Medical Writing

Medical Writing in Oncology

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Contents

Regular Features

Themes of upcoming issues of *Medical Writing*

The theme of the September issue is '**Writing Matters'**. This issue is now closed.

The theme of the December issue is '**Diabetes/obesity**' and the deadline is 3rd September 2012. All correspondence relating to this issue should be addressed to editor@emwa.org as should letters to the editor, general articles on medical writing and suggestions for future theme topics.

The theme of the March 2013 issue is '**Medical Writing Education**'. Articles are requested on the opportunities and resources available, how to become a medical writer, how to teach medical writing, how to teach medical English and where to learn it, how to create a good EMWA workshop, and reviews of textbooks relevant to medical writing or any other topic which prospective authors consider to fall within the Medical Writing Education theme. Correspondence relating to this issue should be address to Phil Leventhal phil.leventhal@gmail.com

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About the Medical Writing Journal

Announcement

The official journal of the European Medical Writers Association (EMWA) has changed its name from *The Write Stuff* to *Medical Writing*, which is being published by Maney Publishing. This marks a leap forward for the journal, which is now in its 19th year of publication. The change of name and publisher results from EMWA's executive committee's decision to open up this valuable resource of medical writing information and education to a wider medical communication community and to fill a niche left vacant by biomedical publishing. The journal is additionally a platform for discussion in its field, covering a wide range of topics from hotly debated medical/publication ethics to the intricacies of English style and grammar.

No one disputes that medical writing is expanding at an incredible pace. Most members of EMWA work in the pharmaceutical, medical communications, or biomedical publications industries, but medical writing has a broader definition and includes communicating to the general public ever eager for health information, with social media becoming increasingly important in this respect. Indeed, medical writing includes any health communication written by academic researchers, medical practitioners, governmental departments, organizations like the WHO, NGOs, patient associations…. The list is endless and the demand for health information continues to grow.

The change of the journal's name reflects the evolution from what was born as a society newsletter and grew up to become a serious resource for an audience working in bioscience. Article format now includes an abstract and keywords, and we will no longer be publishing photographs of authors. Regular readers can rest assured that with all this grown-up seriousness we will still publish playful articles and boxes. Please keep sending amusing anecdotes, photos of funny English signs etc. to: editor@emwa.org.

As before, each issue will have a theme (see box for forthcoming themes and deadlines at the end of the table of content). Original research and feature articles of interest to medical writers but outside the theme are also published. Articles are accepted from non-EMWA members. The journal also has two dedicated sections: the Freelance, or Out On Our Own, section (section editors: Raquel Billiones and Sam Hamilton) and the Translation section (section editor: Gabi Berghammer). It publishes two regular themed articles under the banners of Medical Journalism and Social Media, written by Diana Rafflesburger and Ursula Schoenberg, respectively. The regular features are Regulatory Writing (Greg Morley), Manuscript Writing (Phil Leventhal), Good Writing Practice (Alistair Reeves and Wendy Kingdom), Journal Watch (Nancy Milligan), and The Webscout (Karin Eichele). Each regular feature usually contains an article, often written by the section editor(s), followed by short articles which are contributed by readers. Book reviews are published in the In the Bookstores column; again *MEW* welcomes reviews from readers. Letters to the editor appear under the heading Vital signs. A Clinical Pharmacology series is provided by Graham Blakey. Finally the journal's pages are brightened up by illustrations from Anders Holmqvist.

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Oncology and medical writers

Elise Langdon-Neuner

Editor Medical Writing

Editorial

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Let me start this first editorial in an old journal with a new name by explaining why a medical writing journal has a theme issue on oncology and includes articles that are not directly related to writing. Medical writers write about research that is aimed at preventing, diagnosing or treating a medical disorder. They might receive an assignment that involves a disorder they know little about and need to gain an understanding of the literature on the disorder and its treatment in a very short time to meet a deadline. Quite apart from this, flexibility, curiosity, and a zeal for learning are typical characteristics of medical writers. The fund of articles in this issue cover the gamut from the nature of cancer, its current and developing therapies, management of the disease, educating healthcare workers about treatment, and communicating with patients – to tips for writing clinical trial reports.

The first known written account of the disease was a description of breast cancer in the Egyptian 'Edwin Smith' papyrus from 3000 BC. The cut surface of a solid malignant tumour with veins stretched on all sides is like a crab with its feet on all sides of the body, hence the name 'cancer' which comes from the Greek word *carcinos*, meaning crab.[1] The vocabulary we use for cancer is loaded with metaphors, mostly taken from military quarters. We are 'at war' with and 'fight' cancer, which reflects its devastating effects and urgent need of treatment. The military metaphors also help to rationalize the radical treatments required.

Cancer encompasses many diseases and has a reputation for being a complex and deadly disease even though about one-third of cases are non-melanoma skin cancers, which are easily treated and usually cured, although they are excluded from cancer statistics precisely for this reason. In her article 'The war on cancer' (p. 8) Jo Whelan, a medical journalist, summarizes current thinking on what makes cancer cancer, the question first posed by Hanahan and Weinberg in 2000. She explains how the hallmarks of cancer that they outlined then, and added to in a 2011 update, have had a tremendous influence on scientific opinion and research although they have not been without their critics.

The symptoms of cancer are not immediately evident and few are specific, which means that when they come to light they are often confused with symptoms of other disease, leading to inappropriate treatment. Once detected, cancer is diagnosed by examination of a tissue sample by a pathologist. This work could be taken over by computers in future. In a recent report in *Science Translational Medicine*, Daphne Koller and colleagues describe a program (C-Path) that they have produced by scanning images of slides and survival data from 248 breast-cancer patients.[2] With this information the program was able to grade the slides from other patients and predict whether the patients would survive for 5 years after treatment, a prediction that pathologists have not been able to make. The implications are profound not only for diagnosis, but also for ethics, because as the costs of cancer therapy increase and budgets become tighter more information will be available on which to base decisions as to who does and does not receive treatment.

At present, cancer is usually treated by chemotherapy, radiation therapy, and surgery rather than with drugs. But, as Jo mentions in her article, 900 cancer drugs are currently in phase I–II development. Cannabinoids for instance are usually associated with the palliative care of cancer. However, in The Webscout Karin Eichele (p. 61) explores the potential for using cannabinoids as inhibitors of tumour growth.

Unfortunately, many promising new agents fail, not least because some tumours do not respond or pathways blocked by treatment are circumvented by the disease. Nevertheless, researchers are hopeful that in 10 years' time it will be possible to stop even the most formidable advanced solid tumours from the colon, pancreas, and lungs. Jo quotes Weinberg, who believes that by then patients will have a normal lifestyle with a chronic disease.

Personalized medicine has been hailed as a promising way forward. Interestingly, the term has been

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criticized as more a marketing term than a scientifically meaningful description of using measurements and biomarkers to allocate patients to groups who respond to specific therapies.[4] Stratified medicine as used by Cancer Research UK is more appropriate because the process is a stratification leading to more and smaller groups of patients being matched to more and more specific therapies with the goal of reaching a truly personalized medicine when $N = 1$. But perhaps a treatment under development for ovarian cancer, which Adam Jacobs describes in his article (p. 14), truly deserves the tag 'personalized'. Adam is the project's statistician. The potential treatment, which aims at prolonging remission, involves extracting dendritic cells from the patient and re-injecting the cells after they have been primed to attack the cancer cells.

