Drugs, devices, and the promise of pervasive computing

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Nick Davies and Stuart Henderson explore the ways in which pervasive computing is set to transform drug development and healthcare delivery.

In 1979, the famous science fiction writer Arthur C Clarke published a novel, *The Fountains of Paradise*, in which the protagonist wears a device to monitor his heart rate. CORA, his coronary alarm, tells him to rest when he has overexerted himself and radios for help when he has a heart attack. Now fact is fast catching up with fiction as IBM is developing a heart-rate monitor designed to phone for help when trouble arises.

This new device may lack CORA's sweet mezzo-soprano voice but it certainly represents a big step forward. The heart-rate monitors on the market today are typically strapped to the chest and work by sending a signal to a second device on the wrist, which the patient can track. IBM has devised a way of using Blue-Tooth, a short-range wireless technology, to intercept that signal and redirect it to a cell phone on the same wireless personal area network (PAN), if it shows that the heart rate has exceeded certain thresholds. The prototype device is small enough to fit in a pocket and, like CORA, can intervene when a patient is unconscious.

IBM's heart-rate monitor is just one instance of the way in which pervasive computing promises to shape the future of healthcare. Miniaturized individual tracking devices, mobile telecoms, and wireless technologies will ultimately transform drug development and healthcare delivery.

Disappearing technologies

Mark Weiser, a leading light at the Xerox PARC computer science laboratory, first defined the concept of ubiquitous or pervasive computing. In an article published in Scientific American in 1991, he wrote: "The most profound technologies are those that disappear. They weave themselves into the fabric of everyday life until they are indistinguishable from it."

Weiser argues that what matters most is not technology itself, but its relationship to man. Over the past 50 years that relationship has undergone two major metamorphoses: We began with the mainframe, where many people share a computer, and migrated to the personal computer, where one person has one computer. We have subsequently moved onto the internet, which provides widespread interconnection. But this, says Weiser, is simply a stepping-stone to a third stage – an era of pervasive computing, where many computers share each of us.

"Pervasive computing offers particular potential in the pharmaceutical and healthcare industries"

Some of those computers will be the thousands we access in the course of browsing the internet. Others will be embedded in walls, chairs, light switches, cars, and even the human body. In short, pervasive computing is the antithesis of virtual reality, instead of creating an artificial world inside the computer, it invisibly enhances the world that already exists.

Pervasive healthcare

Pervasive computing has numerous applications, but it offers particular potential in the pharmaceutical and healthcare industries by facilitating the transmission and collection of biological data on a real-time basis outside a clinical setting. That, in turn, means it can be used to monitor patients and manage their health, to test new drugs in totally different ways, and to deliver healthcare anywhere, anytime.

In addition to such direct advantages, pervasive computing has a big social contribution to make. It can be used, for example, to enable patients and their relatives to keep in touch, and to help people with cognitive disabilities function on a daily basis. One illness that lends itself to such treatment is senile dementia - which is likely to be a growing trend in the graying populations of the Western World.

But though 'pervasive healthcare,' as it is sometimes called, promises to deliver huge benefits, there are still numerous challenges to be resolved. For a start, information about the health of patients is very sensitive, so any system that handles such data must be completely secure. It must also be unobtrusive and easy to use, since the vast majority of patients will not be technophiles eager to adopt the latest technology.

Lastly, and for obvious reasons, any system that is used to provide pervasive healthcare must be completely robust - and this is currently the single biggest problem. Pervasive computing is still in its infancy and largely reliant on the methods of experimental computer science, where researchers design, develop, program, and assess prototypes, in other words, it is still at the 'proof of concept' stage. But modern information-based medicine is rooted in statistical significance, repeated iterations of a test to prove that a treatment really works, and does so without causing intolerable side effects. Moreover, the clinical trials that yield such evidence typically involve thousands of patients over a period of several months or years.

At present, most pervasive computing technologies are not sufficiently reliable to be used in such a context - and while there is any doubt about their robustness, the regulators will rightly refuse to accept data collected in this fashion. That said, some of the key components are already beginning to emerge, and though it is difficult to predict the precise crossover point, the moment at which they make the transition from prototype to practical reality is getting much closer (see Figure 1).

