

SPRING 2019
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EDITION #19

PATIENT CENTRICITY ON TRIAL

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Clinical trials are broken and only
patients can help us fix them.
If we let them.

patientcentricityontrial.com

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INTRODUCTION

"Trying to tuck a paradigm shift into the 'way it has always been done' only serves to marginalise the concept of patient centricity."¹

T.J. Sharpe, stage IV melanoma survivor

1. Research interview with T.J. Sharpe, stage IV melanoma survivor.
2. Antidote. Available at: bit.ly/2VBMevQ Accessed: April 2019.
3. Clinical Trials Trends, Charts and Maps. Available at: bit.ly/2Z4cpa3 Accessed: April 2019.

The official crest of the Institute of Naval Medicine centres on a lemon tree. The image celebrates the surgeon's mate, James Lind, whose basic clinical trial aboard a naval ship in 1747 proved that oranges and lemons were a successful treatment for scurvy.

Dr Lind took 12 men suffering from scurvy, divided them into six pairs and treated them with various remedies, ranging from half a pint of sea water to two oranges and one lemon a day. By the end of the week, those on citrus fruits were well enough to nurse the others.

We've come a long way since this first rudimentary clinical trial. The UK Medical Research Council's (MRC) trial of patulin for the common cold in 1943 was the first double blind controlled trial. This paved the way for the first randomised control trial (RCT) of streptomycin in pulmonary tuberculosis carried out in 1946 by the MRC.

 Clinical trials are now established as the lifeblood of medicine. Patients at the centre of these trials have traditionally been viewed through an ethical or regulatory lens, with guidance such as the Nuremberg Code, the Declaration of Helsinki and the International Conference on Harmonisation Good Clinical Practice Guideline ensuring the rights and safety of patients.

Yet there are mounting challenges. The exorbitant costs associated with (the many) trials that fail to recruit or retain enough patients are well known. And these age-old challenges are being compounded by an evolving and more complex environment for clinical research:

- The era of the blockbuster drug has made way for increasingly niched drugs that cater to smaller, harder to find populations, including a larger variety of genetic sub-populations as a result of precision medicine.
- Old data sources such as radiological scans and bloods are fast being joined by newer sources such as wearables and social media.
- The digital age is producing more opportunities to engage, but also more opportunities for potential participants to become disillusioned and distrustful of clinical trials.

While the old clinical trial model was well adapted to the blockbuster era of drug discovery and delivery, the simple 'find patients, test drug' era clearly isn't cutting it any longer. The model must evolve as the types of drugs and demands on RCTs do.

Key to this evolution is the need to add another patient-focussed lens to complement the ethical and regulatory lenses. That of patient experience. We must flip convention on its head and think of clinical trials not simply as a vehicle to answer a research question but as a service to a customer – and about optimising patients' experience of this service.

Clinical trials remain crucial to bringing drugs to market, and those who are successful in recruiting and retaining patients continue to drive forward medicine.

Understanding clinical trials from this vantage point can take you beyond the rigid confines of the 'cut 'n' paste' trial protocol and into the practical everyday of the people you want to participate in your trials.

This white paper explores how some of the world's most innovative companies are bringing the patient experience front and centre in clinical trials, and reaping the benefits of doing so. From protocol design to recruitment and retention, it's about seeing every touchpoint that a patient or their caregiver has with a trial as an opportunity to improve experience and therefore engagement.

 Today, more than 40 million patients are needed in around 300,000 clinical trials worldwide every year,^{2,3} guided by these meticulous ethical and regulatory frameworks.

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PATIENT CENTRICITY ON TRIAL

Clinical trials are broken and only patients can help us fix them. If we let them.

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BUSINESS AS

USUAL ISN'T GOOD



*"We spend a lot of time designing the bridge,
but not enough time thinking about the
people who are crossing it."*⁴

Dr Prabhjot Singh, Director of Systems Design
at the Earth Institute

4. 10 quotes that will spark your design thinking. 2015. Available at: bit.ly/2laKsrl Accessed: April 2019.
5. Diagnosing the decline in pharmaceutical R&D efficiency. 2012. Available at: go.nature.com/2UJuo6h Accessed: April 2019.
6. The enigma of Eroom's law and the Wall Street math stifling Alzheimer's drug discovery. 2018. Available at: bit.ly/2D9CURQ Accessed: April 2019.

We can no longer shrug our shoulders and say "that's just how it is". Too many clinical trials fail to recruit to time or target, or to retain patients. The result? Pharma is haemorrhaging money and patients aren't seeing the benefits they need. More frustratingly, the solution is staring us in the face.

THE PROBLEM OF EROOM

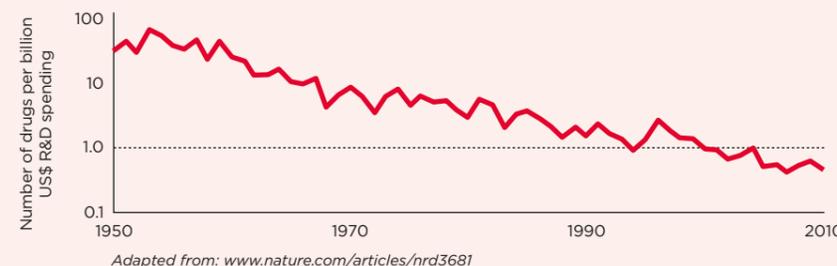
Eroom's law has quickly become the symbol of the troubled state of pharmaceutical research. Coined in 2012 by industry analyst Jack Scannell, it refers to the fact that the average cost of developing a new drug has doubled every nine years since 1950.⁵

Adjusted for inflation, it now costs 80 times more to develop a new drug than it did in 1950.⁵

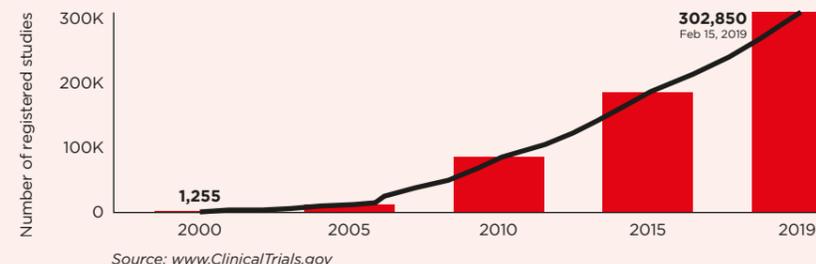
The name is an irony-laden reversal of Moore's law, which shows that transistors become cheaper over time due to lower costs per unit (unlike clinical trials).

This striking contrast with the success of the computer industry's research and development (R&D) efforts is a source of anxiety for pharma execs everywhere. And with good reason - the average current return on investment from internal R&D in the pharmaceutical industry as a whole is hovering around the 5% mark.⁶ Clearly, this exponential decline in the productivity of R&D can't continue.

BALLOONING DRUG DEVELOPMENT COSTS VS. BALLOONING NUMBER OF TRIALS



The number of new drugs developed per \$1BN of R&D spending has halved every 9 years



Over 13,000% more trials were registered in 2018 than in the year 2000



Figure 1

Clinical trials
registered
in 2018

POOR PATIENT EXPERIENCE IS A BILLION-DOLLAR PROBLEM

Patient recruitment and retention in clinical trials, or lack thereof, are a heartsink for pharmaceutical companies. Take your pick, whichever metric or source you look to, the numbers aren't pretty.

Delays, barriers and discontinuations directly cause a loss of investment. But exactly how much money is leaking from the system?

Across the industry, these figures translate into dollars. These delays affect not just study costs but subsequent sales and ultimately less money to reinvest in finding new medicines. Estimates vary on the cost of a failed clinical trial, but one study calculated that, for every drug programme funded, the manufacturer loses more than \$1.1BN in 'time costs'.⁸

The Food and Drug Administration (FDA) approved 309 new drugs between 2011 and 2018, 38 per year on average.⁹ This means that the industry lost roughly \$40BN every year during this period, totalling approximately \$280BN lost over the entire 7 years.^{8,9}

These money losses are truly exorbitant. And unacceptable.

In our current era of cost-prohibitive prescription, pharma companies face extreme scrutiny for their product pricing – the global scale of continued money wastage means that high product profit margins are increasingly unjustifiable. Not just because of the sheer waste and systematic failure, or because pharma companies report loss of profits, the knock-on effect on our increasingly underfunded and overstretched healthcare systems means that, eventually, it's patient care that will fall through the cracks.

 **50%**
of trials are
delayed
due to patient
recruitment⁷

 **80%**
of trials are
delayed by at
least one month⁷

 **85%**
of trials are failing
to retain enough
patients⁷

 **\$40BN**
lost every year⁸

- Clinical Trials Trends, Charts and Maps. Available at: bit.ly/2Z4cpa3 Accessed: April 2019.
- The High Cost of Cancer Treatment. 2018. Available at: bit.ly/2v9cwmL Accessed: April 2019.
- How much money does the NHS need and how much is it actually getting? 2018. Available at: bit.ly/2P39gTd Accessed: April 2019.

In 2018, in the UK alone, the NHS faced a budget gap of about £4BN, which could have funded about a year's worth of cutting edge cancer treatments for 4,000 patients.^{10,11} Saving money could therefore clearly benefit patients. Avoiding drug development losses of up to £40BN per year could extrapolate to the stretched healthcare systems with reduced pricing released by cost savings, relieving some of this budgetary pressure.

It's no wonder that things used to be easier – there were fewer trials for sites to run and fewer choices for patients. Today, the number of trials has ballooned: Over 13,000% more trials were registered in 2018 than in the year 2000 [Figure 1].⁵ The 'good old days' (please note the irony) of patients having less control over their own healthcare journey are over.

This huge growth in competition for clinical trials has coincided with the advent of the internet and the digital age, which has forever changed the rules of engagement.

Clinical trials
registered
in 2000

- Clinical trials and their patients: The rising costs and how to stem the loss. 2016. Available at: bit.ly/2luHtU Accessed: April 2019.
- Counting the cost of failure in drug development. 2017. Available at: bit.ly/2WZ8Q2Y Accessed: April 2019.
- Can The Record Breaking Number Of FDA New Drug Approvals Continue? 2019. Available at: bit.ly/2U82qwL Accessed: April 2019.
- The High Cost of Cancer Treatment. 2018. Available at: bit.ly/2v9cwmL Accessed: April 2019.
- How much money does the NHS need and how much is it actually getting? 2018. Available at: bit.ly/2P39gTd Accessed: April 2019.

DESIGNING FOR THE RIGHT CUSTOMER

The challenge we face is fundamentally one of perspective. Clinical trial experiences and recruitment are still heavily designed around the wrong customers: the research site, healthcare professional or pharma company. Often the last perspective considered is that of the patient.

Mark Evans of Havas Lynx Faze draws parallels between research sites and Apple stores to describe how we need to change our relationship with research sites. “If you look at an Apple store, they’re a critical part of the Apple experience. They connect with customers and deliver the practical products and support. We also judge the whole brand based on how they treat us in their stores,” he says.¹²

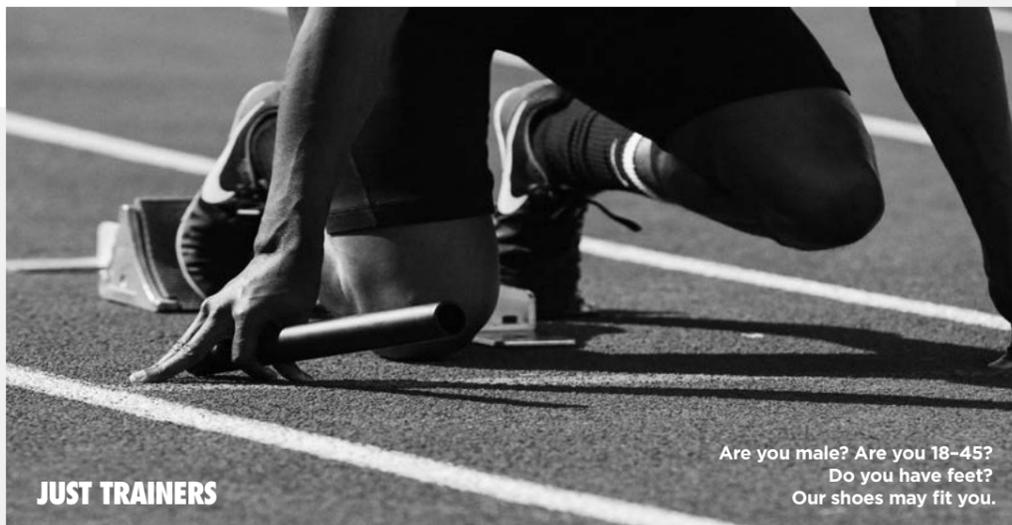
But, crucially, the store and the staff aren’t the end customer for Apple. They are a key stakeholder in delivering the end customer experience, says Evans.¹²

“Compare a research site to an Apple store. They are a crucial part of the patient experience and the only real connection a patient has with a study.

