It is now widely recognised that the traditional model of clinical development is near breaking point. Indeed Tomasz Sablinski, chief executive of Transparency Life Sciences, argues that 80% of clinical trials are studies no-one cares about, using 80s technology, and costing 80% too much.

And as Professor Trevor Jones, non-executive director of Allergan, makes clear, the case for disruptive innovation in clinical trials is not so much whether, or when, as how.

“We simply cannot continue to do clinical studies the way we have been doing them over the past decade or so. It costs far too much, it takes far too long and the problem with attrition at Phase III – now in terms of efficacy rather than safety – is just unacceptable.”

In drug discovery there is already broad recognition that open innovation can stimulate the fresh thinking needed to restock tired R&D pipelines. In pre-competitive areas of drug development, initiatives such as Transcelerate and the Innovative Medicines Initiative are already showing how collaboration can benefit the whole R&D enterprise. Yet companies still struggle with clinical trial mechanisms that fall down on the most basic of objectives: timely delivery of cost-effective medicines addressing the real needs of patients, healthcare systems and societies.

To meet those goals requires a fundamental shake-up of assumptions about how clinical trials should be conducted. Two interlinked factors likely to play a crucial role in driving disruptive change are the emergence of new technologies and the parallel shift in the contribution patients make to those trials – from being passive to active, subject to participant.

The net effect of disruptive innovation, notes Dr Nimita Limaye, vice president, risk-based monitoring at Tata Consultancy Services, has to be reduced complexity in clinical development – not more barriers on the road to market. That means, for example, not only externalising more R&D but better integrating data flows, shifting from site-based to virtual trials, and...
focusing on real-time data and outcomes rather than bolting on analyses at the end of the study – the traditional ‘learn and confirm’ model.

In the meantime, there remains a serious imbalance between cost and effort in drug development. The development phase, for example, accounts for around 60% of overall drug discovery and development costs, Jones points out. And it is by no means uncommon for 30% of clinical trial sites to recruit no patients at all.

Estimates of R&D costs for new medicines now stand at $1.3-$1.8 billion. Yet the past five years have seen 50% fewer new molecular entities reach the market than in the previous five. Moreover, attrition in Phase III has reached 30%-40%, higher even than the 30% seen in Phase I trials. In oncology – the seedbed of genomics and personalised medicine – the failure rate is 93% overall, with 50% of that share in Phase III.

But as well being economic and scientific, the barriers to success are cultural. As Ira Spector, former senior vice president, global development operations at Allergan, explains, clinical trials may be “the only thing standing between great discovery and the patient”, but to management they can look like “an expensive gamble”, while marketing may only be interested in the “right” trial to make a commercial impact. That makes for an altogether tougher sell when the per-product cost of clinical trials is around $500 million, 80% of trials don’t start on time, and 80% don’t complete on time. “We are chasing patients around the world,” Spector comments.

Solutions within reach

Nevertheless, some practical solutions are already within reach. One example is the virtualisation of site visits. A typical clinical trial involves 20-25 patient visits at considerable expense, and most of these are to check compliance with the study protocol. Probably only around three of those visits are really needed, says Spector, while a younger generation would rather check in via smartphone, and those smartphones can be linked up to a portable scanning device to transmit their vital signs back to the trial monitor.

Virtualising clinical trials could have a dramatic impact on the resources needed to support clinical development. According to Limaye, the cost and time saving from Pfizer’s Remote virtual trial pilot amounted to more than $2,500 per patient.

‘The clinical research sector is effectively trying to do the work of a speedboat with an oil tanker’

The availability of patient registries and electronic records also presents opportunities to seed clinical trials more effectively, such as running meta-analyses based on existing patient data, injecting real-world data from clinical practice, or using registries to enhance patient recruitment.

Trim the fat

Another way to trim the fat from development is through innovative trial designs, such as that employed in I-SPY 2, an adaptive North American study designed to develop breast cancer therapies twice as quickly and at one-fifth the cost of current methods. This, Spector notes, points the way forward for real time data-mining and collecting the “signal”, not the “noise” – in other words, focusing on clinical rather than statistical significance.

While traditional clinical trials painstakingly collect and monitor huge volumes of data, “this data is not all equal”, he observes – indeed, only 3% of trial data actually changes post-monitoring. Complexity is built in from the start. Far better, Spector says, to stop treating the protocol as “sacred”, distil it down to just a few fundamental questions, and then use technology to learn from patients, sites, and ultimately the trial itself, as the study moves forward.

One problem with this approach, says Medidata Solutions’ Rebecca Jackson, is that technology in the home has now outstripped technology in the workplace. The clinical research sector is effectively trying to do the work of a speedboat with an oil tanker, and “I don’t understand how we as an industry are still afloat”.

Nevertheless, technology is shifting from enterprise-driven, closed solutions to cloud-based open solutions characterised by social networking and downloadable apps. Everyone has their own apps and patients want to participate, comments Jackson. Indeed 23 of the top 50 pharmaceutical companies are already using social media to engage with patients. What cloud-based clinical research

What is disruptive innovation?

A disruptive innovation is an innovation that helps create a new market and value network, and eventually disrupts an existing market and value network (over a few years or decades), displacing an earlier technology. The term is used in business and technology literature to describe innovations that improve a product or service in ways the market does not expect, typically first by designing for a different set of consumers in a new market and later by lowering prices in the existing market.

‘Patients have moved from being subjects to customers in clinical research’

Lilly has taken tentative steps down this path as part of its clinical open innovation initiative, submitting a completed breast cancer trial to the ChallengePost competition site to get input on the kind of study protocol and informed-consent document patients would like to see. The company has also been working on study designs with the Smart Patients online oncology community in California. We regard these patients as “micro-experts, not subjects”, Kasher stresses.

A proactive patient community could assess the available data on their condition and match it with their own electronic medical records to determine which trials would apply to them, Kasher suggests. The ultimate goal would be on-demand patient enrollment. Indeed, the Michael J Fox Foundation already has 17,000 pre-screened patients ready to enter Parkinson’s disease trials.

Sablinski dismisses the notion that regulators are a sticking point to disruptive innovation, noting that TLS secured approval for an entirely telemonitored trial protocol from the FDA in 30 days, and was encouraged to do more.

Moreover, Dr Kirsty Wydenbach, medical assessor in the clinical trials unit at the UK’s Medicines and Healthcare products Regulatory Agency, stresses that part of the regulator’s role is to support innovation – “if only you’d come and talk to us”.

The clear message for industry is that it needs to get ahead of the curve and make sure technological change translates into process change that will deliver the outcomes sought by an ever-widening range of stakeholders. As Kasher observes, pharma needs to follow the advice of the great footballer Pele, and “go where the ball is going”.

This article is based on talks given at a Health Network Communications meeting held in London recently.