

Commentary

An agenda for UK clinical pharmacology

The potential of the internet

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The internet and the World Wide Web have changed the ways that we function. As technologies grow and adapt, there is a huge potential for the internet to affect drug research and development, as well as many other aspects of clinical pharmacology. We review some of the areas of interest to date and discuss some of the potential areas in which internet-based technology can be exploited. Information retrieval from the web by health-care professionals is common, and bringing evidence-based medicine to the bedside affects the care of patients.

As a primary research tool the web can provide a vast array of information in generating new ideas or exploring previous research findings. This has facilitated systematic reviewing, for example. The content of the web has become a subject of research in its own right.

The web is also widely used as a research facilitator, including enhancement of communication between collaborators, provision of online research tools (such as questionnaires, management of large scale multicentre trials, registration of clinical trials) and distribution of information.

Problems include information overload, ignorance of early data that are not indexed in databases, difficulties in keeping web sites up to date and assessing the validity of information retrieved. Some web-based activities are viewed with suspicion, including analysis by pharmaceutical companies of drug information to facilitate direct-to-consumer advertising of novel pharmaceuticals.

Use of these technologies will continue to expand in often unexpected ways. Clinical pharmacologists must embrace internet technology and include it as a key priority in their research agenda.

Introduction

The first step towards our modern understanding of the internet started as early as 1969, when computer science researchers from California sent a message to fellow scientists at Stanford University (over 300 miles distance away) consisting of a single word [1]. The next two decades showed steady progress, as global data communications systems were constructed. One of the facilitators to ensuring that multiple independent networks could communicate as part of this 'internetworking architecture' came in 1989, when Tim Berners-Lee, himself a scientist and researcher, published the standards and protocols for the exchange of information over the internet: the World Wide Web had been born [2, 3]. The World Wide Web (WWW, or simply the web) allowed for users to have a graphical interface of the internet via specific browsers and put the technology in the hands of the ordinary population. The ability to access documents and other resources over intercon-

nected networks of computers has influenced not only many personal lives, but also the conduct of research and health-care delivery. The information age afforded by the internet and the World Wide Web is likely to continue to influence the way that researchers do their business. We consider here what influence these technologies will have on clinical pharmacologists, reflecting on previous work that has been affected by or conducted using the internet, and we discuss the potential new directions that this technology will afford.

The global importance of the internet

The World Wide Web is an information space in which the items of interest, referred to as resources, are identified by specific identifiers called Uniform Resource Identifiers (URI) [4], more commonly known as Uniform or Universal

Resource Locators (URL). A URL is strictly speaking only one type of URI, but the two terms are often used synonymously.

Today there are interconnections of multiple independent networks covering the globe, and it is almost impossible to recognize the limits of the capability of the technology. We have become used to the new language that the technology brings and may remember that <http://www.bps.ac.uk> (a URI for the British Pharmacological Society) will take us to our society's website, even though we may fail to remember our own telephone number. The global impact of the internet on many aspects of everyday life cannot be overestimated, but have we considered where it has and could have further potential to affect the way that we conduct our professional lives?

Using the internet

Through a complex history of technological, organizational and societal changes, the use of the internet has burgeoned (Figure 1) and the ways in which people use the internet today are incredibly varied. Few skills are actually required to access and manipulate information over the internet, through the modern user interfaces of web-based systems. The web has therefore become a widespread platform for access to information. While information retrieval is one of the fundamental benefits of the internet, how and why we use web technology is actually quite varied [5]. In simple terms there are a few reasons for 'browsing the web':

- 1 information tasks – finding specific information in 'documents'; for example, searching for the latest research protocol;

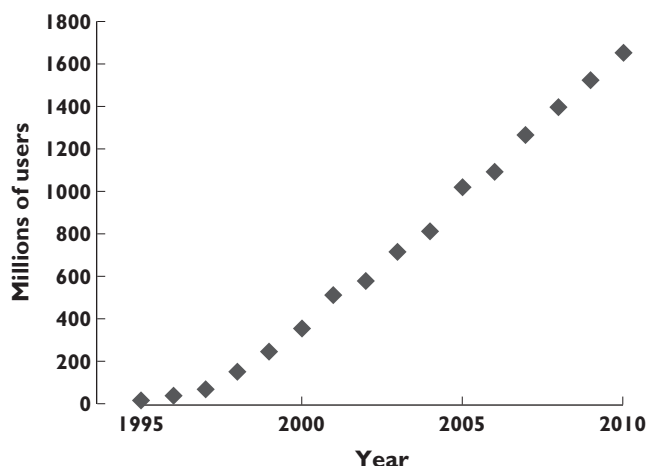


Figure 1

The increase in the numbers of users of the internet between 1995 and 2010

- 2 navigational tasks – finding something such as the website of a company or a resource such as a database;
- 3 transactional tasks – performing a web-mediated activity, for example, buying goods or services.