“Of course, the site and staff need to be well trained and well supported to deliver an excellent experience and care for patients. But they emphatically aren’t the end customer.¹²

“Just because we don’t get to interact with the patient on trials, we should never forget it’s really all about them. They are the only people with choices, without a contract, who can walk away at any point. We need to think of sites not as a customer per se, but as a vehicle for delivering the patient experience,” says Evans.¹²

Take the way clinical trials traditionally communicate with patients as a prime example. Crucial communications such as recruitment adverts are so often couched in impersonal and functional language tailored to the needs of sites and not to the needs of patients. “Do you have asthma? Are you 18-35 years old? You might be eligible for our study.” This is the industry standard for attracting patients to a study. This is the equivalent of Nike saying “Are you male? Are you 18-45? Do you have feet? Our shoes may fit you” in their Times Square billboard ad.



If Nike advertised like a pharmaceutical clinical trial

THE PATIENT PROOF

To address the continued failure of clinical trials, things need to change, says Evans.¹² The good news is that things can be different. And there’s proof.

‘Patient-centric’ trials aren’t simply touchy-feely nicer for patients – the evidence shows they work better than more traditional trials. A recent analysis by the Economist Intelligence Unit found that drugs developed using patient-centric designs, which focus on making participation as easy as possible for patients, showed a 10-20% increase in likelihood of launch compared to drugs developed without a patient-centric methodology.¹³ And in a world where only 10% of drugs make it to launch, every improvement is critical.¹⁴

Patient-centric trials took 3 months less time to recruit 100 participants (4 months) than traditional ones (7 months). That 3-month difference takes on major significance when you consider that every month by which the drug development process can be shortened is worth \$25M in revenue for the average sponsor.¹⁶ Remember too that the additional costs that are incurred during the clinical research process must be recovered through sales or increased prices – the efficiencies of patient-centric trials could clearly benefit both pharma and its customers.

12. Research interview with Mark Evans, Havas Lynx Faze.
13. Patient-centric trials. Available at: bit.ly/2Ggh5kD Accessed: April 2019.
14. The High Price of Failed Clinical Trials: Time To Rethink The Model. 2016. Available at: bit.ly/2U92j3T Accessed: April 2019.
15. Research interview with Michael Mittelman, rare disease patient.
16. White paper: A Paradigm Shift in Patient Recruitment for Clinical Trials. 2017. Available at: bit.ly/2PviJ64 Accessed: April 2019.

“Being a patient isn’t our job – it’s your job to run a clinical trial – but it’s part of our life, alongside jobs, family and everything else. Patients think in terms of everyday life, and a clinical trial can be a big, time-consuming thing to take part in. That’s why ‘addressing everyday practicalities’ along the whole trial is crucial for patients.”¹⁵

Michael Mittelman, rare disease patient

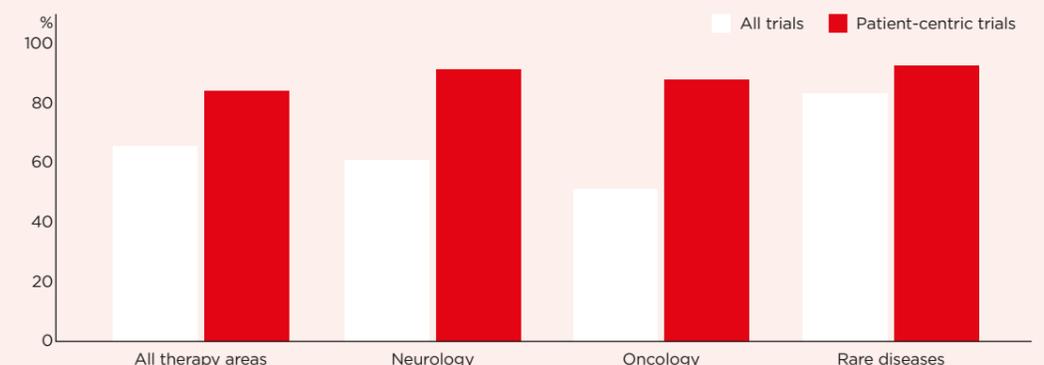


3 MONTHS
Patient-centric trials took 3 months less time to recruit 100 participants than traditional ones¹⁶



\$75M
Potential revenue increase from shortening drug development process by 3 months¹⁶

TRIALS THAT IMPROVE EXPERIENCE IMPROVE CHANCES OF DRUG LAUNCH

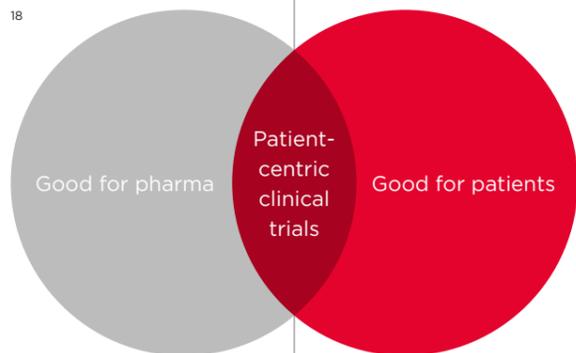


Likelihood of launch for patient-centric trials vs. all trials (Phase II and III)
Figure adapted from www.druginnovation.eu.com

17. Impact of patient and public involvement on enrolment and retention in clinical trials: systematic review and meta-analysis. 2018. Available at: bit.ly/2Z2yXlg Accessed: April 2019.

A HOLISTIC PICTURE OF EXPERIENCE

An extensive review in The BMJ last year also found that involving people with “lived in experience of a health condition” improves clinical trial enrolment. So the evidence is clear: understanding and improving patient experience makes as much sense for pharma’s bottom line as it does for patients’ wellbeing and satisfaction.¹⁷



That moves it firmly into the mission critical column of things to do.

But optimising something that doesn’t work just makes it not work a little less – in a space where approximately 80% of trials fail to get patients on time, tinkering around the edges isn’t good enough.¹⁹ To truly transform the clinical trial experience, we need to think about every touchpoint of the clinical trial as a point to improve patient experience.

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18. Good Pharma. Havas Lynx Group. 2013. Available at: bit.ly/2GECsIH Accessed: April 2019.

CASE STUDY

ONLINE COMMUNITIES: INSPIRE^{20,21}

The social network for health, Inspire, was set up to help patients and caregivers share information about their disease and learn about clinical research opportunities in a secure and controlled environment.

The network has created a community of support groups that are particularly useful for patients and caregivers looking for practical and emotional support in cases where the healthcare system has been unable to help. Inspire partners with commercial research sponsors, connecting its users with those designing clinical trials and working together to make their clinical development programmes more patient-centric.

“Patients are the heart of clinical research. At Inspire, we are committed to advancing medical progress by actively engaging patients who possess an authentic desire to improve the quality of human health.”²¹

Inspire has more than 225 individual communities, 100 patient organisation partnerships and over 1.5 million members, and it continues to grow.

“It’s gratifying and humbling to see the community’s growth. We see it as a testament to the wisdom of empowered patients and caregivers who are leading a movement towards patient-centred care,” says Brian Loew, co-founder and CEO of Inspire.²²



19. Could talking to patients be the biggest innovation in clinical trial recruitment? 2019. Available at: bit.ly/2X8ezU9 Accessed: April 2019.

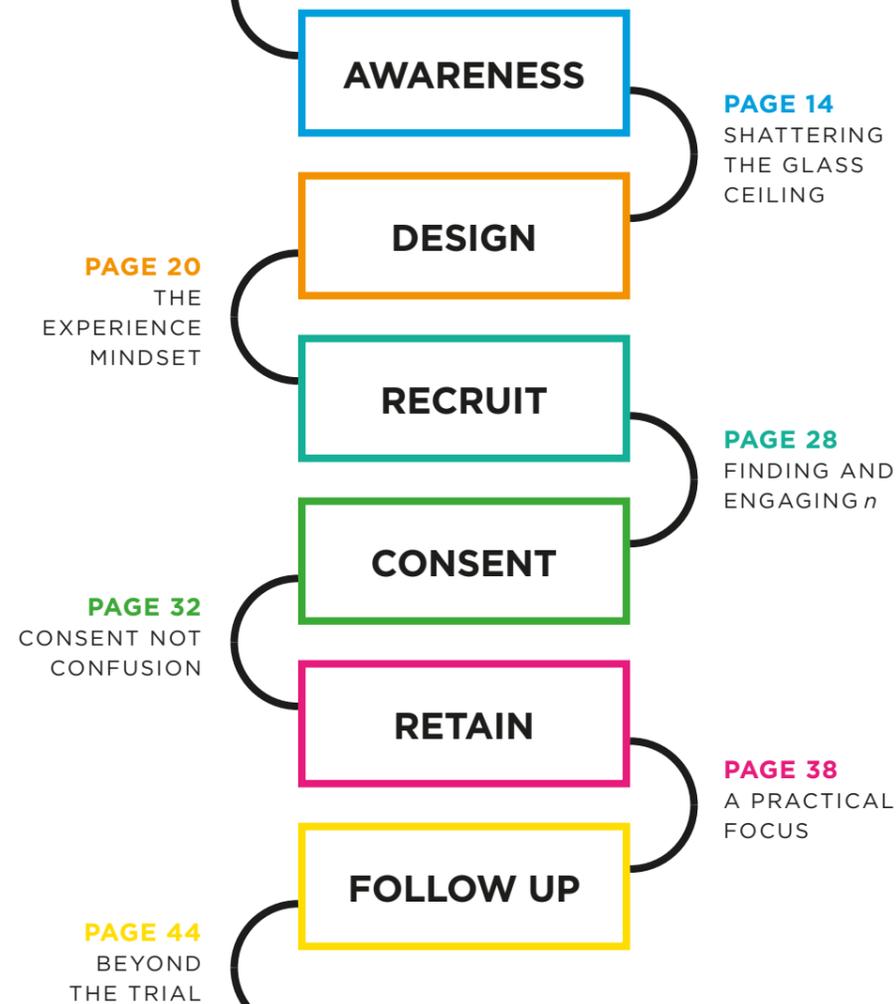
20. Inspire. www.corp.inspire.com Accessed: April 2019.

21. WCG Clinical Services Division Partners with Inspire to Improve Patient Recruitment in Clinical Trials. 2018. Available at: prn.to/2GkNtSX Accessed: April 2019.

22. Inspire grows online patient community to one million strong. 2017. Available at: bit.ly/2KLxPFO Accessed: April 2019.

PUTTING PATIENT CENTRICITY ON TRIAL

This white paper looks at each touchpoint in turn to explore how a focus on patient experience can drive clinical trial success.



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AWARENESS

SHATTERING THE

GLASS CEILING

“No patient should ever feel like they missed their opportunity. Patients have a right to be informed about all treatment options, including clinical trials.”²³

Grace Cordovano, PhD, board-certified patient advocate

23. How to Win at Clinical Trial Recruitment in 2019. Available at: bit.ly/2GekD7W Accessed: April 2019.
24. Role of Clinical Trial Participation in Cancer Research: Barriers, Evidence, and Strategies. 2016. Available at: bit.ly/2U84gOb Accessed: April 2019.
25. State of the Clinical Research Industry Report. Available at: bit.ly/2P0lpqM Accessed: April 2019.
26. Every patient a research patient? Evaluating the current state of research in the NHS. 2015. Available at: bit.ly/2GcFGrn Accessed: April 2019.
27. Global Public Attitudes About Clinical Research and Patient Experiences With Clinical Trials. 2018. Available at: bit.ly/2IDCEPo Accessed: April 2019.
28. Research interview with Rachel Lind, Director of Business Development, Antidote.
29. SCORR Marketing + Antidote Technologies: The Patient Perspective on Clinical Trials. Available at: bit.ly/2Ux6wyA Accessed: April 2019.
30. Research interview with Shwen Gwee, General Manager and Head of Open Innovation, Novartis.

The idea that we distrust trials is an easy excuse for poor recruitment. But the reality is more nuanced. Public opinion often shows that, despite some wariness, most agree clinical trials are important and would consider getting involved. The challenge is telling the right people about the right opportunities. A consumer mindset is therefore key.

