can portray – as Withings themselves put it...

"Styled for life. Built for health."

In parallel to the growth of these new players in the healthcare field, we are beginning to see a positive social change in attitudes towards disability and illness. The 2012 Paralympic games has left a lasting legacy through the positive inclusive coverage in the media, and more recently we've seen global coverage of Sierra Sandison proudly showing off her insulin pump throughout her victory in the Miss Idaho competition. Changes like these suggest we may be reaching a tipping point where medical assistive devices are becoming accepted and even celebrated as part of our identity. Maybe now is the perfect time to begin thinking differently about how we design these objects.



Exhibit B - Nobody wants an aid

During my university major I began exploring this challenge and posed the guestion, "Can medical be beautiful?" I chose an area which I believed had become stagnant, surrounded by negative stigma and a confusing experience for all involved - hearing aids. Spectacles were once a stigmatised visual aid and over time have transcended into objects with connotations of style and intelligence. Why can't hearing aids follow a similar path?

Through an in-depth investigation and time spent putting myself in the user's shoes, I found that whilst most of the users I spoke to told me they were happy with their devices, mainly because they can now hear better and are grateful for that privilege, their body language of tucking the aid behind their hair or choosing a discreet grey or beige coloured device suggested otherwise, almost as if they'd feel guilty complaining about a device which improved their quality of life. I knew that to break the stigma I needed to not only differentiate physically from the current stereotype, but also change branding, retail and marketing – the entire experience. I even went as far as removing the term "hearing aid" from all my content the devices were now Hearwear.

Instead of being designed to be hidden, the new object was designed to have presence, in a sophisticated yet subtle way. The introduction of high quality materials such as gold and silver gave the object properties similar to that of a fine watch or jewellery. The straight profile broke away from the traditional stereotype of how a hearing aid should look, providing an added benefit of conforming to the individual ear. A small touchpoint to help the user feel like this device is theirs, part of their identity, unique to them. All interactions and features were reduced and simplified removing the confusion and intimidation of previous designs.

The brand, 'Listen Carefully', reflected these values in its name, tone of voice, and sales and marketing strategy. The devices would be sold in large department stores alongside fashion and tech brands, and advertised in the likes of GQ and Vogue to further break the medical stereotype. The product would speak for itself, so the brand could focus on making the user feel welcome and stylish.



Exhibit C – One small step

The reality is that the highly regulated products we develop often have constraints which prevent us doing many of these things - we have to be careful not only what we say on drug packaging but even how we say it. It's pretty unlikely that we'll find ourselves in a situation any time soon where our end users can select their preferred device from a shelf in a department store. But we can't ignore the user benefits of this holistically considered experience. If we can't provide end users with a choice, can we persuade the medical industry to acknowledge that these factors might be important, and ultimately design products which better fit the user's environment and lifestyle?

Maybe the first step is to forget that these are medical objects all together. Let's think of them as a vehicle for a technology which provides a solution to a problem. If we start there, we can begin to design an object that fits with its surroundings.



If we consider the end environment these objects will be used in, what values and traits would we begin to look for in an object if we had the choice? Would cheap plastic really be the right material for a device with a long lifespan? Or would beautifully polished ceramic or even glass be more appropriate? Does a scientific looking nebulizer really fit in someone's home environment? Or could it and other home-use devices be designed to sit more comfortably with the furniture you might find in a modern living space?

I truly believe that considerations like these will make for a better life, affecting daily routines in a positive way. If anything, it communicates that someone cares, that our industry cares. It tells the patient that "we aren't just going to provide you with an aid to your ailment, we have considered that you are a human being with needs and wants, we have thought about how you are going to use this device, how it will fit with your life and your personal make-up". If we begin to take this different approach, celebrating the objects for what they are and the environment they exist within - can we begin to help change the way people feel about their assistive devices? I'd like to think so, and hopefully we can see medical products become a proud addition to our personal exhibition. ENDS

The battle to fight lung diseases

Can urine samples be the answer for diagnosing lung diseases?

By Ben Wicks

You probably don't think about your lungs very often but they do a very useful job – delivering oxygen into your blood stream and removing CO₂. Over your lifetime you'll breathe in and breathe out over half a billion times – that's enough air to blow up two full sized, inflatable models of the Empire State Building! Not only are your lungs very durable, they somehow manage to expose each lungful to an area bigger than half a tennis court (50m²) so that gas exchange can occur quickly and efficiently between your blood and the air. If you've ever had a chest infection you'll remember how nasty it felt and how you wished you could give your lungs a rest! Sadly, more than a hundred million people live with chronic lung diseases such as Chronic Obstructive Pulmonary Disease (COPD) and asthma which are not only debilitating for individuals but costly for economies.