James Visanji (p. 10) tackles the specific challenges for the conduct of clinical trials in cancer, including efficacy endpoints and ethical issues. He also provides tips for medical writers on how to deal with adverse events in clinical study reports. The article by Vicente Alfaro (p. 23) focuses on safety sections of clinical study reports in the light of guideline E3 of the International Conference on Harmonisation (ICH).

Medical education is another area where medical writers make a contribution. Oncologists are more willing than specialists in other fields to try new strategies and technologies in an effort to prolong the life of patients in their care. However, they are challenged by the constant changes in the field and 'information overload'. Shanida Nataraja's article (p. 17) is a comprehensive overview of how medical education is ensuring that healthcare professionals working with cancer patients are informed of the latest treatment advances in research and of shifts in thinking about optimum patient management. The article covers the impact of the digital era on medical education, the different audiences that need to be targeted, and how learning preferences can be addressed. She also explores how tighter controls and the shrinking of educational grants can be overcome.

Diarmuid De Faoite and Bárbara Wicki (p. 64) discuss another opportunity for medical writers: communicating directly with the growing body of patients who are seeking information on their disease through the web and often finding it presented in language too difficult for them to understand.

Cancer is not only difficult to manage; treatment is also becoming increasingly expensive. In particular, personalized/stratified medicine is expensive to develop and deliver. This raises the obvious question of whether cancer is preventable. Worldwide ~18% of cancers are related to infectious diseases. Genetic mutations cause <3–10% of all cancers. Can the rest of cancers, i.e., more than 70%, be prevented? Cancer has often carried a stigma of being the fault of the victim. This is epitomized by the talk therapy movement, which provided a popular alternative therapy in the 1970s. The negative attitude of people with the disease was blamed for their plight and it was thought that their cancer could be cured by correcting this attitude through psychotherapy. Few people support this concept today, but our lifestyle and diet, of which certain elements are related to cancer incidence, are personal choices. Diana Raffelsbauer (p. 44) reviews the evidence of associations between lifestyle and incidents of cancer in her medical journalism column. She also discusses the limitations of the research methods used – comprising case-control studies, prospective cohort studies, and randomized clinical trials – and calls for a focus on whole dietary patterns and other lifestyle factors which should be researched through high-quality observational studies.

New research funded by Cancer Research UK has been published since Diana wrote her article. Max Parkin's group at the University of London examined about 134 000 cases of cancers occurring in the UK in 2010 and estimated how many could be attributed to sub-optimal, past exposures to 14 lifestyle and environmental risk factors.[3] They found that the 14 factors were responsible for 42.7% of the cancers cases (45.3% in men, 40.1% in women). The top risk factor by far for both men and women was smoking. Second came a lack of fruit and vegetables for men, and overweight for women. Following publication of the study Diane Abbot, Britain's shadow minister of health, criticized the UK's government's approach to tackling lifestyle-related health problems as completely inadequate. She could have equally said this about any government in the world.

Medical writers are already lined up in the battalions who are fighting the war against cancer. They prepare clinical trial reports, text for the medical education of and communications to physicians and healthcare workers, and, as medical journalists, text for the general public. There are even more opportunities to enlist the expert communication skills of medical writers. They could be looking to improve text for patients on the web, become involved with campaigns (e.g. Jamie Oliver's[5]) lobbying governments to take decisive action in influencing lifestyle, or they could work in government departments which will eventually have to

implement policies on who receives treatment paid for by the shrivelling public purse as well as possible lifestyle-connected adjustments to insurance contribution levels which will need to be communicated to the electorate. In any event, acquiring a broad knowledge of a medical area is the first step to opening new doors in the corridors which lead down the diverse paths of a medical writer's career.

References

1. http://en.wikipedia.org/wiki/Cancer.
2. Beck AH, Sangoi AR, Leung S, Marinelli RJ, Nielsen TO, Vijver MJ, West RB, Rijn MV, Koller D. Systematic analysis of breast cancer morphology uncovers stromal features associated with survival. Sci Transl Med 2011;3:108ra113.
3. Max Parkin D, Boyd L, Darby SC, Mesher D, Sasieni P, Walker LC. The fraction of cancer attributable to lifestyle and environmental factors in the UK in 2010 with a foreword by Professor Sir Richard Peto. 2011; 105(S2):Si–S81. http://www.bbc.co.uk/news/health-16031149.
4. http://scienceblogs.com/insolence/2011/12/personalized_gene-targeted_cancer_therapy.php.
5. http://www.jamieoliver.com/foundation.

Message from the President

Rita Wellens

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Dear MEW reader

Welcome to the first 2012 *Medical Writing* or MEW issue – another EMWA milestone to start off this stellar year. I hope you enjoy the new design and the thematic focus on oncology.

The theme of EMWA's upcoming 34th Spring conference in Cyprus is 'Paediatrics' and other vulnerable populations. The full programme can be accessed through our website www.emwa.org. You are hereby gently nudged into speedy registration to ensure a seat in your preferred workshops or any of the other star-studded events that mark this festive 20th jubilee conference.

A generous number of workshops are again on offer and professionals from around the globe and from agencies that define the rules and regulations in areas pertinent to the medical writing profession (including the European Medical Agency and the Medicines and Healthcare products Regulatory Agency) will share their unique expertise during plenary sessions, lectures and workshops. EMWA's founding veterans will highlight 20 years of EMWA's pioneering achievements.

You are always in great company with EMWA, the prime meeting ground for professional medical writers and healthcare communicators. On that note, I would like to plead your continued support to help grow our membership by sharing EMWA with a friend, colleague, or anyone considering medical writing as a career option. Do generously spread the EMWA passion and do freely distribute EMWA's sponsorship package available at http://www.emwa.org/Sponsor/SPONSORSHIP_OPPORTUNITIES_2012_FINAL.pdf.

EMWA welcomes and honours its many volunteers and their invaluable contributions – they are the driving force behind 20 years of EMWA progress and are key to EMWA's future.

Welcome to sunny Cyprus!

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The war on cancer – What is the enemy, and are we winning?

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Abstract

The so-called 'war on cancer' is now in its fifth decade. This article presents some facts and figures about cancer and the effort to treat it. It outlines updated thinking on the hallmarks and classification of cancer, and draws together published quotes from experts on the state of play in the fight against this disease.

Keywords: War on cancer, Cancer

Alongside the war on terror and the war on drugs, another war is going on. We have been fighting it for 40 years, and although we have made progress, it does not look as though we will win it any time soon. Yes, the 'war on cancer' has just entered its fifth decade. Many of us are involved in this war in some small way, part of the enormous army of medical staff, biological scientists, medicinal chemists, genomics scientists, clinical researchers, and pharmaceutical industry workers who are in a job because of cancer.

A 'war on cancer' was never declared in those exact words, but the term was widely used to describe the signing of America's National Cancer Act by President Nixon in 1971. The fighting gets more intense as the war goes on. According to the Economist (Medco),[1] the world pharmaceutical industry had around 900 cancer drugs in phases I–III development in 2010. The next biggest category, central nervous system, numbered about 350. Cancer accounts for about 13% of deaths worldwide – the same proportion as ischaemic heart disease, with stroke and cerebrovascular disease contributing a further 11% (WHO).[2] Yet, only just under 200 cardiovascular drugs are in pipeline. Cancer is huge business. However, attrition rates for new drugs are high (figures of 74–95% are quoted in the literature I found), with many promising new agents failing to meaningfully alter disease characteristics (phase I or II failures) or patient outcomes (phase III failures).