THE OPPORTUNITY GAP

Only a fraction of eligible patients are ever offered the chance to participate in a clinical trial. Fewer than 1 in 20 cancer patients in the US enrolls in cancer clinical trials, for example.²⁴ And a recent survey of more than 900 clinical research professionals showed that finding enough participants was one of their top three barriers to conducting clinical trials.²⁵

But the problem isn't an unwillingness to participate. In a global survey of over 12,000 people, more than 8 in 10 people said clinical research is very important to the discovery and development of new medicines. And yet more – 9 in 10 – believe research is generally safe.²⁷

Great news!

Here comes the bad – almost half said that clinical trials are rarely considered as an option when discussing treatments or medications with their doctor. And 6 in 10 were unable to name a place where studies were conducted.²⁷

“My own experience... is they're very, very keen to take part... it's one of our great assets... relative lack of cynicism about research and taking part in it.”²⁶
– Clinical academic

Despite the phenomenal medicinal need for clinical trials and large numbers of patients willing to participate, the main challenge is that patients don't have the appropriate information. To succeed in improving trial recruitment and retention, shattering the glass ceiling preventing their access is crucial.

Rachel Lind is from Antidote, a direct-to-patient digital health company focussed on accelerating medical breakthroughs by connecting patients with research. She sums up the challenge as follows: “The biggest barrier is lack of access to information about clinical trials as a care option.”²⁸ She cites a recent survey that Antidote carried out with SCORR Marketing, in which patients were asked what would most help them make informed decisions about participating. The answer was simple: making it easier for them to learn about clinical trials.²⁹

Shwen Gwee is General Manager and Head of Open Innovation at Novartis. He says:

“Don't presume your patients – or their doctors – know exactly what clinical trial is right for them. We need to educate and guide patients to trials that are suitable for them, rather than assume they or their doctor will find that single trial that fits.”³⁰

AWARENESS

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31. Hunt, J., Visual Communication Design: An Introduction to Design Concepts in Everyday Practice. 2017, p35.

THINKING BEYOND HEALTHCARE

We need to make more noise and frame the opportunity of clinical trials to the public, patients, their doctors and patient advocacy groups. And we must remember that patients and doctors don't live in special 'patient'/'doctor' bubbles – they are everyday people living in the real world, where they are bombarded by consumer messaging.

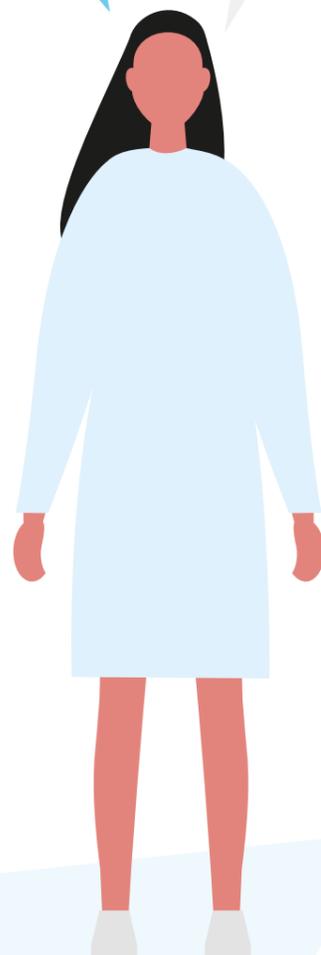
We compete not simply with other clinical trials, but the world of distraction that is modern life.

The average person is thought to see as many as 3,000 advertising messages every day across all media.³¹ The competition for share of voice goes well beyond just competing studies, but has expanded across alternative and holistic therapies, as well as powerful consumer brands such as Apple, Facebook, Amazon and Nike.

To stand out we must use the tools of the very best consumer brands. Those that not only understand the power of advertising, but that have already adapted to the experience or brand-as-a-service way of thinking.

That means not just 'better ads', but mirroring those brands and businesses that truly understand the need to centre their offer around their customers' experiences.

THE AVERAGE PERSON IS
THOUGHT TO SEE UP TO
3,000
ADVERTISING MESSAGES
EVERY DAY³¹



1. Research interview with T.J. Sharpe, stage IV melanoma survivor.
23. How to Win at Clinical Trial Recruitment in 2019. Available at: bit.ly/2GekD7W Accessed: April 2019.
32. Clinical trials and tribulations. 2015. Available at: bit.ly/2lw42ld Accessed: April 2019.
33. Research interview with Lindsey Wahlstrom-Edwards, Antidote.

THE HCP GATEKEEPER

David Richards is a mental health researcher from the University of Exeter, UK. He led the DiReCT study that looked at improving recruitment for mental health related trials. The study piloted a system where patients seeing doctors for help with anxiety and depression were asked to join a large cohort from which they could be randomly selected for several clinical trials. Richards found that most patients were willing to participate in the scheme, but it was reluctance from doctors to ask for their involvement that was holding back recruitment.³²

In this study lies an important point: healthcare professionals (HCPs) are crucial gatekeepers to clinical trials, and so educational outreach should go beyond the confines of the patient and help to build HCP advocates for clinical research.

T.J. Sharpe is a stage IV melanoma survivor and patient advisor to the pharma industry. He says: "As HCPs are often the most trusted source of medical information, when clinical trial participation discussion is ignored or downplayed, the effect on patients can be discouraging to trial participation".¹

Lindsey Wahlstrom-Edwards from Antidote says: "Patients want to hear about research from their physicians, but doctors are overburdened and aren't always aware of what's available, so there's a disconnect there that we need to address."³³

*"Physicians must have the tools they need to seamlessly include discussions on clinical trials at point of care, and patients and care partners need to be able to proactively explore trials."*²³

Grace Cordovano, PhD, board-certified patient advocate

WE MUST HAVE BOTH PUSH AND PULL

"A researcher would hand me a piece of hastily typed A4 paper with some entry criteria on it for their clinical trial and it would be up to me to speak to patients to help with recruitment. In between having 20 patients to see, a slow computer to load results on, and a waiting room full of impatient people awaiting their turn, the chance of having a meaningful conversation about a trial I'd not heard of before was pretty much non-existent."

Dr Tapas Mukherjee, Respiratory Physician and Associate Medical Director, Havas Lynx Group



By developing the 'push' factor from patients in tandem, so that more patients are aware of research and will ask to be involved in suitable trials, we will create an environment where clinical trials become part of the everyday for patients and the public alike.

34. PopUp Star Changing Awareness of Clinical Research. Available at: bit.ly/2ld9qq1 Accessed: April 2019.

CASE STUDY

#POPUPSTAR: RAISING AWARENESS THROUGH COMPETITION³⁴



What if every stakeholder in healthcare and research could participate in creating awareness for clinical research as a care option? With that lofty aim, the #PopUpStar contest launched in November 2017.

An industry sponsored contest, #PopUpStar hopes to bring clinical trial awareness to the masses by challenging stakeholders to lead teams that will create the “ultimate clinical trial community awareness event”.

Each team is provided with seed money to help them with their events, which are encouraged to explore themes such as:

How can different grassroots community-based events have an impact on awareness for clinical trials as a care option?

What methods will help us better engage the community?

In what ways might we create champions for research long after these events are over?

How can we improve root cause issues that affect participation in research such as health literacy?



Over 1,500 people were exposed to clinical trials through the events in the 2018 competition, and the 2019 competition launches on International Clinical Trials Day, 20th May.

35. Public urged to take part in clinical research to find new NHS treatments. 2018. Available at: bit.ly/2lowKAN Accessed: April 2019.

36. Research interview with Jenny Preston, Senior Patient and Public Involvement Manager, University of Liverpool.

SPOTLIGHT



COMMON MISCONCEPTIONS ABOUT CLINICAL TRIALS³⁵

Increasing awareness of clinical trials isn't simply about telling people that they exist, but about countering the many misconceptions people have about clinical research.

A 2018 survey from the National Institute for Health Research (NIHR) in the UK revealed a number of public misconceptions about clinical trials.³⁵

The survey was part of the NIHR's I Am Research campaign, which aims to raise awareness of the benefits of research and the positive impact it has on people's lives.

“Research has to be demystified and not portrayed (especially in the media) as something that only a handful of people participate in. The advances of science and the implications this has on our care must be shared in ways that are understandable to patients and families.”³⁶

Jenny Preston, Senior Patient and Public Involvement Manager, University of Liverpool



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PATIENT EXPERIENCE MINDSET

“We need to be more thoughtful of the burden protocols place on patients and caregivers, and work with these groups at all stages of trial design to ensure trials are meeting patient needs.”³³

Lindsey Wahlstrom-Edwards, Antidote

33. Research interview with Lindsey Wahlstrom-Edwards, Antidote.

37. Global Public Attitudes About Clinical Research and Patient Experiences With Clinical Trials. 2018. Available at: bit.ly/2l8u3E8 Accessed: April 2019.

38. How Facebook and Twitter could be the next disruptive force in clinical trials. 2018. Available at: go.nature.com/2U6vbtr Accessed: April 2019.

39. Research interview with Lilly Stairs, patient advocate and Head of Growth & Partnerships at Savvy Cooperative.

Protocol design has historically been the domain of clinical research scientists. But that’s changing. Once seen primarily as ‘study subjects’ who had research performed on them, the culture is shifting towards **engaging patient partners** who contribute across the spectrum of clinical development, including in the design of trial protocols. The early adopters are reaping the benefits. The imperative for the rest of the industry is to embed patient experience as a must-have input **sooner rather than later.**

SIMPLE INNOVATION

When we hear the word innovation we often leap to thinking about things like artificial intelligence, blockchain and other cutting-edge technologies that – let’s be honest – most of us are in the dark about.

But innovation can be so much simpler than an app or other tech-centric solutions. Innovation is about thinking differently. Patients can help you do that, if you let them.

In a 68-country survey examining patients’ attitudes, perceptions and experiences of clinical research, three quarters of respondents listed ‘types of medical procedure required by the protocol’ as a very important consideration that influenced their decision on whether to participate or not.³⁷

And yet it’s been estimated that as many as one-third of clinical trial procedures – such as blood tests or biopsies – are not crucial to the applications for drug approval.³⁸ The involvement of patients in trial protocol design can shine a light on these superfluous tests and help shape trial protocols that are more convenient and therefore more likely to recruit.

“ We need to design to fit the patient’s lifestyle, not the other way around.”³⁹

Lilly Stairs, patient advocate and Head of Growth & Partnerships at Savvy Cooperative

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- 15. Research interview with Michael Mittelman, rare disease patient.
- 30. Research interview with Shwen Gwee, General Manager and Head of Open Innovation, Novartis.
- 39. Research interview with Lilly Stairs, patient advocate and Head of Growth & Partnerships at Savvy Cooperative.
- 40. A. Anderson and K. A. Getz, Ther. Innov. Regul. Sci. 52, 469-473; 2018.
- 41. Research interview with Kelly McKee, Head of Patient Recruitment, Rare Diseases, Vertex.

CONVENIENCE FACTOR

Convenience is hugely important to patients. An evaluation of 30 patient advisory boards found that most were making recommendations about the convenience and feasibility of study visits, and the schedule of procedures performed.⁴⁰ This shows that focussing on patient experience goes beyond simply thinking about disease factors. It's about immersing yourself in a patient's disease as well as their everyday life, and viewing the impact of clinical trial interactions on this level.