Box 1. Small and beautiful

Miniaturization and new fabrics have massively increased the opportunities for developing devices that monitor a patient's health. Here are a few of the most promising examples.

- *The GlucoWatch.* In mid-2001, the first wristwatch device designed to monitor blood glucose levels in patients with diabetes reached the market. It uses a small electrical current to extract a tiny amount of fluid through the skin. A thin plastic sensor on the back of the watch measures glucose levels in this fluid every 20 minutes for 12 hours. The device sounds an alarm if the wearer's glucose reaches dangerously high or low levels.
- *The clip-on pedometer.* Titan Industries is developing a clip-on device that tracks various parameters, including the number of calories the wearer has burned while walking around. The company is also exploring the potential for a similar device that monitors blood pressure.
- *PC in a pill.* Scientists in Israel have developed a wireless digital camera so small that it can be sealed in a capsule and swallowed. It takes high-quality color images while passing through the digestive tract. The images are transmitted to a portable recorder worn on a special belt and can be downloaded on a PC.
- *The smart shirt.* Sensatex, a New York-based company, is developing a shirt that is used to monitor patients' vital signs. The shirt is made of an electro-optical fabric that transfers data from the wearer to the garment. A transceiver on the shirt records the data and sends it to a wireless gateway, from which it can be transmitted to the doctor.
- *Smart dust.* Researchers at the University of California, Berkeley, have developed smart dust - tiny, intelligent wireless sensors that can communicate with each other, form autonomous networks, reprogram themselves and monitor almost anything. They have already been tested for various military and non-military applications, but their potential in providing pervasive healthcare is equally huge.

Wireless networks

Thanks to advances in miniaturization and developments in sensors and measurement technologies, it is already possible to collect a considerable amount of health-related information from wearable or embedded devices, and numerous new devices are also in the pipeline (see Box 1). Some of these devices function on a constant basis, while others take intermittent measurements. The surrogate markers they track determine which mode is most suitable; a device that monitors the heart rate in a patient with a history of cardiac events must be constant, for example, whereas a device that monitors lipid levels in the bloodstream of a patient who has high cholesterol need only be intermittent.

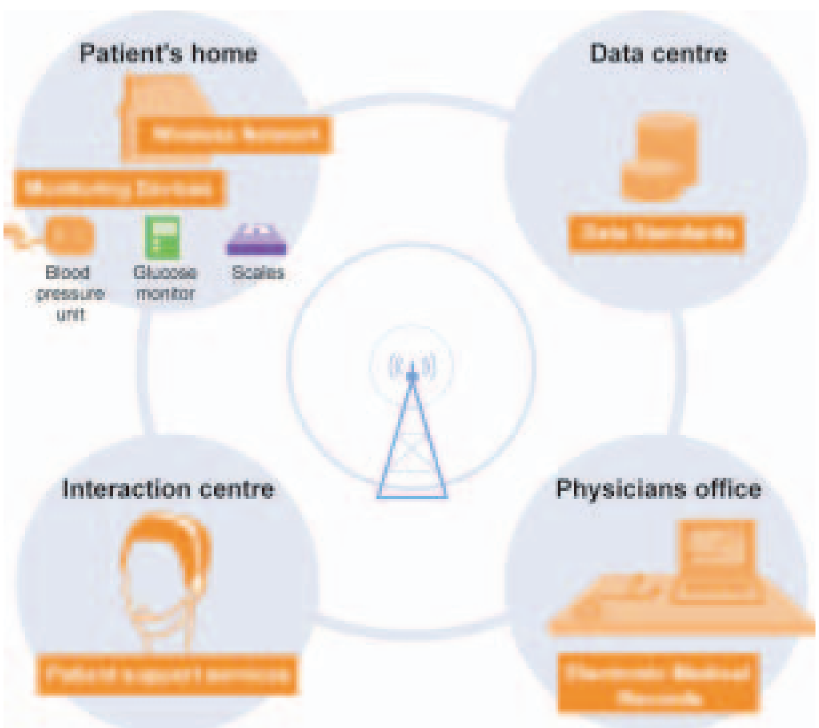

Figure 1. The infrastructure required to support pervasive healthcare.

Reliable, portable monitoring devices are only one element in the equation. The second is the network across which the data they collect can be sent - and here two new technologies are particularly relevant: third-generation (3G) mobile telephony, and a wireless network protocol known formally as 802.11 and colloquially as Wi-Fi.