The explosion in the number of cancer drugs in development is being driven by an enormous growth in our knowledge of cancer biology. The more we know about the behaviour of cancer cells, the more potential drug targets emerge. We have known for some time that cancer is not one disease but many, but only in the last decade have we begun to realize how many. Take lung cancer. Lung cancer is one of the few diseases that have entered the era of personalized medicine – where treatment is selected according to the genetic makeup of the patient (or in this case, their cancer). There are two main types, small cell and non-small cell lung cancer (NSCLC, which accounts for about 80%).

NSCLC is subdivided into adenocarcinoma and squamous cell carcinoma: the type matters, in terms of both prognosis and treatment selection. Now, even this degree of classification is not enough. Adenocarcinoma of the lung is now analysed to see whether it has an activating mutation of EGFR (epidermal growth factor receptor), because patients with such mutations are much more likely to respond to tyrosine kinase inhibitors that target the receptor. The approval of a second targeted agent, crizotinib, will bring pressure to test for its target mutation also, the EML4-ALK translocation. In the case of advanced lung cancer, which is inoperable, all this information must be gathered from small biopsy samples – access to tissue for testing is a major issue in both clinical practice and clinical trials.

These targeted agents are not for everyone: a paper presented in 2011[3] found that only 17% of lung adenocarcinomas had an EGFR mutation and 7% had the EML4-ALK mutation. Twenty-two per cent had a KRas mutation, for which there is no drug approved yet. And 46% of tumours had none of the mutations known to drive lung cancer, so are not currently treatable with targeted agents. Even when targeted agents work, responses are relatively short-lived, and relapse (in advanced disease) is almost inevitable.[4] This is because of cancer cells' ability to change. When one pathway is blocked, their genetic instability means that it is not long before clones that have circumvented the blockage develop and thrive. This is helped by the fact that the network of signalling pathways in cells is extremely complex and has inbuilt redundancy, so several pathways can lead to the same result. Because of this, there is an increasing recognition that targeted

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agents (with rare exceptions) will be most useful as part of combinations, rather than acting as a single magic bullet as was once hoped.

Given that it has so many types and subtypes, and is so changeable, what makes cancer cancer? This question was addressed in an influential paper by Hanahan and Weinberg published in 2000, called *The Hallmarks of Cancer*.[5] They suggested that 'most if not all cancers have acquired the same set of functional capabilities during their development, albeit through various mechanistic strategies'. They described six hallmarks that set cancer cells apart from other cells: evading apoptosis; self-sufficiency in growth signals; insensitivity to anti-growth signals; sustained angiogenesis; limitless replicative potential (i.e. immortality); and tissue invasion and metastasis. In the years since, much more has been learned about the way in which cancer cells interact with and subvert non-malignant cells to serve their own ends. Tumours are not pure lumps of cancer cells growing in isolation. They are like dirty snowballs, full of white cells, cytokines, blood vessels and scaffold tissue as well as malignant cells. This mix is called the tumour microenvironment. Many researchers now believe that targeting the microenvironment is a promising new line of attack against cancer.

The year 2011 saw the publication of the eagerly awaited *Hallmarks of Cancer – The Next Generation*.[4] In their update to the original paper, Hanahan and Weinberg added two more hallmarks: deregulating cellular energetics (cancer cells can use metabolic pathways in ways that normal cells do not) and avoiding immune destruction (cancer cells can sabotage the immune cells that are sent to attack them). They also described two 'enabling characteristics' of cancer: genome instability and mutation, and tumour-promoting inflammation (a characteristic of the tumour microenvironment). They observe that: 'Given that the number of parallel signalling pathways supporting a given hallmark must be limited, it may become possible to target all of these supporting pathways therapeutically, thereby preventing the development of adaptive resistance'.

The hallmarks of cancer have been tremendously influential, but the emphasis on them was questioned in a 2010 commentary in Nature Reviews Cancer.[6] Yuri Lazebnik noted that of the six original hallmarks, five were also characteristic of benign tumours. These can grow extremely large but do not kill because they do not spread to other parts of the body. Only the capability for tissue invasion and metastasis is unique to malignant cells, he argued, continuing: 'If five of the proposed hallmarks of cancer are also characteristic of benign tumours, why has it become so widely accepted to consider these features in the same league as tissue invasion and metastasis, which are responsible for most cancer mortalities?'.

Lazebnik suggests that the terms 'cancer' and 'tumour' are too often used interchangeably. He says: 'Keeping in mind the difference between tumors and cancers might [also] help us to focus more on mechanisms underlying the key emergent property of cancers, their malignancy. This change might help to correct the situation in which, after producing nearly two million papers on cancer, we are yet to understand when and how cancer cells metastasize, or to learn the underlying mechanisms sufficiently well to have a sizable impact on cancer mortality'. However, Hanahan and Weinberg[4] say that they 'envision significant advances during the coming decade in our understanding of invasion and metastasis'.

So after 2 million papers and billions spent, where are we in the war against cancer? In an interview for the Naked Scientist,[7] Robert Weinberg said: 'Right now, advanced solid tumours from the colon and the pancreas, and the lungs are really formidable enemies, and we don't really know how to stop them. It would be nice – I think it's even realistic, to assume that 10 years from now, some of those tumours will be stopped in their tracks, caused to shrink. They may not be caused to totally disappear, but they will be kept at a small size that will render the patient fully normal in terms of his or her lifestyle, and will create a chronic – albeit, tolerable disease'.

References

1. Medco. R&D Directions, *Economist* [cited on 26 May 2011].
2. WHO Media Center. Fact Sheets 297 and 310.
3. Kris, *et al.* ASCO 2011. J Clin Oncol 2011.
4. Hanahan D, Weinberg RA. The hallmarks of cancer – the next generation. Cell 2011;144:646–74.
5. Hanahan D, Weinberg RA. The hallmarks of cancer. Cell 2000;100:57–70.
6. Lazebnik Y. What are the hallmarks of cancer? Nat Rev Cancer 2010;10:232–3.
7. The Naked Scientist 2010. Available from: http://www.thenaked-scientists.com/HTML/content/interviews/interview/1476/.

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Medical writing for cancer trials and submissions

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Abstract

Cancer is currently a high-priority area for drug development. Most cancers are immediately life-threatening diseases demanding urgent treatment and therapies are usually highly toxic. This poses a range of specific challenges for the ethical conduct of clinical trials in cancer, including difficulties with performing placebo-controlled studies, blinding, and restricting off-protocol treatments that may impact on trial results. Overall survival is the gold-standard efficacy endpoint for cancer trials, but reliable results can require a long duration of follow-up. Other endpoints such as time to progression and tumour response rates are therefore also used. Where treatments are targeted at specific disease mechanisms, biological endpoints may also be assessed. Safety evaluations require an understanding of the effects of the disease and its treatment on the likely observed events and abnormalities. A thorough understanding of the specifics of the disease under investigation and established as well as experimental approaches to its treatment can help medical writers to produce consistent and accurate documentation throughout clinical development.