As Michael Mittelman, a rare disease patient, puts it: "The decision to enter a clinical trial isn't simply binary – 'yes I want to' or 'no I don't want to' – the practicality of it isn't as simple as the industry makes out."¹⁵

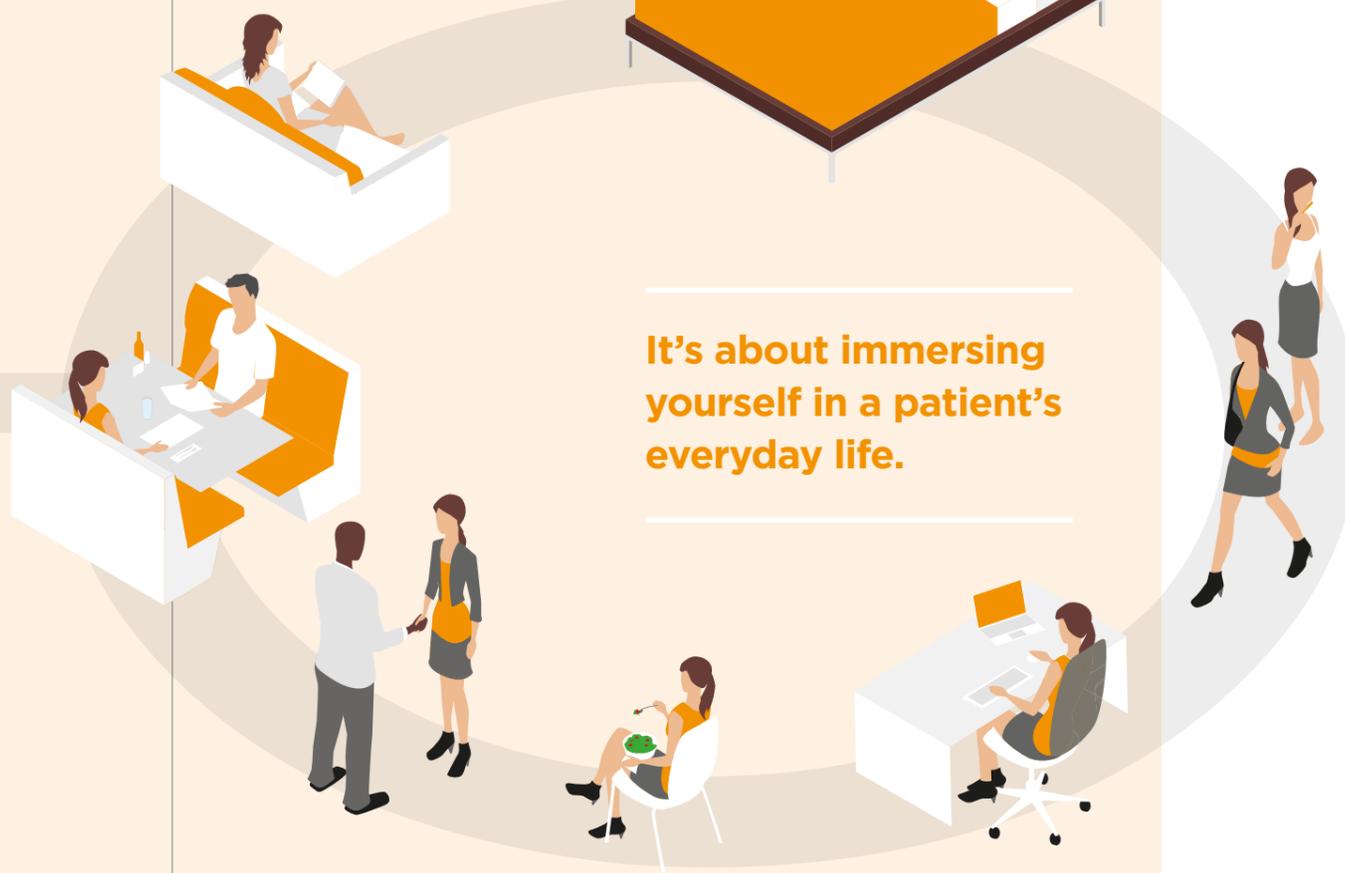
The problem, according to Shwen Gwee from Novartis, is that we've been focussing on the wrong customers.

"Oftentimes pharma only talks to healthcare professionals (investigators) to understand patients, which is an important, but skewed perspective," he says.³⁰

Kelly McKee from Vertex agrees: "We must design clinical trials to fit the needs of patients and not just researchers and clinicians."⁴¹

Patient advocate Lilly Stairs gives an example of home infusion as a way to improve patient experience. "If a medicine needs to be delivered, then why can't we send an at-home infusion nurse so that patients don't have to travel when they're already not feeling well?"³⁹

While strides are being made, we need to accelerate and spread the change throughout the industry. Clinical trials are about improving patient outcomes, and convenience shouldn't be a barrier for them to overcome so they can participate and help pursue those outcomes.



It's about immersing yourself in a patient's everyday life.

USER EXPERIENCE MENTALITY

Adapting to the increasingly competitive age of clinical trial recruitment means adapting to a user experience mindset, seeing patients not as an amorphous group to be targeted by mass marketing, but as individuals or sub-groups of people with particular shared characteristics and needs.

For example, how do patients who need to visit a dialysis centre a few times a week become aware, motivated and enrolled in a study? And how does that differ from people who participate in an outpatient, acute-disease study?

As Shwen Gwee from Novartis puts it: "We've been too transactional up until now in our approach to clinical trials, and tactical in execution, rather than thinking in terms of service design and changing the overall experience for every patient touchpoint along the journey."³⁰

Thinking in this more nuanced and strategic way is part and parcel of the consumer advertising world, which is replete with examples of how to effectively use digital tools and social media to engage different types of customers.

"We need to start thinking about taking the consumer tech approach rather than the scientific approach to how we present information, how we engage with patients, and how we create the overall experience for what patients go through in a clinical trial," Gwee says.³⁰

He adds that we need to dramatically shift how we think about clinical trials. "The traditional model of handing off to the sites is more a business-to-business type transaction rather than a business-to-consumer, which means we've been focussing on site experience more than patient experience," he says. This needs to change, though we still need to continue to engage and support sites to help drive better experiences through and for them as well.³⁰

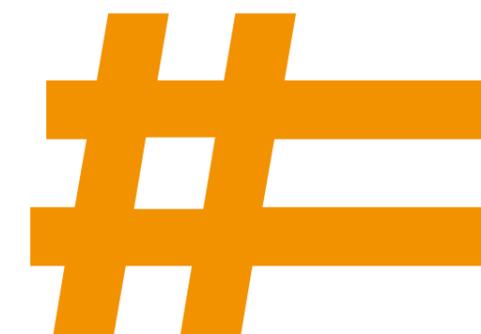


Kelly McKee from Vertex says: "We need to establish value propositions for our studies."⁴¹

"If you wouldn't participate in a clinical trial, how can you expect anyone else to participate?"⁴¹

Designing clinical trials with patients as partners, providing educational materials and communications using health literacy principles, eliminating unnecessary visits and procedures, incorporating telemedicine and technology, and providing study results to patients, are all tangible tactics that can be employed by study teams and will, ultimately, improve the understanding and appreciation of clinical trials.

Lindsey Wahlstrom-Edwards from Antidote adds that we need to stop trying to find a "one size fits all" solution. She says that patient motivators participating in research and how they would like to receive information about research vary greatly by condition and demographics.³³



ELIGIBILITY FRUSTRATIONS

150% increase in eligibility criteria 2008-2013⁷

Such criteria are often there to protect either the patients or the study. But are all these eligibility criteria needed, or are they a symptom of a cut 'n' paste mentality, leading researchers to use previous trial protocols as templates for their next studies?

ELIGIBILITY CRITERIA

These are guidelines describing characteristics of all participants of a clinical trial. They help make the trial a fair test. The specific characteristics will vary from trial to trial and often include patient age, gender and medical history.

In the US, a joint project by the FDA, ASCO (American Society of Clinical Oncology) and the advocacy group Friends of Cancer Research found that five common criteria for cancer-trial eligibility could frequently be amended without harming participants or the integrity of the trial.⁴²

Whatever the reason, patients – and their doctors – often grow frustrated when they encounter the sometimes overwhelming requirements to join a study.

“What really frustrates me are instances when, in my mind and in my heart, it really seemed that the patients should be eligible. If I had the exact same treatment outside of a clinical trial, I would give it to them without a concern.”⁴³

David Gerber, lung-cancer specialist at the University of Texas Southwestern Medical Center, Dallas

Sharon Allin works on clinical trials at Biogen. When asked what she thinks is holding back clinical trials, she lamented the industry’s habit of “writing protocols for the perfect patient that doesn’t exist”.⁴⁴

Clearly the issue of inclusion and exclusion criteria isn’t a simple case of removing all those that are a barrier to patient participation – they are intended to avoid harm to patients or confounding factors for trials. But an open and honest interrogation of the often lengthy eligibility criteria – with patients – could at least sometimes lead to an easing of criteria, giving more patients the chance to try new treatments and a greater chance of a clinical trial meeting recruitment targets. Surely that’s worth the effort?

For those who are sceptical, “run an A/B test”, suggests patient advocate Lilly Stairs.

“Run one trial where you work with patients from day one, then pick another trial in a similar therapeutic area and don’t involve patients. See what the difference is. I guarantee you the one where you work with the patient is going to enrol faster, it’s going to have a much higher retention rate and you’re going to see a better patient experience,” she says.³⁹

45. Levitan B, Getz K, Eisenstein EL et al. Assessing the financial value of patient engagement: a quantitative approach from CTTI’s patient groups and clinical trials project. *Ther Innov Regul Sci* 2018;52(2):220–229. doi: 10.1177/2168479017716715.

46. Improving Protocol Design Feasibility to Drive Drug Development Economics and Performance. 2014. Available at: bit.ly/2P631Yc Accessed: April 2019.

47. Getz K.A., Zuckerman R., Cropp A.B., Hindle A.L., Krauss R., Kaitlin K.I. Measuring the incidence, causes, and repercussions of protocol amendments. *Drug Inf. J.* 2011;45:265–275.

FINANCIAL VALUE OF PATIENT ENGAGEMENT

“Protocol design is uniquely positioned to fundamentally and directly impact – positively or negatively – drug development efficiency and economics.”⁴⁶

Int J Environ Res Public Health. 2014 May; 11(5): 5069–5080.

The choice of inclusion and exclusion criteria can affect the duration and cost of a clinical trial, not to mention the likelihood of the trial meeting desired enrolment levels and retaining patients. A study of thousands of clinical trials showed that more than 40% had amended protocols prior to the first patient visit, delaying trials by an average of 4 months.⁴⁷ Of course, some protocol amendments can’t be avoided. But the potential for amendments can be reduced with better planning, with and for patients.

And the evidence shows just how valuable this patient involvement can be. A recent study that looked at return on investment for engaging patients in trial design showed eye-opening results.⁴⁵

Researchers looked at an oncology research project in which a patient review of the pre-phase II protocol had avoided one amendment to the trial, increased enrolment and adherence, and reduced dropout rates.

They then used a financial modelling technique called expected net present value (ENPV), which is a cumulative measure of cost, time, revenue, and risk.

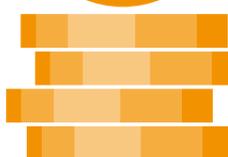
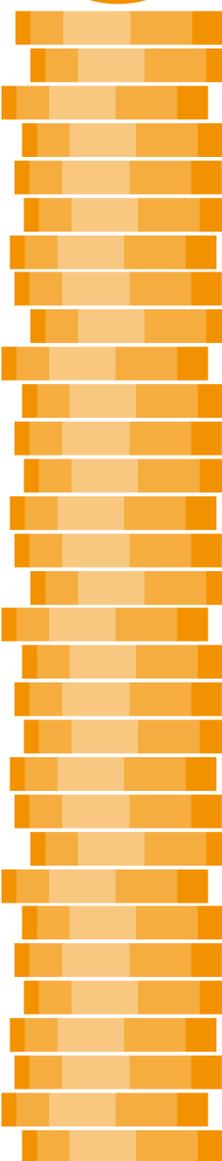
The ENPV was found to be an astonishing US\$35M, rising to US\$75M by Phase III.⁴⁵

Depending on the scenario, the researchers conclude that a US\$100K investment in patient engagement in the design of a trial could produce an ENPV 500 times that figure.⁴⁵

Clearly, understanding patient experience pays.

“It’s not only the right thing to do, it’s a smart business decision to incorporate the patient experience.”³⁹

Lilly Stairs, patient advocate and Head of Growth and Partnerships, Savvy Cooperative



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CASE STUDY

ACT FOR CANCER UK NATIONAL GRID FOR SMART TRIALS⁴⁸



48. ACT. Adaptive Collaborative Treatments. Available at: bit.ly/2ZybCOD Accessed: April 2019.

In the UK, Jess Mills, daughter of Dame Tessa Jowell, and Dr Jack Kreindler, have founded a charity that is working with the UK government and various cancer charities to introduce a new type of complete personalised, adaptive trial design in cancer care.



49. Cancer Statistics for UK. Available at: bit.ly/2ISJ50y Accessed: April 2019.

50. Office for National Statistics. Available at: ons.gov.uk Accessed: April 2019.

51. Adaptive designs in clinical trials: why use them, and how to run and report them. 2018. Available at: bit.ly/2UzSX1l Accessed: April 2019.

Adaptive combination therapy is aimed at the patients with untreatable cancers, where patients tumours are deeply profiled and their treatments and trial experience are adapted and refined in real time based on their response.

The aim for these trials is to find the treatment that works for the patient.

Never giving up the pursuit of trying to find a bespoke solution and moving away from the traditional process of trying to prove if one investigational drug works better than a placebo.

Such new trial models, called Adaptive, Matrix, Platform or Bayesian trials completely challenge the current thinking as to how trials are run, truly putting patients at the heart of the experience.