All of these are useful on a personal level, but also influence the conduct of professional interactions, including health-care delivery and research.

The internet as a professional tool

Information retrieval from the web by health-care professionals may have previously been regarded with suspicion by their colleagues and patients, but is now commonly undertaken. Computerized access to information in health-care settings has changed remarkably over the last decade and even early research has shown that bringing evidence-based medicine to the bedside affects the care of patients [6]. Modern information and communication technologies bring information, quite literally, into the palm of providers' hands and take us beyond information tasks into the realms of transactional tasks, with the use of online tools (such as calculators and clinical algorithms). These tools are often accessed on mobile computing terminals or telephones connected to the internet as web applications (or 'apps').

However, having all of this technology at one's fingertips may bring its own problems, as it is usually impossible to ensure the validity of information on the web. This is not surprising, as it is estimated that online information has now exceeded all human documents generated in the first 40 000 years of human history and is vastly more than all the information on earth that humans can learn [7]. The solutions to effective information retrieval include developing effective search strategies, as one would do when conducting a systematic review, and using efficient tools to assist in the process. This has become one of the important skills of modern researchers.

The internet has become a research tool in its own right, whether for information retrieval to help with research, searching information as the main focus of research or facilitating research in some other manner. These are worth examining individually.

The internet as a research tool

The web can provide a vast array of information that can be useful to current research if it is used appropriately. Whether it be in the generation of new ideas or an exploration of previous research findings, researchers can find information much more efficiently than ever before. Performing a literature search has changed from a laborious process of driving to a library, thumbing through a hard copy of Index Medicus, and searching shelves for a specific issue of a journal (or requesting an inter-library loan) to a simple task of typing a few terms into a database such as

MEDLINE® (Medical Literature Analysis and Retrieval System Online), Pubmed or EMBASE, clicking a few buttons, and downloading an article from a remote online server. The exponential growth in information available on the web in general is also reflected in the volume of scientific literature available. For example, there are now more than 18 million records from about 5000 selected publications in the MEDLINE® database [8]. Therefore, while systematic reviewing could become an armchair hobby for academic researchers, there are still challenges due to information overload. Specific bibliographic user interfaces can help to make searches more specific. Researchers are also helped by colleagues who are willing to publish search strategies for finding information on specific topics (see for example [9]). Problems also exist when information is not appropriately indexed, is not in the public domain or is too old to show in some databases. An interesting pharmacological example of a perceived failure in effective information retrieval was the case of a young healthy male volunteer who died in an experimental trial of inhaled hexamethonium, despite the known association between hexamethonium and lung toxicity that was reported in the 1950s and early 1960s [10]. Since the reports of lung toxicity occurred before 1966, the researchers' information searches failed to reveal the historical online information.

While old information can be revealing, new information can go out of date. Although some websites are updated regularly, much of the information relevant to research remains indefinitely available to access. Information obsolescence therefore becomes a problem for researchers. Shojania and colleagues observed that new signals that significantly affected the outcomes of systematic reviews occurred at a median time of 5.5 years after publication, but also noted that new relevant data were evident for 7% of reviews by the time they were published [11]. The internet may allow for contemporaneous updating of materials, but it is likely to confound rather than resolve the issues related to obsolete information.

Describing the distribution and content of information on the web has become the main focus for some research studies. Examples include studies that have analyzed the content of various websites, such as regulatory information on the web [12], direct-to-consumer television prescription drug advertisements [13] and pharmacovigilance websites [14]. Passive analyses of content on the internet may be limited if the internet population is unrepresentative of the general population. However, it is often well-suited to qualitative research [15]. The web represents collections of many communities that can be exploited in internet-based research. Topics suited to this type of research include analysis of interactive communications (for example e-mail), study of online communities and exploration of the quality of health information on the internet [16]. Seeking to understand people and cultures outside experimental settings has given rise to new knowledge in an area that has been described as pharmacosociology. Examples include

narrative studies of specific adverse drug reactions [17] and other drug-related problems [18].

The internet as a research facilitator

The web is now widely used as a research facilitator. Some examples include a tool to aid communication between researchers, specific online tools (for example web-based questionnaires, trial management) and the distribution of information. Internet-based communication can allow collaboration between and within research groups or networks of researchers, allowing progression of a range of medical and pharmacological trials. Fostering efficient virtual research efforts in geographically dispersed scientists is particularly important in areas such as neglected diseases and orphan drugs [19]. Some researchers have also taken advantage of internet-based technologies to facilitate research processes that benefit from fast communication, such as the conduct of electronic Delphi studies [20]. Whether other types of internet communication, such as the social networking sites Facebook or LinkedIn, become credible resources for scientific endeavours remains uncertain [21].