Keywords: Cancer, Clinical trials, Medical writing

Introduction

Cancer has been a top priority in drug development for over 50 years. Cancer drugs, whether already marketed or in development, represent a critical part of the portfolio of most major drug companies, and may be the sole focus for smaller pharmaceutical and biotechnology companies. Annual healthcare spending on cancer exceeds $125 billion in the USA alone and is projected to exceed $200 billion within 10 years.[1]

Late-stage malignant cancers are invariably fatal without adequate treatment, and there is a large unmet clinical need for several common cancers (e.g. lung, colon, and breast). Although the advent of chemotherapy, as well as radiotherapy and improved surgical options has turned many cancers from a short-order death sentence into a chronic condition that is manageable over at least a period of months or years, many cancers, when not identified early enough, remain incurable, and others are difficult to treat adequately at any stage.

The law of diminishing returns is clearly applicable to cancer drug development, with fewer genuine breakthroughs, and ever-smaller incremental advances. Nevertheless, despite the high cost of developing new cancer medicines and the inevitability of political discussions about how extravagantly we as a society are prepared to fund treatments of increasingly marginal benefit, there is no sign as yet of reduced investment in cancer research, with annual research and development spending by the top 18 pharmaceutical companies exceeding €3 billion.[2] Companies are confronting the financial pressures imposed by the regulatory and patent protection environment by devoting resources more strategically, for example, by cancelling unpromising leads at an earlier stage and instead spending on increasing the range of indications for effective products.

Cancer is not a single disease. Even when cancer is exhaustively classified by variables such as primary tumour site and location and extent of metastasis, every individual patient's disease is unique. What all cancers have in common is that they are a consequence of genetic mutations that result in a loss of normal control over cell growth and division. Classical chemotherapy for cancer tends to use a broad cytotoxic approach, aimed at killing the tumour or stopping its growth before the treatment kills the patient. Combination chemotherapy regimes have been developed, often specific to cancer types, and treatment is often delivered in cycles, allowing breaks in treatment so that the patient can recover. In contrast, modern approaches are often based on our ever-increasing

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understanding of disease mechanisms. They attempt to target specific aspects of tumour biology in the hope that this is both more effective and less harmful. Tumour markers may consist of specific mutations or over-expression of specific genes such as growth factor receptors or signalling pathway components. Some markers are now being used prognostically to identify patients who are expected to respond to a particular treatment. As cancer classification becomes ever more sophisticated, treatment is destined to become increasingly personalized in the future. As the target populations for novel therapies become smaller, this will create further challenges for the design and conduct of studies, and for the financial viability of effective products.

Ethical issues

Cancer, being a life-threatening disease demanding urgent treatment, poses several ethical and technical problems for study design that would not usually apply to other indications.

Thus, it is unusual to find placebo-controlled trials of cancer drugs. On the one hand, the test drug is typically applied in combination with an established chemotherapy or radiotherapy regime so that in controlled studies, all groups receive at least an established standard of treatment. Similarly, 'best supportive care' may be offered to all patients in a (effectively) placebo-controlled trial. On the other hand, when new products are tested in isolation, this is generally done in patients who have failed to respond to several established treatments and who are not eligible for other standard treatment regimes.

For first-in-man and other phase I trials, cancer drugs are rarely if ever piloted in the usual healthy male subjects, as most cancer drugs are so toxic that the risk to individuals who will not benefit personally is unacceptably high. Early development is typically performed in patients with advanced, usually incurable disease. Toxicity, which may result in characteristic side-effects, also presents challenges for blinding of trials, and usually investigators (and sometimes subjects) are not blinded to trial treatment. Where 'softer' efficacy endpoints such as progression-free survival are used, it is common to have a blinded independent committee assess patient data such as X-rays and computed tomography (CT) scans to determine progression. It is important to present both investigator and independent assessments when both are available, and you should not be surprised that investigator assessments, regardless of treatment, tend to be more optimistic than independent assessments.

Trial treatment may be for a defined duration or number of cycles, and typically patients who are still alive or show response may continue receiving treatment beyond the planned trial duration. An overly strict definition of concomitant treatments that cancer patients may receive during a clinical trial is also ethically questionable. Compared with other indications, cancer trials demand greater tolerance of reduced compliance due to missed treatments, and you can expect a wider range of permissible concomitant therapies. Cancer specialists have considerable freedom to determine the best treatment for each individual patient, and when a new product is administered alongside a particular established chemotherapy regimen, recruitment should be restricted to patients who would otherwise qualify for that regimen. Once patients leave a trial, they may receive a wide range of further lines of therapy for their underlying disease. Ideally, data on second- and further-line treatments are collected during follow-up in order to evaluate whether such treatments have influenced efficacy results.

Early development

Dose-finding studies will typically evaluate dose-limiting toxicities, i.e. adverse events serious and frequent enough to prevent further administration of treatment, or to prevent dose escalation. Dose-limiting toxicities will vary between indications and treatments.[3] They should be carefully defined in the trial protocol in conjunction with the number of such events, or the number of patients experiencing such events. As a single excess patient with a dose-limiting toxicity can prevent dose escalation, the study population should closely reflect the intended treatment population.[4]

Efficacy evaluations

As most products in development aim to cure or at least extend life, rather than providing purely palliative care, cancer trials lend themselves to the most solid endpoint available – survival. The gold standard endpoint is overall survival, which is typically expressed as the proportion of patients alive at one or more time points, survival over time (e.g. Kaplan–Meier analysis), and mean or median duration of survival. If overall survival endpoints are defined in advance, data are often not mature by the time the report has to be written. For example, if most patients in both treatment groups remain alive it may be difficult to establish any treatment effect on long-term survival. Conversely, a treatment effect resulting in increased (or even

decreased) short-term survival may not have the same effect on long-term survival. Comparison of survival between treatment groups may also be confounded by protocols allowing cross-over from the control to the experimental arm after treatment failure. Mature survival data as well as updates of survival and efficacy analyses may have to be provided in the form of report addenda or revisions after the first report.

Rather than survival itself, a commonly used endpoint is time to progression, or progression-free survival time. In this case, patients undergo regular clinical or radiological investigations (or both) to determine indicators of disease progression, such as further growth of the primary tumour, or new metastases. Data are often assessed by a blinded, independent committee to overcome investigator bias and any lack of investigator blinding.

Response to treatment may be assessed according to common criteria such as the Response Evaluation Criteria in Solid Tumors (RECIST)[5] or WHO response criteria, alternatively disease-specific response criteria may be defined. The frequency of different response categories will be compared between groups and across studies, so response definitions should be standardized within a development programme. Surrogate or biological endpoints (such as tumour markers) may also be assessed, but are not adequate for licensing purposes.[6] Both the European Medicines Agency and Food and Drug Administration have published guidelines on acceptable endpoints in cancer clinical trials.

Follow-up can last almost indefinitely, and may range from simple survival follow-up at regular intervals until the patient has died to full data collection for patients continuing with trial treatment after having completed the defined treatment period.

New cancer drugs are increasingly targeted at specific molecular abnormalities of tumours. Specific pharmacodynamic endpoints may be evaluated alongside genetic characteristics of the patient population or detailed analysis of tumour characteristics, such as expression of specific genes, or presence of specific mutations. These may be compared among treatment groups, or be used to define subgroups, or (particularly at later stages of drug development) used as inclusion criteria.