Jess Mills & Baroness Tessa Jowell, co-founders, ACT for Cancer



Dr Jack Kreindler, co-founder, ACT for Cancer

ADAPTIVE TRIALS ARE REVOLUTIONARY

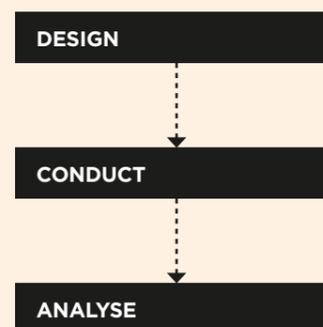
Dr Jack Kreindler, physician and co-founder of ACT for Cancer, argues that adaptive trials are revolutionary. A much needed but equally contentious new approach. He says, “for many highly complex, fast-evolving diseases like cancers, currently over 1 in 4 die within a year of diagnosis and 44% within 5 years, our gold standard RCT has not helped make breakthroughs.”^{49,50}

CURRENTLY OVER 1 IN 4 DIE WITHIN A YEAR OF DIAGNOSIS^{49,50}

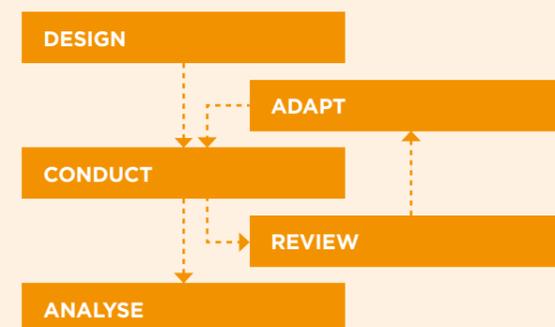
“We now have the technology to add, alongside the gold standard in trials, algorithmically supported, massively multi-arm trials that adapt as the disease evolves. Here we are not determining if therapy A or B is better, we are measuring how model A for adapting a combination of personalised therapies, perhaps never before tested together, may be yielding longer progression free survival, higher quality of life and longer lives for those for whom standard of care, and indeed every attempt at trialing effective treatments one at a time, has not made enough difference. It is true moonshot thinking that molecular sequencing, AI and connected data now makes this possible and economical. Trials like Precision Panc, Lung Matrix, and Brain Matrix have started on this path. My opinion is that this, with the right systems and education supporting them, will become the standard of care and research within the next decade.”

Dr Jack Kreindler, physician, founder of Centre for Health and Human Performance (CHHP) and co-founder of ACT for Cancer

TRADITIONAL RANDOMISED CONTROL TRIAL DESIGN

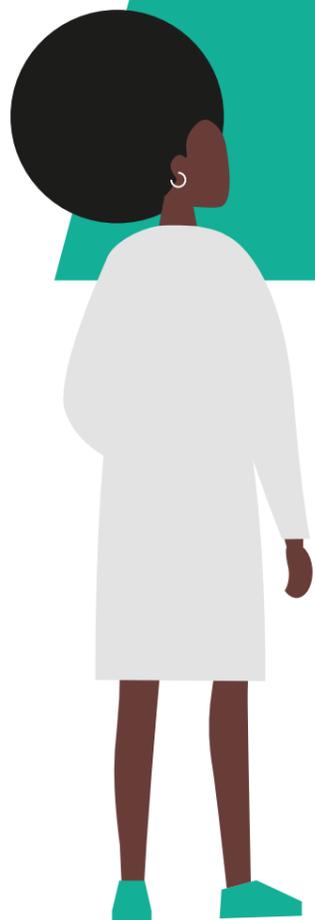


ADAPTIVE DESIGN



RECRUIT

FINDING AND
ENGAGING



*"I see recruitment as being a by-product of good patient engagement... Patients should become part of the process, and that translates into them signing up for the project and being included. It can't just be tokenism."*⁵²

Deborah Collyar, founder and President,
PAIR: Patient Advocates in Research

29. SCORR Marketing + Antidote Technologies: The Patient Perspective on Clinical Trials. Available at: bit.ly/2Ux6wyA Accessed: April 2019.
52. Making the Patient-Centric Trial a Reality. 2016. Available at: bit.ly/2KHerkb Accessed: April 2019.
53. e-Recruiting: Using Digital Platforms, Social Media, and Mobile Technologies to Improve Clinical Trial Enrollment. 2013. Available at: bit.ly/2W2K9mb Accessed: April 2019.
54. Times they are a changin' - how technology can help with patient recruitment. 2016. Available at: bit.ly/2UrTXcJ Accessed: April 2019.
55. Five Trends in Clinical Trials We'll See in 2019. Available at: bit.ly/2VfpPko Accessed: April 2019.
56. Citruslabs. Available at: bit.ly/2Z4GRRq Accessed: April 2019.

Recruitment is the thorn in the side of trial coordinators. Nearly a third of clinical trials' time is spent on recruitment. The explosion in the trial numbers and a rare disease shift aren't making things easier. But solutions exist. It's about communicating to the right patients more effectively.⁵³

A COMPETITIVE ENVIRONMENT

Competition for trial patients is intense. Regulatory agencies are demanding more studies that are larger and longer, plus increasingly targeting niche populations. There are only so many potential patients to go around - reaching that perfect *n* number for your trial is becoming harder.

Yet sponsors and clinical research organisations (CROs) still heavily rely on traditional recruitment tactics, such as physician referrals and mass media advertising. In fact, according to The Tufts Center for the Study of Drug Development, the majority of studies that run outside of North America use these approaches. And even in North America, only about 14% of studies use non-traditional forms of recruitment.⁵³

As Dr Bob Phillips, Honorary Consultant in Paediatric Oncology Centre for Reviews and Dissemination (CRD) University of York, UK, puts it, we have "endless possibilities" to reach people, "...so why on earth do we still expect to let research participants know about our studies with very formal letters, 6-page patient-information booklets and A4 posters in hospital corridors?"⁵⁴

FINDING UNDIAGNOSED PATIENTS

HVH Precision Analytics are using electronic medical records and predictive analytics to identify and activate potential trial participants before they are even diagnosed.

Learn more about HVH at
www.hvhprecision.com

Of course these tried-and-tested methods can and should be part of the mix, but we're in the age of e-patients and e-caregivers. This established breed of health consumers uses the web to understand a medical condition, engage with online patient communities, and simply live significant chunks of their everyday online.

According to Antidote's survey of 4,000 patients, advertising remains the foremost way that patients hear about clinical trials. But we need to find smarter ways to approach patients, particularly for conditions that they are not actively presenting with.²⁹

"While we have made some headway in moving toward more effective social and digital advertising, recruitment is still largely 'push' marketing."⁵⁵
- Angela Radcliffe, R&D Practice Lead, Life Science, Capgemini Invent

For instance, in Alzheimer's and other neurodegenerative diseases, these smarter ways might include integrating with companies like Citruslabs,⁵⁶ who use brain training games to pre-screen users who self-select as caring about their brain health. They could also include reaching concerned friends and family through Facebook, or while they are Googling about memory problems.

Ultimately, the challenges and solutions that face clinical trial recruiters have been tackled by consumer brands for years, grounded in behavioural science research. Some sponsors are starting to see the opportunity. For example, Novartis bringing in consumer expert Bertrand Bodson as Chief Digital Officer is one of several signals that pharma appreciates that consumer expertise is crucial to unlocking future opportunities.

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COMMON CONCERNS OF POTENTIAL CLINICAL TRIAL PARTICIPANTS⁵⁷



58. Blueprint for Truly Patient Centric Research. 2018. Available at: bit.ly/2UcHWD1 Accessed: April 2019.

CASE STUDY

BEYOND INVESTIGATOR-INITIATED STUDIES⁵⁸

Research in the pre-approval setting is by definition intervention centric, even if the ultimate aim is to provide new medicines to patients. Kai Langel, a clinical trial innovator, asks whether truly patient-centric research should go beyond incorporating the patient voice to existing research programmes to an entirely new model of research, at least the post-approval setting.

In an analogous way to how consumer services like Carwow work – where customers dictate what make and model of car they want and invite dealers to come to them with an offer – Langel sees the status quo flipped on its head: “In this kind of a model, it would not necessarily be the pharma company inviting patients to take part in their research, it would be patients inviting research partners to join in and to use their data,” says Langel.

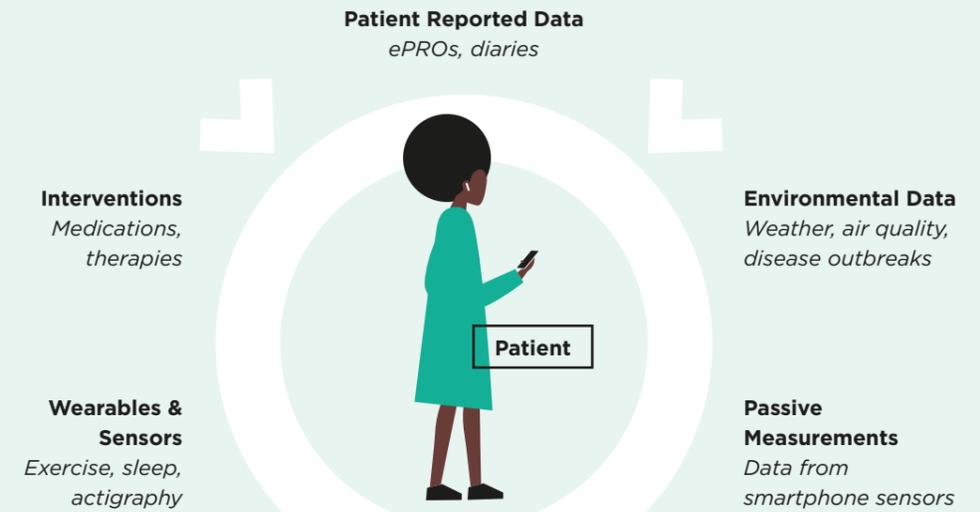
“I’m quite aware that I’m generating data that may be very interesting to some organisations that are interested in some particular diseases or interventions that I may be using, and to understand how these perform in the ‘real world’,” says Langel.

“The pharma industry supports a lot of investigator initiated studies, but I have never really heard of patient initiated studies?”

Langel envisages a world where research partner organisations give patients or the public access to a research platform with connected apps for data capture, and access to existing health data via electronic health records.

Such a flexible platform would allow patients to define their areas of health interest, track them, and give access to validated health questionnaires and diaries. Patients could even be given medical grade sensors like activity or sleep trackers in exchange for sharing data with research organisations.

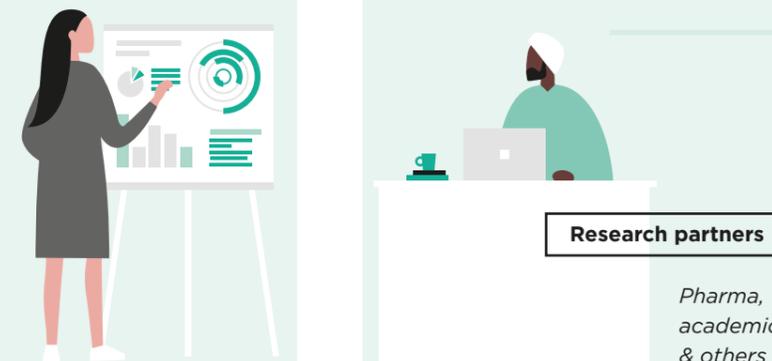
PATIENT CENTRIC DATA CAPTURE



Shares data



Supports



“Like many people, I would be quite happy to share the data I generate with some of these organisations if I understand what the data is used for and especially if these organisations actually support my efforts. So could we think of a new kind of a research paradigm where the patient is really in the driver’s seat?”⁵⁸

Kai Langel, clinical trial innovator

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CONSENT NOT CONFUSION

“It’s really important that we get our informed consent right and that we recognise this as a process rather than a box that needs to be ticked... moving away from the idea that it’s your sample I’m interested in but you, as a partner, I think is important.”²⁶

Clinical academic

- 26. Every patient a research patient? Evaluating the current state of research in the NHS. 2015. Available at: bit.ly/2GcFGrn Accessed: April 2019.
- 59. Final rule enhances protections for research participants, modernizes oversight system. 2017. Available at: bit.ly/2D6smDi Accessed: April 2019.
- 60. 5 things you need to know about the revised Common Rule. 2018. Available at: bit.ly/2WXUWQ Accessed: April 2019.
- 61. 2013 CISCRP Perceptions and Insights Study: Ineligible Participants and Those Who Terminate Participation Early. Available at: bit.ly/2lpDHBH Accessed: April 2019.

Too often consent is seen as a necessary evil, a legally driven form-filling exercise that neither investigator nor patient truly engages with. But this view of consent is flawed. Looking at the consent process through your patients’ eyes helps you see it as a crucial step of engagement in a clinical trial.