Large scale multicentre trials can take advantage of the internet for many different parts of clinical trial management, such as remote randomization, data acquisition and validation, protocol distribution and data exporting [22]. For example, Lindh and colleagues have demonstrated the usability of web-based tools to coordinate a complex study of warfarin pharmacogenetics across 39 dispersed centres [23]. The potential benefits of web-based management of clinical trials include reduced administrative costs, centralized and secure data storage, automation of various tasks (for example data quality assurance), standardization and real-time monitoring. The monitoring aspects are clearly only possible through computerized data capture and specifically allow for continuous surveillance of study participants as part of pharmacovigilance plans [24], akin to the online data-driven frameworks for managing post-marketing surveillance that also currently exist [25].

One final area in which the internet can affect research facilitation is the registration of clinical trials. The world's largest clinical trials repository (<http://www.ClinicalTrials.gov>) has more than 100 000 registered studies and is administered by the US National Library of Medicine [26]. Researchers are encouraged to register clinical trials prospectively via such websites. Indeed, paragraph 19 of the 7th revision of the Declaration of Helsinki, which was adopted by the 59th World Medical Association General Assembly in Seoul in October 2008, states that 'every clinical trial must be registered in a publicly accessible database before recruitment of the first subject' [27]. This allows knowledge and participation in clinical trials, in addition to providing results when known, and in particular can prevent unintended duplication of clinical research.

The internet as a clinical tool

While not strictly a research priority, it is important to understand how and when the internet is used as a clinical tool. Discovering how the internet can be applied to clinical problems is itself a defined research question. There is increasing interest in how web-based tools can facilitate health-care delivery. A paper in the BMJ reported a simple study undertaken by two Australian physicians [28], which was inspired by a letter published in the New England Journal of Medicine, lamenting the fact that a diagnosis had been made by 'googling' (a word that has entered the vernacular) the diagnosis [29]. The physicians found that by entering three to five search terms into Google, they could correctly identify 15 of 26 cases from the case records series in the New England Journal of Medicine.

Google is a sophisticated search engine and is making billions of dollars a year from its worldwide use, which includes a significant advertising section. It is more fascinating perhaps to marvel at the complexity of modern search capabilities, which incorporate various important strategies to maximize their search relevance, including page rank technology and semantic analysis, and consider how these technologies can influence health-care and research. As more health care delivery relies on the use of information technology, such as electronic prescribing, order entry, digital image repositories and electronic health records, the need to take advantage of powerful search technologies may be advantageous for care management and clinical decision making. The capability of indexing and structuring medical data in the background of electronic records has a huge potential to facilitate trial recruitment and generate new types of knowledge.

The internet as a surveillance tool

There are some technophobes who view the internet with suspicion. This is not helped by various illicit online activities, including the spread of computer viruses, the use of spyware and other forms of cyberterrorism. Surveillance can be used more positively, and there have been reports of the use of the internet as an epidemiological tool to study various health-related issues. For example, various studies have investigated the link between web access and other social media sites and the distribution of cases of influenza [30, 31]. Similar methods have been used by commercial enterprises to provide information relevant to pharmaceutical companies about drug information searches on the internet, either by conducting specific surveys or by analyzing web access logs (see, for example, Cybercitizen Health® [32]). By careful analysis of consumer interactions with online drug information, these companies aim to establish knowledge about treatment and product decisions that can be used in the advertising and promotion of new products, particularly in regions where direct-to-consumer advertising of novel pharmaceuticals

is permitted. The advent of new consumer-facing health repositories as online personal health records, such as HealthSpace and Google Health (although the latter was discontinued in late 2011), gives additional capability to obtain richer information about consumer interactions with medicinal products [33].

The internet in the future

Trying to predict how the internet will change research priorities in the next 5 years is not easy. A popular science book by Jonathan Zittrain has described the future of the internet in terms of either 'unsettling levels of control' or 'generative technology and collaboration for scientific 'netizens'' [34]. However, Zittrain, a Professor of Law at Harvard University, concludes that the saviour of the internet will be the positive creativeness and collaboration of tens of millions of users.

Some web-based technologies have the potential to change the way we conduct our business and yet have not realized their potential. The ability to conduct a virtual medical conference while being logged on to your computer terminal has not replaced traditional conferencing, probably because of the importance of body language. Other technologies have been revolutionary in their widespread acceptance, for example, mobile internet.

The internet is no longer simply something from which many of us access web information; it is something with which we interact. The creation of new knowledge, a key research output, must use the internet to its best advantage to distribute and disseminate data in ever more creative ways. More than this, we must embrace internet technology and ensure that clinical pharmacologists become academic 'netizens' and have the internet as one of the key priorities in our research agenda.

Competing Interests

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