Safety evaluations

Consequences of the severity of cancer and its treatment are a high rate of adverse events (AEs), serious AEs, and a high fatality rate. Differences between treatment groups may become exaggerated if the test drug is effective and results in increased treatment duration, whereas obvious differences in AE frequency may be apparent for established safety issues. Keep in-text AE presentations manageable by not presenting less common events that occur at similar frequencies across treatment groups in-text (these data should of course be available in the end-of-text tables). It is common to focus on related AEs or AEs of grade 3 or 4 by the National Cancer Institute Common Toxicity Criteria for Adverse Events (NCICTCAE)[7] criteria rather than overall frequencies. Depending on the study design, relatedness may be attributed to individual components of treatment or to treatment in general: the approach used will determine the best way to present related AEs.

As patient narratives (required for clinical study reports) are often not adequately planned in advance, you should seek agreement with the study team as early as possible on criteria for narrative writing, and if necessary explain this policy in the report. There is no regulatory requirement to write narratives for Serious Adverse Events (SAEs) or deaths that were clearly unrelated to the product but unless criteria are set in advance, there is the risk that you will be asked to write large numbers of narratives for patients dying, entirely expectedly, of their underlying disease. A consistent policy should be applied to all reports for any given product and indication.

Laboratory evaluations can be difficult to interpret: the underlying disease and co-morbidities in the study populations can cause wide variations in several laboratory parameters. Individual frequencies of abnormalities and shifts by severity are more informative than mean or median values. You should also consider the possible effects on laboratory evaluations of any differences in time on study between treatment groups, or established toxicities of the trial drug.

Concluding remarks

This is not a comprehensive overview of all of the specific challenges you may face as a medical writer working in the cancer field. All the skills you apply when writing about other indications apply to writing about cancer. Medical writers working in this field are, however, expected to have some understanding of the molecular basis of cancer, the principles underlying cancer therapies, and to have an awareness of some of the specific issues that affect the conduct and evaluation of cancer studies. Although a medical writer has little direct influence on the business decisions made for individual products, this understanding can help

you to prepare high-quality documentation to ensure that the decisions on a product's future, whether made by regulators or the board of directors, are based on well-presented and accurately interpreted evidence.

References

1. Mariotto AB, Yabroff KR, Shao Y, Feuer EJ, Brown ML. Projections of the cost of cancer care in the United States: 2010–2020. J Natl Cancer Inst 2011;103:117–28.
2. http://www.ecancermedicalscience.com/cache/pdf/ECRM%20LR%20Survey.pdf.
3. Le Tourneau C, Razak AR, Gan HK, Pop S, Diéras V, Tresca P, *et al.* Heterogeneity in the definition of dose-limiting toxicity in phase I cancer clinical trials of molecularly targeted agents: a review of the literature. Eur J Cancer 2011;47:1468–75.
4. LoConte NK, Cleary JF, Bozeman J, Wilding G, Alberti D, Setala A, *et al.* Predictors of dose limiting toxicities in phase I clinical trials: the impact of age, comorbidity, and other clinical and non-clinical factors. J Clin Oncol 2008;15S:9525.
5. Therasse P, Arbuck SG, Eisenhauer EA, Wanders J, Kaplan RS, Rubinstein L, *et al.* New guidelines to evaluate the response to treatment in solid tumors. J Natl Cancer Inst 2000;92:205–16.
6. Schilsky L. End points in cancer clinical trials and the drug approval process. Clin Cancer Res 2002;8:935–8.
7. http://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03_2010-06-14_QuickReference_5×7.pdf.

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Bar Jokes from Graham Guest

A split infinitive decides to slowly walk into a bar.
It's a bar that a terminal preposition walks into.
Two misplaced apostrophe's walk into a bar.
And a conjunction walks into a bar first.
A reflexive pronoun walks itself into a bar.
An ellipsis […] a bar.
A diaeresis walks into a bär.
A Swedish accent walks into a bår.
A tag question walks into a bar, doesn't it?
An anagram walks into a bra.
A spoonerism baulks into a wahr.
A malapropism stalks into a car.

Graham Guest (graham@guest.org.uk) offers coaching for simplicity, grammar coaching, and consulting on the English language, continuing professional development and lifelong learning. He has a background in the management and administration of international professional associations, and experience as a career coach and a psychological counsellor.

Developing a treatment for ovarian cancer

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Abstract

Ovarian cancer is a really nasty disease. Although, like most cancers, it is curable if caught early enough, in practice it is not usually diagnosed until it is too late for curative treatment. It initially responds well to treatment and patients can go into remission for months or even years, but it usually returns and ultimately proves fatal. In this article, I describe a project I have been working on designing clinical trials with a high-tech immunological product, Cvac™, which uses modified autologous dendritic cells to prime the patient's immune system to attack ovarian cancer cells. We hope that Cvac™ will prolong the period of time in which women can remain in remission from ovarian cancer, but we will have to wait for the results of the clinical trials to know whether it does.

Keywords: Cancer, Immunology, Clinical trials, Outcome measures

There are many reasons why I love my job, but one of them is that I sometimes get to work on projects which are not only interesting, but also have the potential to make a real difference to human health. In this article, I would like to tell you about a project I have been working on recently which fits firmly into that category.

One of the reasons why I originally wanted to become a scientist was that I had this crazy idea that I might make important discoveries that would make the world a better place, like finding a cure for cancer or something like that. Well, I am never going to do that in the way I originally imagined, as my career as a lab scientist was over long before I ever got to do anything useful. Those of you who have sat within earshot of me in the bar at an EMWA conference will doubtless have heard the story of the little phosgene gas incident that was partly responsible for cutting my lab career short.

But of course 'finding a cure for cancer' is not as simple as just making a discovery in a lab one day. It is a hugely complex multidisciplinary process, involving lab scientists for sure, but also doctors, statisticians, medical writers, clinical project managers, etc. Potential cures must not only be discovered, but also investigated thoroughly in a series of laboratory experiments, animal studies, and of course clinical trials in humans. Every part of that complex process is necessary if a discovery is ever going to make it from the lab to clinical use.

So even though I never got to discover anything of interest in my lab career, I now find myself contributing to the process of improved cancer treatments in my work as a clinical trials statistician, helping to design trials that may show a potential new treatment really does have clinical benefit. I will settle for that. Although I got there by an extremely roundabout route, it is remarkably close to what I thought as a child that I'd do when I grew up.

I should point out at this point, although I am sure you already knew, that there is no such thing as a 'cure' for cancer. Cancer is not just one disease, but a generic term for a whole series of different pathological conditions. So a treatment that may have huge benefits for one particular cancer may be useless for other types of cancer. Think of tamoxifen, for example, which has been a great advance in the treatment of breast cancer, but is not much use for anything else. And it is pretty rare for any of the treatments currently at our disposal, with the exception of surgery, to be anything like a 'cure'. Although genuine cures may come one day, the best we can hope for at the moment for those patients unlucky enough not to have been cured by surgery is to prolong the time in which they can enjoy a reasonable quality of life before the cancer finally gets them. But even that, of course, is a thoroughly worthwhile aim.