INFORMED CHOICE

Jerry Menikoff is Director of the US Department of Health and Human Services’ Office for Human Research Protections. He says consent has become unwieldy for patients.

“Over the years, many have argued that consent forms have become these incredibly lengthy and complex documents that are designed to protect institutions from lawsuits, rather than providing potential research subjects with the information they need in order to make an informed choice about whether to participate in a research study.”⁵⁹

This is partly why the Common Rule – a regulation governing the use of human participants in federal research in the US – has been revised for the first time since its publication in 1991. Starting 21st January 2019, every new federally funded study that involves human participants must comply with the updated Common Rule, which includes stipulations around improving consent. Specifically, the regulation focusses on making consent language and consent forms more understandable to patients.⁶⁰

Pharma can and should follow suit. After all, the more unwieldy a consent process, the more likely it is that a patient becomes confused, frustrated or distrustful. A recent study showed that 35% of potential participants dropped out from a study because they couldn’t understand the informed consent documents, for example.⁶¹

“There are trial information leaflets that are not done for the benefit of the patients. They’re done for the benefit of the regulators and to cover people’s backs. They’re unhelpful and they’re obstructive.”²⁶ – Consultant surgeon

But avoiding such negative feelings isn’t just about stopping patients refusing consent.

It’s about improving a patient’s experience at a crucial time in a clinical trial, and so adding to the overall positive experience of participating in research.

Just as a good experience of visiting a NikeTown shop is a consequence of a myriad of touchpoints that reflect the Nike brand – from the window display, in-store DJ and individual sports products, to the way enthusiastic staff interact with customers – a good clinical trial experience comes from a patient having a series of positive experiences across their whole journey, not only at the disjointed times and places where their perspective may have been considered.

AWARENESS

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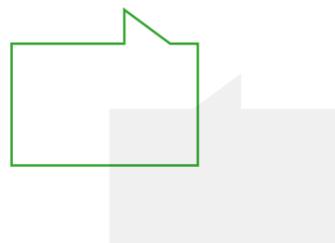
62. Alder Play: Revolutionising patient care for children and their families. Available at: bit.ly/2W2Yhvi Accessed: April 2019.

CONSENT AS A CONVERSATION

Making consent information simple is therefore crucial. And we must remember that consent should be more than reading a form, understanding it, and signing it.

It should be a conversation and a two-way exchange, whereby a patient is encouraged to speak on their own terms with a study representative and feel comfortable and confident that they're making an informed decision to participate.

As such, the principal investigators and study coordinators involved in procuring consent need to make sure the patients involved fully appreciate and understand the potential safety risks and benefits of participating in the trial. And pharma has a key role in supporting trial staff with the expertise and tools to have meaningful patient conversations on consent.



63. Key Considerations for the Adoption of eConsent for Sites. 2018. Available at: bit.ly/2VBokdj Accessed: April 2019.

64. Use of Electronic Informed Consent. 2016. Available at: bit.ly/2UxFXhy Accessed: April 2019.

65. What is eConsent? Available at: bit.ly/2UxavuR Accessed: April 2019.

THE RISE OF eCONSENT

While the shift to digital technologies is widespread across many industries, the informed consent process for clinical trials has been historically paper-based. But change is afoot. Well over half (66%) of the top 50 pharma companies are engaged in or planning an eConsent initiative in the near future. And all of the top 10 already have an eConsent strategy in place.⁶³

It seems inevitable that eConsent will ultimately replace or at least augment the traditional paper-based consenting process, a fact reflected by an expanding number of published guidelines from regulatory bodies such as the FDA and MHRA (Medicines & Healthcare products Regulatory Agency).⁶⁴

There is an understandable focus on regulatory considerations such as 21 CFR (Code of Federal Regulations) Part 11 on electronic signatures, or on security and privacy aligned to HIPAA (Health Insurance

Portability and Accountability Act of 1996) and GDPR (General Data Protection Regulation). But alongside these important administrative considerations, we mustn't lose sight of the patient.⁶⁴

An eConsent process is only 'better' than a paper-based system if a patient or caregiver finds it easier to engage with and understand the information. We can't just transpose paper information into a few screens on an iPad and say "job done" – we need to apply the principles of great UX (user experience) and UI (user interface) to create a digital experience that aids comprehension and engagement.

Done right, there's a tremendous opportunity to hit the sweet spot between making consent easier for the patient and for the site.

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FOCUSING ON PATIENT EXPERIENCE⁶²



Working for patient centricity also demonstrates remarkable effects in health organisations outside of clinical trials. Alder Hey Children's Hospital, in collaboration with digital agency ustwo, improved paediatric patient experience with an innovative approach.

Visiting the hospital is often daunting and scary for children, so Alder Hey and ustwo set out to create an enhanced and personalised experience for both patients and their families. They focussed on three key themes 'familiarising children with the hospital', 'distracting children at difficult moments' and 'rewarding children for bravery' and created an entire patient experience through their app, Alder Play. The app uses a combination of games, augmented reality and chatbots to support children throughout their patient journey.

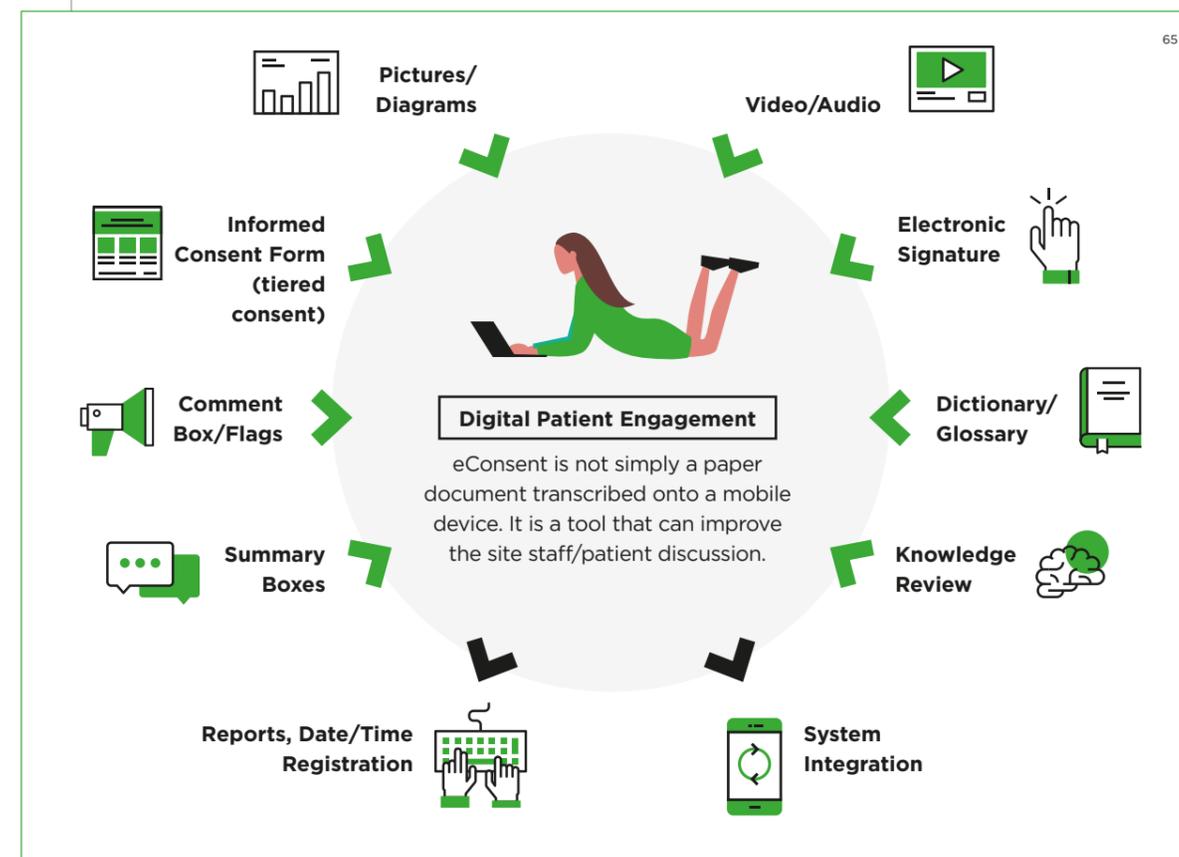


"The time honoured way of rewarding children in hospital is with stickers. So we're going to use stickers, but we're going to use them with a little bit of digital extra. They'll get upgrades, games and specific rewards for doing positive health behaviours. One of the great things about this app is it's been created in conjunction with NHS Digital as part of our Global Digital Exemplar programme. If we can create an enormous platform across NHS, I think we can really trailblaze how you do digital interaction."

– Dr Iain Hennessy, Clinical Director of Innovation at Alder Hey Children's Hospital

With the consent process consistently introducing challenges within paediatric research, initiatives such as Alder Play provide unique opportunities to improve the entire informed consent experience not only for patients, but for everyone involved.

Using augmented reality, Alder Play helps children engage with and understand their surroundings while in hospital



63. Key Considerations for the Adoption of eConsent for Sites. 2018. Available at: bit.ly/2VBokdj. Accessed: April 2019.

POTENTIAL BENEFITS OF eCONSENT FOR PARTICIPANTS⁶³



More convenient

The participants can start the consenting process at home and, in some cases, not have to go to a research site.



More consideration

The participant can start the consent and take a break as needed, and then continue from where they left off. Participants may feel less pressure to sign straight away. They have time to review without feeling anxious and can involve family, friends and caregivers in their decision.



More informed

The presentation of the consent information with multimedia offers links to additional resources for supporting an informed decision.



More engaged

Paper consent documents are not interactive and more challenging to reference information later than user digital technologies. eConsent sessions document when and what type of questions they have, better supporting the site to assist the participant in getting questions answered.



SPOT LIGHT

66. Readability of consent form templates: a second look. 2013. Available at: bit.ly/2UM1x1f. Accessed: April 2019.

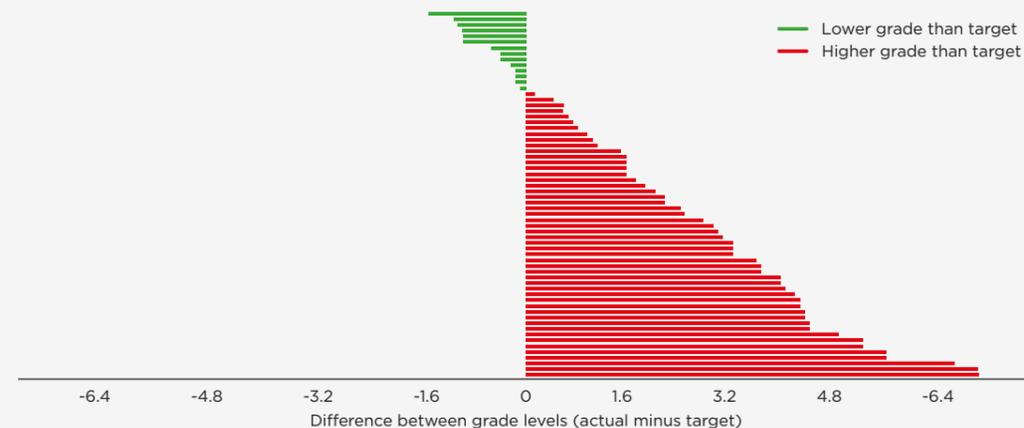
67. Research interview with Jeremy Parks, cystic fibrosis patient.

MAKING IT SIMPLER: A HEALTH LITERATE APPROACH

“Low health literacy affects more adults in the US than obesity, diabetes, HIV and breast cancer combined,” says Oliver Childs, Director of Anatomy Health, a patient information and support specialist. Low health literacy is a challenge in every part of the world, “yet we continue to write and design patient information in ways that hinder – not help – comprehension,” he adds.

Even simple things like readability guidelines for consent forms are rarely followed, as shown by the majority of consent form templates that score too high in readability tests.

TARGET VS. ACTUAL READABILITY SCORE FOR CONSENT FORMS FROM 64 INSTITUTIONS WITH STATED STANDARDS⁶⁶



Each bar represents 1 of the 64 institutional review boards that indicated a specific grade-level target as a readability target. SOURCE: Paasche-Orlow et al., 2013.

People with limited health literacy are less likely to understand terminology, risks and benefits described in traditional consent documents. But a health literate approach to clinical trials and informed consent can reduce barriers to participation by improving the patient experience.

As Jeremy Parks, a cystic fibrosis patient and clinical trial veteran puts it: “I get there is a liability aspect and certain amount of legal terminology, but it seems like there’s got to be a better way to write and design consent for those without a clinical background.