The first 3G networks using the Universal Mobile Telecommunications Systems standard came into operation earlier this year. They offer an enormous increase in bandwidth and can theoretically transmit data at speeds of as much as two megabits per second (Mbps). They are also relatively easy to use.

Wi-Fi runs at even faster speeds; the most common standard can transmit data at a blistering 11 Mbps, although access is limited, except in large urban areas, and the technology itself is less secure. However, both these problems are likely to be resolved quite shortly. In the US, for example, IBM, Intel and AT&T have formed a consortium to develop a nationwide wireless data network. Similarly, a number of wireless initiatives have been launched in the UK, the most ambitious being The Cloud. Founding fathers Inspired Broadcast Networks and Leisure Link Group have already rolled out the service to 1000 sites (all pubs), and aim to provide 3000 Wi-Fi hot spots by the end of the year. A new and much more secure encryption standard, Wi-Fi Protected Access, is also under development.

The third element required for pervasive healthcare is a hub at the relevant hospital or doctor's surgery, to which the data can be sent. The frequency of collection and transmission determines whether the data are electronically filtered and programmed to trigger an alert only when they fall outside certain preset parameters or checked by a human agent.

A package job

The tools for pervasive healthcare are evolving quite rapidly, but how will they work in practice? In it's latest report on the future of the pharmaceutical sector, Pharma 2010: *The Threshold of Innovation*, IBM Business Consulting Services outlines some of the implications.

Most of the drugs currently on the market come in a one-size-fits-all format and are aimed at a mass population. But complex biomolecular and genetic variations in individuals, as well as the different environmental influences to which they are exposed, mean that many drugs do not work for a significant percentage of the patient population. Worse still, some drugs cause serious side effects in some people. Research conducted at University College, London, shows, for example, that every year more than 800,000 patients using the UK National Health Service experience adverse drug reactions.

High-throughput biology - genomics, proteomics, metabonomics, and so forth - will eventually enable the pharmaceutical industry to develop healthcare packages for patients with different genetic profiles and different disease subtypes. These 'targeted treatment solutions' will include diagnostics for evaluating a patient's susceptibility to a particular disease; biomarkers for identifying the specific subtype from which he suffers, and for measuring its severity and progression; drugs for treating that disease subtype; and monitoring mechanisms to check the efficacy of the treatment and help him comply with his individual medical regimen.

Pervasive computing is one of the vital pieces in this transition. In the future, any company that wants to produce a new drug will develop relevant biomarkers as an intrinsic part of the target validation process (see Box 2). These biomarkers will be used to assess the toxicity and efficacy of the drug during the preclinical phase. They will also be used, in conjunction with remote monitoring devices, to determine how patients respond during clinical trials, both in terms of adverse effects such as hepatic toxicity and in terms of how effectively the drug impedes the progress of the disease subtype for which it is designed.

In-life testing

However, pervasive computing will ultimately do much more: it will change the very way in which new drugs are tested.

At present, all drugs go through three clinical phases, but the process is both very costly and very inefficient. Clinical trials cannot detect rare side effects and drug interactions, or even fairly common reactions sometimes. In fact, one recent study conducted by Harvard Medical School and Public Citizen, the US consumer advocacy group estimates that 20% of all new drugs are eventually found to have serious side effects which are unknown or unclear at the time of their approval.

Pervasive computing will help to overcome these problems, by providing the means with which to conduct 'in-life testing'. Promising new drugs will first be tested in man during late-stage discovery to prove their safety and efficacy. They will be tested still further in phase II trials and submitted to the regulators for conditional approval. They will then be launched on the market and subjected to extensive additional in-life testing, using a wide range of remote monitoring devices and networks.

Box 2. Biomarkers

The value of using biomarkers to measure diseases that are hard to track or slow to run their course is well established. One such instance is the CD4+ lymphocyte count - a biomarker for assessing the efficacy of antiretroviral therapies in patients with HIV, the number of CD4+ cells falls as the disease progresses. But it is no accident that this is one of the very few biomarkers approved to date; developing new biomarkers is difficult. Moreover, the biomarkers used for proof of concept may not necessarily be the same as those used in the clinic.