So what is this exciting project I have been working on recently? It's a pleasingly hi-tech treatment called Cvac™, produced by the Australian biotech company Prima BioMed

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(http://www.primabiomed.com.au/), which we are trialling for patients with epithelial ovarian cancer.

Ovarian cancer is a really nasty disease. Like most cancers, it can be cured with surgery if caught early enough, but becomes metastatic and ultimately fatal if it is not. But unlike many other cancers, it is rare for it to be caught early enough. As the tumour is on an internal organ, it is not obviously noticeable, and as initial symptoms are non-specific, such as abdominal pain or irregular periods, they are often not identified as being due to cancer. So usually, by the time the symptoms have become severe enough that the diagnosis is made, it is already too late for surgery to have a good chance of being curative.

Now, the good news is that ovarian cancer often responds well to chemotherapy (a combination of platinum-based drugs and a taxane is usually the treatment of choice), and patients can often go into remission and be quite healthy after initial chemotherapy. But this happy state of affairs does not usually persist, as the disease usually recurs after a period of months or at best a few years. The recurrence may also respond well to chemotherapy, but by that stage future recurrences at ever-decreasing intervals are more or less guaranteed. One large trial that reported in 2009 found a median progression-free survival (time until either disease recurrence or death) of 16 months and a median overall survival (time to death) of 44 months in patients with stage III or IV ovarian cancer after initial surgery.[1]

Cvac™ is unusual in that it is designed to treat patients while they are in remission, with the hope that remission will be prolonged. The way it does this is really quite cunning. Cvac™ is an immunotherapeutic product, which is designed to stimulate the patient's own immune system to fight the cancer. The idea is that once the immune system is primed to attack the cancer cells, then any recurrences will be destroyed by the immune system before they grow to the point where they cause trouble.

So how does it work, exactly? Well, it relies on the fact that many ovarian cancer cells over-express a surface protein called mucin 1. Normal mucin 1 appears in some healthy cells, but a modified form is expressed in cancer cells. The main difference is that mucin 1 is normally extensively glycosylated in healthy cells, but much less so in ovarian cancer cells. The more exposed mucin 1 in the cancer cells is therefore an easier target for immunological attack.

And how is the immune system primed to attack mucin 1? Well, this is where it gets quite tricky, because Cvac™ is an autologous cellular product, which has to be individually prepared for each patient. The patient has to undergo leukapheresis, during which her mononuclear cells are harvested, which are subsequently differentiated into dendritic cells. The dendritic cells are then cultured, together with a fusion protein of mannan (which acts as an adjuvant) and modified mucin 1. Thus Cvac™ is autologous dendritic cells primed with modified mucin 1. It must, of course, be injected back into the same patient from whom the cells were harvested in the first place.

The modified dendritic cells are now in a position to activate the T cells of the immune system to recognize the modified mucin 1, and kill any cells that are expressing it in any quantity, which hopefully includes ovarian cancer cells. That is probably a hideously simplified explanation of how it really works, as I do get a bit hazy on some of the details of complex immunology, but I dare say that it will do as an overview.

I have had the pleasure to work on two clinical trials with Cvac™. They are still at an early stage, so we do not yet know whether the product works as well as we hope it will (or even at all). We have recently finished recruitment into a phase II study in about 60 patients, although it will be another year or two before the study is complete. We probably will not learn very much about efficacy from such a small study, but we might see some hint that the product works if it works well. We should, however, learn about the safety of the product, and initial results seem to be very promising, with no sign so far of the sort of toxicity that might be expected from conventional cancer chemotherapies. This is the great advantage of using such a precisely targeted therapy, as opposed to the sledgehammer approach of cytotoxic chemotherapy.

We will soon be starting a phase III study, and being involved (as the project statistician) in the design of that study has been fascinating. We have thought about the design very carefully, and have received advice from both the European Medicines Agency and the American Food and Drugs Administration on the study. One of the most important questions we have had to grapple with is the choice of primary endpoint. Phase III studies in cancer typically use either progression-free survival or overall survival as their primary endpoint, and the choice is not straightforward. Overall survival has the benefit of being a thoroughly objective and clinically relevant measure, and is preferred by regulators. In contrast, using progression-free survival means that you have results sooner,

which is advantageous not only commercially but also ethically, in that a treatment that may have significant benefits can be brought to patients sooner. Furthermore, you could make a strong argument than when patients are in remission and enjoying a good quality of life, the time they spend in remission before the disease returns is highly clinically relevant, perhaps even more so than overall survival. The time spent between when incurable cancer returns and death is not much fun, as anyone who has lost a friend or relative to cancer will be aware. One could argue (and I absolutely would) that there is little benefit to prolonging that period of time, whereas prolonging the time spent in good health until the disease returns is self evidently of great benefit.

In the end, that last argument won, and progression-free survival will be the primary endpoint of the trial. The trial will be starting very soon (and perhaps will have started already by the time you are reading this), but will take a few years before we see the results. If the results are as we hope they will be, then this could transform the outlook for patients with ovarian cancer. Being a part of that is the sort of thing that makes going to work seem all worthwhile.

Reference

1. Bookman MA, Brady MF, McGuire WP, Harper PG, Alberts DS, Friedlander M, *et al.* Evaluation of new platinum-based treatment regimens in advanced-stage ovarian cancer: a phase III trial of the gynecologic cancer InterGroup. J Clin Oncol 2009;27:1419–25.

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The evolving landscape of medical education in oncology

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Abstract

The field of oncology is continuously evolving. The way in which cancer is diagnosed, staged, and managed has changed so much in the last decade, and awareness of the need for a 'personalized medicine' approach to patient management is growing. In the age of 'information overload' and tight time and budgetary restrictions, medical education plays a key role in ensuring that healthcare professionals involved in the care of patients with cancer are informed of the latest treatment advances and shifts in thinking around optimal patient management. The way in which medical education is targeted, designed, and delivered in the oncology setting has had to evolve in line with the changes in the oncology landscape. This article addresses some of the emerging trends in medical education, particularly those that are key drivers of the way in which medical education is executed in the oncology arena. It explores who is now being targeted through medical education, how medical education is being designed and delivered, whether medical education can be delivered strategically, and what impact tighter regulations and budgetary constraints have had on the way in which medical education can be executed.

Keywords: Oncology, Medical education, Adult learning styles, Communication strategy, Accreditation, Compliance

Introduction

The field of oncology is continuously changing. The findings of a single clinical trial have the potential to transform clinical practice and, as a consequence, the *right* treatment approach today may not be the *best* approach for tomorrow. In the age of resource restrictions, where physicians' time is precious, keeping up-to-date with the latest treatment advances can be challenging. UC on the whole, oncologists and other healthcare professionals working with patients with cancer do strive to keep abreast of the latest data. Compared with other specialties, oncologists are 'early adopters' and are willing to try out novel strategies and technologies in the clinical trial setting that they believe might bring benefit to their patients. Many patients with cancer can often only expect to survive one or two years after diagnosis, and therefore any treatment that can offer an incremental benefit over standard of care, even if that benefit is only a couple of months, is one worth exploring. The combination of these two factors means that oncologists feel compelled to be 'ahead of the curve' with respect to treatment advances. They need to be able to access the information that will allow them to be so in an easily digestible and convenient way, so this learning can take place around time in the clinic.