“I can remember the first research trial I was involved with and being very overwhelmed by this very thick consent form. I can see how this could be a deterrent for patients, especially those without any clinical knowledge, which is most people!”⁶⁷

Oliver Childs agrees. “This isn’t about dumbing down,” he says, but simply thinking about user needs and meeting the abilities of everyday people. “It sounds obvious – and it is – but the evidence shows the industry isn’t doing this routinely,” says Childs.



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*“Most trials I’ve participated in have been through one particular pharmaceutical company. There was one that was not, and I remember it for all the wrong reasons – it did not go as smoothly; things weren’t as clearly defined in the trial materials; the structure of the study wasn’t as convenient. I just wasn’t a fan and would think twice about participating in a trial from that company again.”*⁶⁷

Jeremy Parks, cystic fibrosis patient

⁶⁷ Research interview with Jeremy Parks, cystic fibrosis patient.

⁶⁸ Amazon’s first checkout-free grocery store opens on Monday, 2018. Available at: bit.ly/2G71rYr Accessed: April 2019.

EASIER EXPERIENCES

Imagine a new health food store opens in your city, promising to provide you with healthy and tasty foods at cheap-as-chips prices. Great news. But before you can shop at this particular store, you have to apply to be a customer by filling out several complex, jargon-filled forms about organic, pesticide-free veg, omega-3 oils and free-radical busting antioxidants.

Then on the day you decide to do your first shop you find the supermarket car park is crazy expensive and a 5 minute walk from the store. And, oh, the store is closed because it’s only open for a few hours each day when you’re at work. Then you can’t buy or even view products online. Worse still, when you try to phone an actual real person to enquire about a particular product, you’re kept on hold for what seems like an eternity before finally being connected to the wrong department.

Then think of Amazon Go,⁶⁸ the world’s first checkout-free grocery store. The Seattle shop relies on cameras and sensors to track what shoppers remove from the shelves, and what they put back. Cash registers and checkout lines become superfluous: customers are billed after leaving using a credit card on file. Seamless shopping.

The examples are extreme, but highlight two completely different experiences of grocery shopping. And in many cases, it’s the former, it-could-never-be-that-bad scenario, that’s a better metaphor for the current clinical trial experience for patients.

Face it, clinical trials are inconvenient. Mountains of paperwork, endless hospital visits and invasive tests, not to mention the personal cost in time, money and emotions. And with no guarantee that they’re on a treatment that’ll work for them – or indeed anything other than a sugar pill – it’s no wonder people drop out. Using a common sense, user-centred viewpoint can uncover both low and high-tech solutions to help make trials more convenient for patients.

AWARENESS

DESIGN

RECRUIT

CONSENT

RETAIN

FOLLOW UP





- 15. Research interview with Michael Mittelman, rare disease patient.
- 38. Research interview with Lilly Stairs, patient advocate and Head of Growth & Partnerships at Savvy Cooperative.
- 69. Family Caregivers Are Central to the Clinical Trial Experience, 2013. Available at: bit.ly/2Gj9lza Accessed: April 2019.

For example, frequent site visits, time and cost of travel, and the impact of these trips on families and caregivers, are regularly cited for opting out of trial participation or dropping out. In other words, it's the practical everyday experience of taking part in a clinical trial that puts a lot of people off.

What Amazon know better than many others is that customer experience is key. Making it easier or simpler for somebody to interact with – and continue to interact with – a brand or product is a core focus of the pioneers of the so-called experience economy like Amazon or Disney.

*"Why do some industries seem to get it better than others..? Maybe because they listened more. And acted on what they learned."*¹⁵

Michael Mittelman, rare disease patient

ENGAGING THE INVISIBLE ARMY⁶⁹

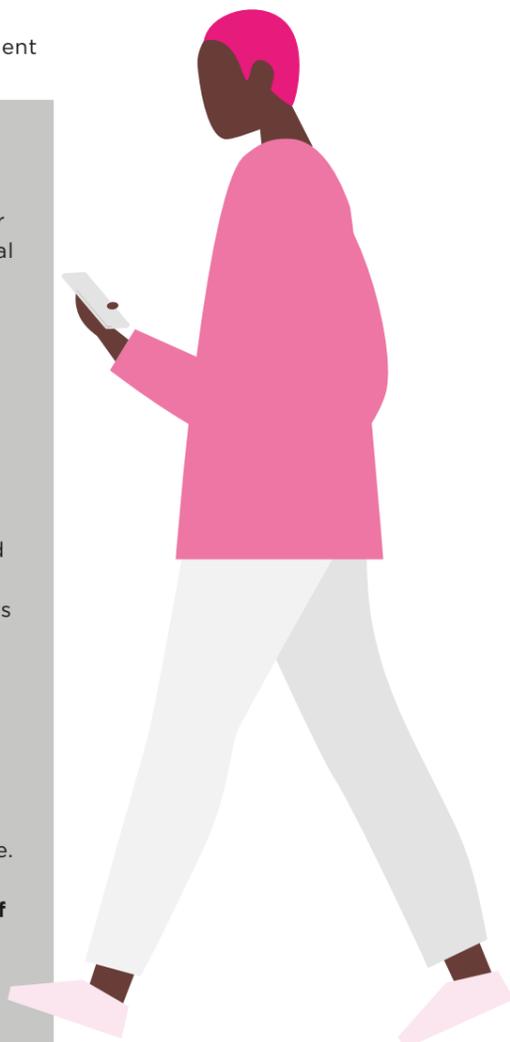
John Schall, CEO of the Caregiver Action Network (formerly National Family Caregivers Association), believes that caregivers are key to the success of a patient's participation in a clinical trial, because they are the closest and most constant observer of the patient.

Sue Sheridan, Director of Patient Engagement for Patient-Centered Outcomes Research Institute, agrees in the value that caregivers bring. "We are finding that caregivers are asking some of the best research questions," says Sue. She adds that clinical trial leaders "need to encourage caregivers to speak up" to help them effectively support patients through the clinical trial experience.

Find out about the crucial role of the caregiver in our white paper, In Search of the Invisible Army, at www.invisible-army.com

Pharma needs to catch up. Because if we don't, we won't see the improvements in trial recruitment and retention that we so desperately need.

Patient advocate Lilly Stairs agrees: "I look at all of these other industries that are consumer facing and that consult their consumers. They run focus groups with their consumers. Their job is to understand their end user. And they do that so well. But we don't do that in healthcare. And that has to change."³⁸



CASE STUDY

A PATIENT LYFT⁷⁰



The Global Alzheimer's Platform Foundation is a non-profit organisation dedicated to speeding up the delivery of innovative therapies to those afflicted with Alzheimer's. They found that participants often stop participating because they don't have convenient or affordable ways to get to and from research facilities.

The solution? They teamed up with the transportation service Lyft to help those who are participating in an Alzheimer's trial get to and from US and Canadian research sites. Under the agreement, Lyft is providing transportation for those taking part in Eli Lilly's Phase 2 TRAILBLAZER-ALZ (NCT03367403) trial and their caregivers.

"Our partnership with Lyft makes the trial experience as easy as possible for study participants and their study partner," says John Dwyer, the foundation's president.



THE PRACTICAL PATIENT JOURNEY

Park 'emotional axes', 'personas' and other buzzwords for a moment and think about what patients are actually having to do each day to participate in a trial, and what could be done to lighten the load. Technology can sometimes be part of the solution, but only as an enabler for better experience.



As Mark Evans of Havas Lynx Faze puts it:

*"The key is understanding the basic human needs. It is easy to overthink the requirements in a world where sophisticated technology appears to be the answer to all our problems, but in reality it is the simple things that make a study more convenient, less costly and ultimately less of a burden on a patient's life. Ultimately improving all of these things will increase the overall probability of success."*¹⁹

Patient advocate Grace Cordovano agrees: "Technology must play a role but we must carefully understand where it will bring authentic value."⁷¹

- 19. Could talking to patients be the biggest innovation in clinical trial recruitment? 2019. Available at: bit.ly/2X8ezU9 Accessed: April 2019.
- 70. Lyft Volunteers to Transport Alzheimer's Patients to and from Clinical Trial Sites. 2018. Available at: bit.ly/2VEvnBP Accessed: April 2019.
- 71. Research interview with Grace Cordovano, PhD, board-certified, patient advocate.

CASE STUDY

CHEMOTHERAPY 'SUPERFORMULA'⁷²



JWT joined up with Warner Bros. and the A.C. Camargo Cancer Center in São Paulo, Brazil, to craft a super-powerful campaign designed to help children with cancer better understand and face their chemotherapy. The initiative revolves around superheroes.



The hospital game room is a mock-up of the Justice League's interior. The children can read specially drawn comic books with medically realistic tales of the Dark Knight and his friends, defeating cancer-like diseases to resume their war against evil. Finally, branded IV bag covers bear the insignia of Superman, Batman, Wonder Woman and Green Lantern, transforming the frightening drugs into a 'Superformula'.

A truly patient-centric approach to learn from. Taking a problem and turning it into an opportunity to enhance the users' experience, perfectly positioned to speak to the audience in their own language and drive understanding and empowerment.

AROUND THE PROTOCOL

Interrogating the patient journey isn't always about fundamentally changing a study protocol or design. We're used to 'around the pill' as an idea, how about 'around the protocol' services?

Examples include arranging transport for patients and their caregivers through Uber Health, or using prepaid study credit cards to cover study expenses so that patients are never out of pocket due to their involvement.

The golden rule - think patient first, trial second.

In doing so, the trial will look after itself. This practical focus can be the difference between a satisfied or unsatisfied patient, and ultimately a successful or unsuccessful trial.



71. Research interview with Grace Cordovano, PhD, board-certified, patient advocate.

72. Chemotherapy Rebranded as 'Superformula' in JWT's Brilliant Campaign for Child Cancer Center. 2014. Available at: bit.ly/2GHzdEf Accessed: April 2019.

73. eClinicalHealth Announces Successful Results for an Entirely Remote Online Clinical Trial. 2016. Available at: bit.ly/2Gaj0XF Accessed: April 2019.

74. Boehringer Ingelheim Initiates a Collaborative Partnership with Science 37 to Accelerate Patient Centricity in the Development of Novel Therapies. 2019. Available at: bit.ly/2DoQeSH Accessed: April 2019.

REDUCING THE BURDEN

Smartphones, tablets, wearables and mobile apps offer great potential for patients because of the convenience they offer. Most consumers can now shop, pay bills and order takeaway food at any time without leaving the comfort of their home - can they take part in a trial in the same way?

The model is compelling because it fits around the needs of the patient, rather than the patient fitting around the needs of the site.

Participating in study visits from home eases the patient burden and allows investigators to interact with more patients and be more productive. As Grace Cordovano puts it, "trials need to be where patients are and that's not in the traditional four walls of medicine; it's online, it's at home".⁷¹

In 2016 Sanofi completed a virtual Phase IV diabetes trial called VERKKO, which used a patient-centric online clinical trial platform, integrated with a 3G-enabled wireless blood glucose meter, in a completely remote clinical trial setting. Sixty patients - all recruited through Facebook - participated in the study. The results exceeded expectations, with an 81% conversion rate among patients who showed interest in participating and a less than 10% dropout rate. This valuable proof-of-concept trial shows new models of clinical trial recruitment and retention can work.⁷³



And the industry is taking note. In January 2019, Boehringer Ingelheim announced a collaboration with Science 37, a specialist provider of siteless/virtual clinical trials. Thor Voigt, Chief Medical Officer of Boehringer Ingelheim, said of the partnership:

*"We will be able to allow patients to participate in clinical trials on their schedule and timetable. This is pivotal in ensuring patients feel they are invaluable partners in helping us to develop and deliver novel therapies worldwide."*⁷⁴

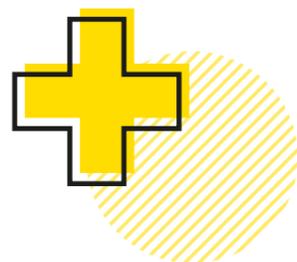
Clearly not every solution is a trivial one, and building operational capacity to deliver large scope improvements to patient experience is crucial in the long term. But the good news is that there are countless routes to improve patient experience today. And every route starts the same way - by talking to patients.