Even so, scientists are now exploring suitable biomarkers for numerous diseases, and some look very promising. The standard test for prostate cancer cannot, for example, discriminate between benign and aggressive tumors, but researchers using high-density tissue microarrays have recently discovered that almost all tissue samples with localized prostate cancer show high levels of alpha methylacyl co-enzyme A racemase, while normal tissue has none. Other studies suggest that overexpression of the EZH2 gene distinguishes metastatic from localized prostate cancer.

Both these findings pave the way for the development of new biomarkers that can identify localized and lethal forms of the disease.

In-life testing has various practical and economic advantages. It will dispense with the need to expose patients to placebos or dosing levels that are pharmacologically ineffective. It will be better able to pick up rare side effects and drug interactions, thus making the move from the laboratory to real life much safer. It will also reduce the frequency of the visits patients need to make to their doctor or hospital – and travel was one of the two biggest obstacles cited in a recent survey of potential trial patients. Similarly, it will reduce the amount of time healthcare professionals need to spend in consultation with individual patients, enabling them to look after more patients more effectively.

Round-the-clock health management

The same technologies that support in-life testing will enable healthcare professionals to monitor the rest of their patients from a distance. Pervasive computing is particularly suitable for monitoring people with chronic illnesses such as diabetes and coronary heart disease, by measuring their blood sugar levels, blood pressure, lipid levels and other such biomarkers. It can also be used to track the constant elements of acute diseases, like the white blood cell count in patients with cancer, or to detect the danger signs suggesting an acute incident such as a heart attack or stroke. The data can then be fed into electronic medical records such as those the NHS plans to introduce throughout the UK by 2005 - a process that will ultimately both reduce the frequency with which patients have to visit their doctor and improve healthcare delivery.

But the power of pervasive computing is not simply its ability to monitor the health of individual patients and trigger remedial action, it will also encourage compliance and persistence. Many patients do not stick to their treatment regimen, even when they risk becoming seriously ill. In one recent study of persistence levels in patients with high cholesterol, for example, only 33% of patients were still using a statin at the end of 12 months, and only 13% were still doing so at the end of five years. A number of factors contribute to such low levels of persistence, but a patient who knows that a drug is doing him good because there is visible proof of its efficacy is far more likely to keep taking it than one who has to rely on infrequent visits to the doctor.

However, it is important to identify where pervasive computing cannot add value, and to distinguish between what it can and cannot do. There is no point, for example, in using it for one-off tests to identify whether a patient has a particular disease subtype, such as breast cancer arising from overexpression of the Her-2 gene. It is only useful for measuring changes in an existing condition on a repeat basis. There is probably little point, either, in trying to monitor side effects that are better measured qualitatively, such as dizziness, rashes, headaches and nausea; although these are common adverse reactions, they are essentially subjective.

Similarly, pervasive computing can only be used to monitor the known risks associated with a particular disease or drug, or those associated with a common drug combination (such as the cocktail of drugs for high blood pressure, angina, and high cholesterol which many elderly patients require). It cannot be used to measure unknown risks or unusual drug combinations.

Pervasive impact?

Although pervasive computing may not be a universal panacea, it will certainly have a profound impact on drug development and healthcare delivery. Moreover, one of the areas in which it promises to yield greatest results is in the treatment of the diseases that are now the world's biggest killers. According to a report published by the World Health Organization in 2002: "Non-communicable conditions, including cardiovascular diseases, diabetes, obesity, cancer, and respiratory diseases, now account for 59% of the 56.5 million deaths annually and 45.9% of the global burden of disease."

Pervasive computing will be one of the most potent tools in combating this burden by aiding the development of effective new drugs for patients with different disease subtypes, helping healthcare professionals and patients alike to monitor their condition, and enabling patients who might otherwise require hospitalization to enjoy an active, independent life for as long as possible.

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FURTHER READING

Weiser M (1991) **The computer for the 21st century**. *Scientific American* **265**:66-75.

Stanford V (2002) **Using pervasive computing to deliver elder care.** *IEEE Pervasive Computing: Mobile and Ubiquitous Systems* **1**:10-13.

Ananthaswamy A (2003) **March of the motes.** *New Scientist* **23 August**:26-31.

Pharma 2010: The threshold of innovation. (2002) *IBM Business Consulting Services.*