Furthermore, in the last decade or so, advances in our understanding of the pathogenesis of cancer, as well as the prognostic and predictive markers that can dictate patient outcomes, have led to significant changes in the way in which cancer is diagnosed, staged, and managed. Clearly advances have been more prominent in some cancers than others. The use of tyrosine kinase inhibitors in chronic myeloid leukaemia has, for example, transformed a fatal disease into a chronic, manageable condition. In head and neck cancer, on the other hand, there has been no significant treatment breakthrough in the last 30 years, and researchers are still exploring therapeutic options that might prolong survival in these patients. However, overall, advances in our understanding about how cancer develops have led to an era of 'personalized medicine', in which physicians are presented with the challenge of implementing increasingly complex treatment strategies, and making increasingly complex treatment decisions. Although in the Edwin Smith Surgical papyrus, which dates from the 17th century BC, eight cases of breast cancer are described as being removed with a 'fire drill', these days physicians need to choose the optimal combination of surgery, radiotherapy, chemotherapy, and targeted therapies to offer their patients the best chances of

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survival. No one size fits all and, as a result, physicians need to assimilate an enormous amount of evidence in order to make the right treatment decision for the right patient. This can be challenging in the era of 'information overload', where an abundance of information often makes the task of filtering out the noise to reveal best practice difficult.

As a result of these challenges, there is an increasing need for medical education that builds on the training offered to physicians in medical school and keeps physicians abreast of the important treatment advances and changes in treatment guidelines. There is also the need to expose them to the latest thinking around what optimal patient management is and how to manage their budgets to ensure that this optimal care can be delivered to their patients consistently. The term 'medical education' captures any educational activity that has been designed to maintain, develop, or expand the awareness, understanding, skills, or performance of healthcare professionals. In some cases, this medical education is provided by medical societies, such as the American Society for Clinical Oncology (ASCO) or the European Society for Medical Oncology (ESMO), or by specialty societies, such as the Association of Cancer Physicians (ACP) in the UK. In other cases, this medical education is supported by unrestricted educational grants from pharmaceutical and device companies active in the oncology arena. Although some critics have challenged the objectivity of industry-sponsored educational programmes, the general consensus is that academic medicine and industry cannot operate independently of each other. Both parties play a unique and crucial role in driving the advancement of healthcare through the delivery of educational programmes.

Who are we trying to educate?

Historically, physicians have been the primary target for medical education; however, the changing healthcare environment means that other important targets are emerging, such as specialist nurses, pharmacists, patients, carers, and even payors. Pharmaceutical and device companies are therefore increasingly investing resources into delivering medical education to these new target groups. This is particularly relevant in the field of oncology. Specialist nurses play a key role in patient management in many countries, and are often in the best position to monitor and manage side effects. Pharmacists often play a key role in determining the treatments that can be prescribed, as well as taking a more practical role in reconstituting drugs for intravenous administration. Patients are encouraged to take an active role in making the decisions about their treatment, and carers often need advice on how to best support the patient during and after treatment. And finally, payors influence what treatments are available to a particular patient. All these different groups of stakeholders need to be educated in order for a treatment advance or shift in thinking to emerge in clinical practice.

Educational programmes that help patients understand, either directly or through their nurses or carers, their diagnosis, treatment options, possible side effects, and the importance of treatment adherence are valuable tools that can enhance the partnership between healthcare professionals and patients and thus promote better care and outcomes. Traditional channels used to communicate with physicians, such as peer-reviewed publications and scientific symposia at key congresses, are not appropriate for nurses, patients, or their carers. These traditional approaches have therefore been accompanied by more innovative approaches that reach out to these wider target audiences, such as electronic side-effect management toolkits for nurses and support websites or information booklets for patients and carers. An effective medical education programme evaluates which stakeholders influence treatment decisions, and targets specific educational messages to these stakeholders through the most appropriate communication channels.

In recent years, we have also seen an increased focus on the role of the multidisciplinary team in decision-making. In oncology, effective treatment strategies often require close collaboration between different specialties, and thus different mind-sets. The management of prostate cancer, for example, is traditionally led by urologists, as surgical and hormonal treatments have long been the mainstay of treatment. However, with the launch of new chemotherapy regimens offering survival benefits in patients with hormone-refractory prostate cancer, it is becoming increasingly important to involve oncologists at the earliest possible stage. This ensures that the treatment plan devised incorporates surgery, hormonal therapy, chemotherapy, and supportive care strategies, where appropriate. Medical education can play a key role in facilitating dialogue between these different specialties, creating opportunities for discussion on common issues and challenges. In this way, sometimes medical education is merely about bringing people together so they learn from each other.

Are all learners the same?

The delivery of effective medical education should be guided by a number of key principles, and these must be borne in mind when developing medical education programmes in the field of oncology. Firstly, learners must acknowledge that they need to learn, and to clearly understand what they are going to learn, in order to benefit from training. The training must therefore be designed with clearly stated and relevant objectives, so that the learners can understand what they need to learn, how the education/training addresses these needs, and how the training will benefit them. Secondly, learning cannot be purely didactic in nature, it must also allow the learner to experience what is being taught. Effective medical education should therefore comprise a practical element that allows learners to practice what they have learnt. Finally, medical education needs to take into account the different ways in which people learn and their preferences with respect to how they want to learn.

Generally speaking, the greatest pull for a learner to attend an educational event is the topics that are going to be covered, and who will be speaking about these topics. Key thought leaders (KTLs) remain the most effective way to deliver education to job-in physicians. As a result, the first thing to consider when developing an education programme is who your audience is most likely to want to learn from, and then involve these key individuals, wherever possible, in delivering the education. There are a number of ways, however, that learners differ. A deeper understanding of the different adult learning styles, and the design of medical educational programmes that address these different learning styles, is another key way in which the delivery of medical education has evolved over recent years.

In 1986, Honey and Mumford proposed that there were four main adult learning styles: activist, reflector, theorist, and pragmatist. An activist likes new experiences and ideas, and enjoys collaborative group learning. A reflector likes considering different perspectives, and enjoys listening to others. A theorist likes step-by-step analytical approaches, and enjoys testing learned ideas by applying them to practical situations. A pragmatist likes ideas with immediate applicability, and enjoys hands-on testing and practice. Any medical education programme must therefore speak to these different types of learning and incorporate a mixture of plenary presentations, case-study-based discussions, practical 'hands-on' sessions, and interactive breakout workshops. A recent standalone event supported by an educational grant by a pharmaceutical company marketing a number of oncology products, for example, used a mixture of keynote plenary presentations by KTLs to provide an overview of the disease area and treatment landscape, breakout workshops to address clinical challenges, case-study-based discussions to identify the most appropriate treatment strategy in hard-to-treat patients, and interactive keypad voting throughout the event to assess attendee opinions and how these opinions changed as a result of the educational programme. By providing this variety in the way in which medical education is delivered, the attendees are more likely to retain the educational messages inherent in the programme.

Crucial to the success of any educational activity is also the skill of the educator. In a setting in which peer-to-peer education is the most effective way of delivering education, often educational programmes need to be implemented by KTLs who have a varying level of experience as educators. An important step in the preparation for the educational activity is therefore training the trainer. Not only is it important to involve the trainers at the outset, when the programme is being developed, so that they can input into the educational objectives of the activity, it is also crucial that they are provided with guidance on how to best present or facilitate particular sessions, so the overall programme is as impactful as possible. Clearly, linking this guidance with the educational content of the activity can help to deliver any necessary training to the trainer in a setting in which they are more likely to be receptive to it.