FOLLOW UP

BE- YOND THE TRIAL

*"Patients want transparency... Treat patients taking part in a clinical trial as investors; they are investing their bodies in your trial so keep them informed about that investment. They also want to be thanked afterwards. These are basic things."*⁷⁵

Andrew Schorr, two-time cancer survivor and founder of cancer patient community Patient Power



- 75. Patient-centricity: Ghost in the machine. 2016. Available at: bit.ly/2GIL9gm Accessed: April 2019.
- 76. Staying Connected After The Clinical Trial. 2015. Available at: bit.ly/2vjwGLa Accessed: April 2019.
- 77. Creating a Standard Practice for Communicating Lay Language Trial Results to Study Volunteers. Available at: bit.ly/2UasCH3 Accessed: April 2019.
- 78. Patients' Attitudes and Preferences About Participation and Recruitment Strategies in Clinical Trials. 2009. Available at: bit.ly/2lhrv6D Accessed: April 2019.
- 79. Key Facts about Communicating Trial Results with Study Volunteers. Available at: bit.ly/2XEZwIo Accessed: April 2019.

Once a trial finishes for a patient, then what? Too often, patients walk away empty-handed or with scant information about the results of the trial. Understanding that a patient's experience shouldn't simply stop at the moment of their last dose or follow-up visit, is crucial to improving patient experience.

FEELING APPRECIATED

Nobody should leave a study feeling underappreciated. Yet how many studies finish and still fail to thank participants, or communicate the results to trial participants, alongside the research community? How many trial participants or family members are told if the experimental drug they were on got to market or not, for instance? Or indeed if they were on the experimental drug or a placebo.

An Eli Lilly representative, in a plea to the industry to do better, says:

*"Research is about asking questions. Patients help us answer those questions, yet they don't get to hear the punchline."*⁷⁶

While more sponsors than ever before are planning and executing trial result communication programmes - from 1 in 2010 to 30 in 2014⁷⁷, at last count - there's still a long way to go until these patient comms are seen as business as usual across the industry.

"Respecting the heck out of participants is key to making clinical trial participation a positive experience and to helping encourage more people to participate," says the Lilly representative on LillyPad, the company's blog.⁷⁶

And patients agree. Research shows that:

90%

of patients say that it's important that they are told about the results of a trial they participated in⁷⁸

70%

of patients say that not being told would put them off participating in future research⁷⁸

86%

of patients say they want not only to be told the results of their trial, but also to be updated regularly in the time between when their participation ends and the trial results are made public and beyond⁷⁹

AWARENESS

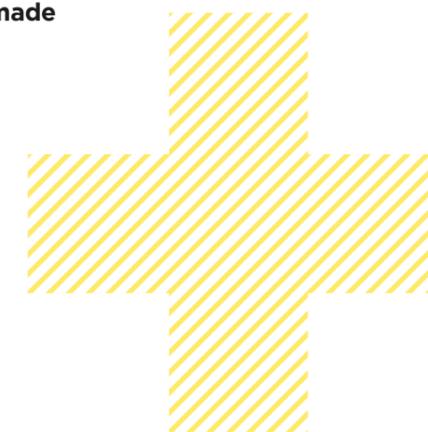
DESIGN

RECRUIT

CONSENT

RETAIN

FOLLOW UP



1. Research interview with T.J. Sharpe, stage IV melanoma survivor.

HOLISTIC EXPERIENCE

A trivial example: have you ever had a lovely meal out ruined by waiting too long for your bill or by an impolite waiter? The same logic applies to clinical experiences: if we fail to maintain a good experience across the whole clinical trial journey – from the very first time a patient hears about a trial through to screening, consent, site visits and continued communication once they’ve completed their participation – then we run the risk of leaving patients unsatisfied with their experience, despite some good intent along the way.

Melanoma survivor T.J. Sharpe sums up the need for this truly holistic view of patient experience eloquently:

“ Patient centricity isn’t something that can be simply bolted onto a trial design by adding an advisory board and incorporating a few comments and insights. Co-creating the entire trial from conception through to approval requires a change in philosophy from ‘get regulatory approval ASAP’ to ‘how can we best serve the patients who rely on us to bring them medicines?’ ”¹

Until that shift happens, he says, patient experience will remain on the outskirts of therapeutics development, instead of at the forefront.



80. Medgadget Joins the Verily Project Baseline Study, Part 3: Onward to Year Two! 2018. Available at: bit.ly/2P0PgRd Accessed: April 2019.

CASE STUDY

PROSUMERS AND WEARABLE-ENABLED TRIALS - PROJECT BASELINE⁸⁰



The Project Baseline Study is a landmark trial sponsored by Verily Life Sciences, the life science division of Google’s holding company Alphabet, who are coupling the opportunity to be part of the future of medicine with consumer brand language to attract patients to take part. Coordinated in partnership with Stanford University and Duke University, the study is using a combination of at home/remote data collection such as sleep and patient-reported outcomes and in-clinic medical tests such as blood counts and deep molecular profiling.

The goal is to learn what the ‘normal’ measures of health are for a population and how genetics, lifestyle choices and other factors affect health. Verily is using three key devices: a wrist-worn wearable containing multiple sensors called the Verily Study Watch; a bed sensor developed by Israel-based EarlySense called EarlySense Live; and a wireless hub called the Verily Study Hub. There is also an optional mobile Android or iOS Baseline app.

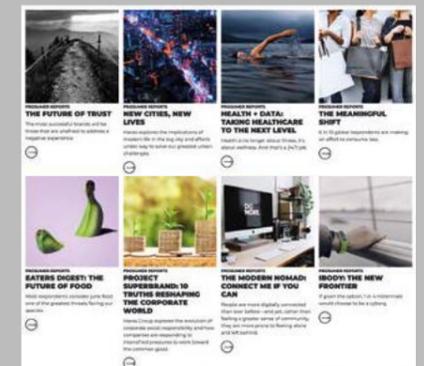
Verily are also experimenting with ways to creatively present research data back to participants. For instance, in the first year, they sent sleep and step data as a personalised snowflake for their holiday card to participants, and are providing comprehensive reports of lab test results to those on the study.

The study is already enrolling and aims to recruit a total of 10,000 patients.

 **Project Baseline** by verily

TOO MUCH OF A GOOD THING?

Read our range of prosumer reports on topics such as Health & Data and the Future of Food.



<https://download.havas.com/posts/category/prosumer-reports/>

AWARENESS

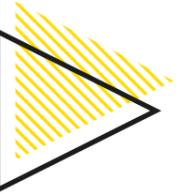
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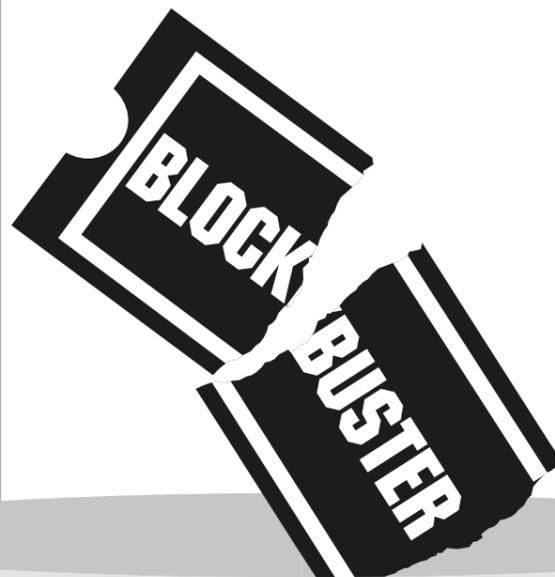
FOLLOW UP



CONCLUSION:

BECOMING NETFLIX

NOT



12. Research interview
with Mark Evans,
Havas Lynx Faze.

The world is going through a customer-centric revolution, with almost every industry focussing on the power and choice their customers have, and on improving experience as a business-critical differentiator.

Clinical trials are at a Blockbuster Video vs. Netflix moment. Blockbuster had the chance to evolve but chose to hold onto a dying business model. We all know trials aren't working, yet it's so tempting to hold onto the way we've always done things.

It's no surprise that companies like Google and Amazon are starting to play in healthcare. They can see that it's a customer-centric future and they believe their strength in this area will give them the edge over current players, as they buy in to backfill the healthcare experience.

For pharma, this isn't about 'brave' business decisions. It's about evolving to meet our customer demand, instead of following the tried-and-failed Blockbuster model of slowly losing relevance. It's about changing or dying. According to Mark Evans of Havas Lynx Faze, we must look at how consumer brands have behaved and follow suit.

They have involved customers in every part of their communication for years. Not because they think it makes them look good, but because they know it's a sound commercial decision and that you can't create or sell products and services for people who you don't understand.

*"Patient centricity is a misused buzzword to signpost all manner of token efforts, but the real winners will be those who embrace it throughout their organisation. Not just because it's the right thing to do, but because it is the only way to fix a broken model."*¹²

Mark Evans, Managing Director, Havas Lynx Faze

OPTIMISING CLINICAL TRIALS USING PATIENT CENTRICITY FROM START TO FINISH

CHALLENGES KEY

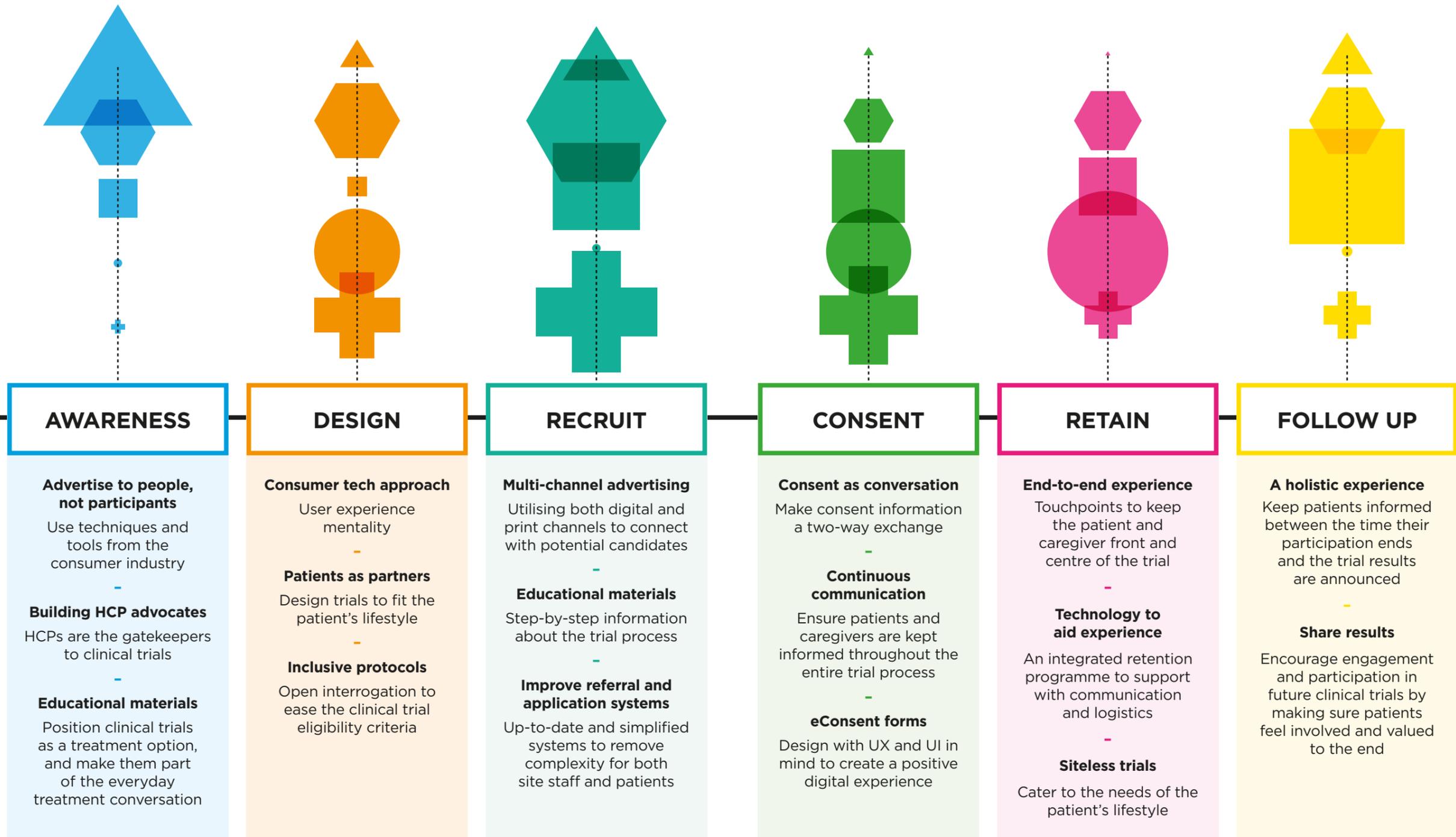
■ Timely Communication

▲ Promotional Outreach

⬡ Education & Information

● Financial & Practical Support

⊕ Site Staff & HCP Upskilling



There are a number of opportunities throughout the clinical trial programme to put the patient front and centre, to improve their overall experience and to ultimately drive clinical trial success.

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