The current approach to managing most respiratory diseases involves waiting for lung function to deteriorate until the patient seeks medical help, measuring lung function (how well they can breathe in and out) and providing drugs which can alleviate short-term and long term symptoms. Compared with many other diseases this overall care pathway is still very rudimentary. Thankfully two global trends offer some hope that care for respiratory diseases will be improved. Firstly, the rising costs of healthcare provision is focusing attention on better diagnosis, prevention and management – particularly for chronic diseases such as COPD and asthma. Secondly, biomedical research is shedding new light on the underlying disease mechanisms which cause lung problems.

However, neither COPD or asthma are simple diseases so finding a cure for either won't be easy. The immune system plays an important role in both diseases, and therein lies a big part of the problem. Your immune system is extremely clever but also unimaginably complicated. It has to be very sophisticated because it's constantly fighting off infection from all manner of bacteria and viruses. It also needs to keep watch over your own body's cells and kill any that show signs of going rogue, multiplying on their own and becoming cancerous.

Most of the time your immune system does a great job – if it didn't you'd be dead. But sometimes it gets a bit confused and freaks out when it sees things it thinks are a threat but are actually harmless. This can be things in the environment such as a bit of peanut, pollen or dust, but can also be parts of your body such as your joints. Either way the immune system starts fighting what it perceives to be an enemy – with detrimental consequences Sadly, immune malfunctions aren't just confined to cases of mistaken identity. Sometimes the communication and coordination systems get muddled and send out spurious messages putting the whole immune system on high alert. Your immune cells will then kick off at the slightest thing, causing all kinds of mayhem. This is one of the things that happens in the airways of an asthma sufferer during an asthma attack. The trigger can be an allergen such as dust or pollen or even something as benign as a lungful of cold air on a frosty morning. The trigger causes immune cells to start sending out chemical signals, starting a chain reaction which results in the constriction of the smooth muscles in the airways making it very difficult to breathe. Since breathing is an important thing to keep doing, asthma sufferers must be armed with inhaled steroids and bronchodilators to calm down the immune system and relax the smooth muscle in their airways in case of an attack. \rightarrow COPD also involves the immune system, but unlike asthma it isn't a rapid problem, it's a gradual progressive disease. The immune system is aggravated over many years by repeated exposure to irritants like smoke, dust and fumes. This constant assault by irritating particles and caustic chemicals, combined with the aggressive response from the immune system, results in collateral damage to the lung tissue. The lung tissues become scarred, calloused and unable to do their job properly. The problem is a result of both the inhaled irritants themselves and the overreaction which is illicited by the immune system.

Lung damage in COPD is a bit like an area of lush countryside which is occasionally invaded by small numbers of troops from a nearby enemy. On each incursion the local army sends in tanks and troops to quickly expunge the invaders, who aren't heavily armed. Each incursion doesn't cause a tremendous amount of damage to the environment but as time goes by, the fighting and continual influx of defensive forces damages the roads, landscape and vegetation. Attempts are made to repair any destruction after each incident but there is always some residual damage to the landscape. To make matters worse, the army decides to retain troops in the area who grow ever more volatile under the constant threat of invasion and shoot at anything or anyone that looks like a potential threat. After several decades, the once-pristine countryside is irreparably scarred. This is similar to the damage which gradually takes place in the lungs of COPD patients.

Thankfully the medical profession now has a variety of new drugs which can specifically dial-down parts of the immune system, and other new drugs are currently in clinical trials. It's hoped that these highly targeted drugs will help tackle the underlying involvement of the immune system in respiratory diseases, not simply treat symptoms. Scientists are also becoming increasingly aware that complex diseases such as asthma aren't actually a single disease but are a collection of distinct immune problems which manifest in a similar way. This deeper level of understanding goes some way to explain why not all patients respond to therapy in the same way. he hope is that by diagnosing disease ub-types more accurately it should be ossible to provide more tailored and ffective therapy.

All this progress in research makes it more important than ever to accurately dentify patients with lung problems, to categorise their particular type of disease and objectively monitor how they are responding to therapy. It is no longer sufficient to simply measure the lung function of wheezy patients every six months. Whole-body imaging modalities such as CT and MRI are very informative out pulmonologists ideally need cheaper, quicker and more accessible diagnostic tools to use on a day-to-day basis. Progress in the diagnostics world means that plenty of sophisticated invitro diagnostic technologies are now available.

Unfortunately the lungs and airways aren't easy to access and take samples from. Several approaches have been adopted over recent years to make cellular and biochemical measurements from the upper airways. Exhaled breath is the easiest sample to access but it only contains gases and volatile compounds, it doesn't contain any liquid or cells. That makes it a tricky sample to learn much from. However, that hasn't dissuaded people from investigating exhaled breath for tell-tale diagnostic compounds. In 1991 scientists discovered that the gas nitric oxide (NO) was an important cell-signalling molecule, involved in immune regulation and found in exhaled breath. Twenty years, 2,000 academic publications and several diagnostic products later and there is still no unequivocal evidence that nitric oxide measurements have clinical utility. Other than breathalysers for measuring exhaled ethanol, no clinical or commercial products have gained significant traction in this field. Research is continuing and complex gas analysis systems are being successfully miniaturised and applied to clinical breath analysis¹, so there may yet be breakthroughs in diagnosing and monitoring respiratory disease using exhaled breath over the coming years.

Sputum is useful because it contains cells and biomarkers directly from the respiratory tract, but it's challenging to access and difficult to physically manage in the lab. Cell samples scraped from the lining of the airways would be good but also can't be sampled routinely.

Urine isn't a sample you'd naturally think of as being useful for diagnosing lung disease but, surprisingly, researchers have found a biomarker which appears in the urine of COPD patients. Healthy lung tissue contains a flexible structural protein called 'elastin'. One result of COPD is the accelerated breakdown of elastin, causing the lungs to be become hardened and inflexible.

Blood (and plasma) testing is a well established and mature technology but as it only reflects the systemic concentration of cells or biomarkers, it isn't necessarily very informative about the lungs and airways. Blood testing is useful but is often insufficiently specific to diagnose lung problems from other inflammatory problems. he overactive immune system of a OPD patient starts attacking the elastin in healthy cells. A by-product of this egradation is a specific group of amino cids called desmosines which aren't ormally found in the body. Desmosines re removed from the body via the idneys and therefore can be detected in he urine of COPD patients via a simple est. Usefully, when COPD patients xperience a worsening or exacerbation in disease, the levels of desmosines in rine jump even higher. This increase ccurs because the overactive immune ystem causes the kidneys to leach more roteins and amino acids than normal not the urine. Thus it makes detection if desmosines in urine even easier uring an exacerbation, and therefore it is possible that we may see desmosine rine tests becoming a routine tool for ulmonologists in the coming years.

It's hoped that management of respiratory disease in the next decade should improve significantly. It needs to, because many millions of patients in an aging population across the developed and developing world will be faced with living for many years with chronic lung disease. It will require respiratory clinicians to embrace new diagnostic tools and technologies as well as new medicines but hopefully the shared goal of improving health for millions of patients will fuel progress. ENDS

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ravel Q

A personal account of medical devices

By Vicky Shipton







Past

It's hard to imagine anyone who hasn't had contact with spectacles, syringes or a stethoscope in their life. I, for one, am delighted that spectacles exist! If not for the invention of this device, I suspect that my family tree would have been very short: my parents, grandparents and great-grandparents were myopic; without glasses surely one of my ancestors would have stepped off a cliff, eaten poisonous berries or merrily approached a dangerous animal. My short-sighted family members aren't alone; scientists have identified twenty-four genes that pass on myopia (King's College London -Chris Hammond). Now in the developed world, 60% of people need to wear glasses/contacts or have corrective surgery, and this percentage is increasing - possibly caused by too much time looking at screens or studying (Hammond et al - King's College London).

But even as alternative treatments for poor evesight become more common, not everyone is ready to bid farewell to glasses. My own father, who has worn glasses since adolescence, needed cataract surgery once he reached his 80s - for his age group, 70% of white, American men have cataracts (this figure varies significantly by race)¹. After successful surgery, he had 20/20 vision, and yet he still refused to give up his glasses. 'Why?' I asked him – was it his vision? His answer was simple: although his vision was fine now, wearing glasses was a lifetime's habit that he just couldn't break; he felt exposed and he said he needed his glasses to protect his eyes. Sometimes psychological factors of habit and comfort may lead people to stick with a medical device when it is no longer needed. With glasses the consequences are unlikely to be serious – glasses can just be a fashion statement! - but the same is not necessarily true for all medical devices. Such psychological attachments are worth bearing in mind in the development process.



Having had ankle surgery in recent months, I myself have had need to use syringes. After my surgery, I was prescribed blood-thinning medication. This was not prescribed, as I'd expected, in pill form but instead came in prefilled syringes. Injections don't usually bother me but an array of twenty-eight syringes – all my responsibility to administer – was a little daunting to see.

I wasn't allowed to leave the hospital until I had given myself the first injection. The nurse gave careful instructions to pinch an area of skin on my stomach and then insert the syringe into the subsequent fold. Once at home and needing to give myself the next shot, I saw that I had bruised badly from my first injection. Had I done something wrong?

I hurriedly consulted the written instructions and realised they were somewhat different from what the nurse showed me to do. I gave the new instructions a go ... and still ended up with considerable bruising. Over the course of my twenty-eight injections, I never quite managed to find the correct technique for me. one that delivered the full dose with a minimum of discomfort and bruising. The instructions that came with my medicine seemed factually correct but unhelpful. I was certainly relieved when I came to the final dose, and I had new respect for those who must give themselves regular injections for life. But what else did I learn from the experience? It made me appreciate how well Team considers the user's experience and just how important the packaging and instructions are.

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Fut -Ut

What could the future hold for the stethoscope?

A smart device

One smart stethoscope is already available and FDA-approved. It looks similar to a traditional stethoscope but has hidden powers! The Eko Core by Eko Devices is a digital stethoscope offering both analogue and digital modes. With the analogue/digital toggle, users have "a calibrated high-pass audio filter, and a re-engineered dynamic driver, providing superior audio quality, white noise reduction and enhanced 40x amplification."² The stethoscope is bluetooth connected to help analyse and share patients' heart sounds, murmurs, bruits and other heart and lung sounds. The data can be analysed on a laptop, tablet or smart phone.

A new shape

The Ekuore is a hand-held device which records auscultation (the listening to the body's internal sounds as part of a medical diagnosis). The data is collected and sent securely through a WiFi connection. The auscultation sounds can be recorded, edited, shared, displayed on a device or simply listened to. The data is seen on the Ekuore App. Ekuore has joined with SensiCardiac to develop this device further in determining heart murmurs.³

A new use

Lithocheck, devised by Tim Leighton (Southampton University) and Andy Coleman (Guys and St Thomas' Health Trust), is a probe that looks much like a stethoscope to the patient but instead of a doctor listening to the sounds, the information is directly uploaded to a



Prediction is a tricky business, especially in an evolving field like medical devices, but it is interesting to consider what the future holds for medical devices. How many will still be used in five, ten or twenty years? With advances taking place in gene therapy the need for glasses might be reduced for future generations.

However, we can safely assume that some devices will be around for a very long time. What modifications and improvements might they face in the short term? As an example, let's consider the stethoscope. First a little historical background: the stethoscope - from the Ancient Greek stethos (chest) and scopos (examination) – was invented in 1816 by René Laenne, who gallantly devised a wooden tube that allowed him to listen to the heartbeats of his female patients without the need to put his ear directly on the patient's chest! In 1851 an Irish physician Arthur Leared designed the now-familiar shape of the bi-aural model, one further refined in 1852 by George Cammann.

computer which automatically makes a diagnosis. The Lithocheck is currently used to assess the success of Shock Wave Therapy (SWT) for kidney stone sufferers. SWT breaks up kidney stones by sending 3000 shockwaves into the human body. It's difficult to assess whether this treatment has been effective in removing the kidney stones: most clinicians use x-rays to assess the success of surgery, but over a third of the patients need to be retreated. "The Lithocheck correctly diagnoses whether the SWT has been successful by listening to the echoes that are created when the shocks are sent through the body. Sensors are placed on the abdomen. The Lithocheck correctly interprets what the sensors "hear" and whether the SWT was successful. Its prediction rate is correct 94.7% of the time.4

With so many exciting new developments to the stethoscope, it will be fascinating to see what future modifications and improvements are made. What will be the next ubiquitous medical device? What simple device will help future generations? ENDS



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