How has the digital era impacted on medical education?

The use of digital media is also becoming much more commonplace in medical education. Increasingly healthcare professionals, particularly younger physicians, are turning to the Internet in order to remain informed on recent treatment advances or changes in treatment guidelines. As such, the Internet is becoming an important way of connecting with and engaging healthcare professionals. Oncologists who, like most healthcare professionals, have substantial constraints on their time, and restrictions on financial support to attend congresses, are no longer able to attend every congress or read every important medical journal. In response, not only are scientific symposia run at these congresses increasingly also broadcast as webcasts and/or podcasts, but numerous online services have also sprung up that attempt to summarize the findings of recent research in an easily

digestible format. This trend has been further strengthened by the explosion, in recent years, in the use of Smartphones and tablet PCs in the medical setting. Physicians now receive updates via RSS feeds delivered to their phones, browse journals via iPhone/iPad applications, and have access to online textbooks and other resources at the patient's bedside.

In addition to offering physicians a convenient way of accessing education, the digital delivery of medical education also has other advantages. Firstly, in the digital environment, it is easy to collect information about the individuals taking part in the training – their experience, awareness of certain topics, and opinions on controversial issues. This can provide invaluable information about educational needs, as well as allowing the educator to map out how opinions are changed, if at all, as a result of the educational programme. Monitoring the online activity following a digital educational event can give an indication of the 'stickiness' of the educational programme, tracking how the educational messages are being received and how they shape opinion in the long run. Secondly, digital education creates a forum in which the individuals taking part in the training event can discuss the topics at hand either during or after the event. It also allows them to forward the link to the training to their colleagues or post it online through social media platforms. Medscape remains one of the most popular online resources for medical information and their oncology section (http://www.medscape.com/oncology), for example, offers healthcare professionals access to numerous continuing medical education (CME) accredited educational modules on oncology topics and allows them to email a link to the module to a colleague or share it via Facebook™ and Twitter™.

Furthermore, in recognition of the fact that physicians prefer to learn from their peers, numerous healthcare sites are now offering social networking, discussion forums, blogs, and other interactive features, all of which encourage dialogue and create vibrant online communities in which physicians can share their expertise. In many cases, therefore, medical education is now not solely about delivering education in the traditional settings of faculty-led scientific symposia and other standalone educational events, but also about providing online forums in which physicians can take the lead in driving medical advancement by sharing opinions, posting case studies, and debating controversial issues.

Patients too are increasingly looking to the Internet for information about their disease and possible treatments. The concept of the 'informed patient' is commonplace in modern healthcare. It is particularly prominent in oncology, where the diversity in different treatment strategies, with different risk–benefit ratios, calls for a greater contribution from patients in guiding the way in which their disease is managed. The abundance of health-related websites has necessitated the need for tighter control over the content of these websites, and organizations, such as the Health On the Net (HON) Foundation, are at the forefront of the drive to improve the quality and transparency of health information posted online. In oncology, patient and carer support websites can be important tools that empower patients and their carers to become more involved in the management of their disease. Some of the best websites now offer patients forums to share their experiences, gain from the insights and experiences of other so-called 'expert patients', and download useful tools, such as treatment diaries and information leaflets. Furthermore, a deeper understanding of patient segmentation has also allowed website developers to tailor online experiences to specific users; targeted educational messages can be delivered to specific, identified patient segments, thereby maximizing the benefit of the information in the eyes of the patient.

How much can we allow education to be defined by strategy?

Given the breadth of different audiences being targeted through medical education activities in oncology, and the variety of different communication vehicles through which medical education is delivered, it is becoming increasingly important to ensure that the *right* educational messages are delivered to the *right* audience through the most appropriate communication channel. Designing impactful educational messages depends on gaining an in-depth understanding of what physicians currently think about a particular topic, as well as what, as educators, you would like them to eventually think about the topic. Educational messages should aim to bridge this gap between current and desired thinking, shifting healthcare professionals' mind-sets, so they can recognize unmet needs, understand the place of novel management approaches, and implement changes in patient management.

As mentioned before, medical education is both provided by medical societies and supported by unrestricted educational grants from pharmaceutical and device companies. In the case of the latter, the delivered medical education must

address the educational needs within the field in the context of the commercial strategy and vision for the products marketed or being developed within that company. This means that the educational messages delivered through industry-sponsored educational events need to be driven by a clear and robust communication strategy. This strategy should underpin all the medical educational activities for a particular product. The importance of strategic communications is especially evident in oncology. Given their mechanisms of action, many new agents are concurrently investigated for numerous different oncology indications. As the strategic considerations for these agents likely differ from one indication to the next, the educational messages must be tailored to the indication, addressing the particular issues and unmet needs of that indication and the likely different target audiences involved. Yet, at the same time, it is also important that all educational messages for a particular agent are aligned, and that the messages developed for one indication do not contradict or undermine the impact of messages in another.

The strategic delivery of educational messages needs, of course, to be done with sensitivity. Physicians involved in delivering educational programmes, as faculty members, need to be given the freedom to express their own opinions, and highlight what they believe the audience needs to know. Transparency is key. It is therefore crucial that these faculty members are involved from the outset, in terms of defining the educational objectives of a particular activity and discussing the most appropriate way of achieving these objectives.

What can we do, and what can we not do?

As the means through which to deliver medical education have become more inventive and diverse, and the healthcare audiences targeted broader, those designing and implementing medical education programmes face some significant challenges. Tighter control over the format, content, and delivery of medical education means that special care must be taken to ensure that all medical education initiatives are designed in line with the codex requirements of the country in which they are being delivered. Not only is there a need to create 'fair and balanced' educational programmes, it is also crucial that appropriate measures are taken to ensure that there is full transparency with regard to industry sponsorship and author/speaker conflicts of interest.

Perceptions of bias in industry-sponsored medical education have led to an increasing importance of the bodies that govern and regulate CME or continuing professional development (CPD), such as the Accreditation Council for Continuing Medical Education (ACCME). ACCME's mission is:

> the identification, development, and promotion of standards for quality CME utilised by physicians in their maintenance of competence and incorporation of new knowledge to improve quality medical care for patients and their communities.

By providing accreditation for medical education programmes, bodies such as ACCME address concerns over objectivity and independence of these educational programmes from commercial goals, and ensure that medical education is delivered in an environment free from brand promotion. However, it is important to note that non-accredited medical education can still be of very high quality. Strict Codes of Conduct defined by bodies, such as the International Pharmaceutical Congress Advisory Association (IPCAA), European Federation of Pharmaceutical Industries and Associations (EFPIA), and the Association of the British Pharmaceutical Industry (ABPI) mean that all major pharmaceutical and device companies have entire medical and legal teams dedicated to ensuring that all of their sponsored medical education activities are fully compliant, fair balanced, and non-promotional in nature.

What should we do as educational grants shrink?

In our current global economic crisis, many pharmaceutical and device companies are finding that their budgets for medical education have been cut dramatically. As a consequence, there is increasing pressure to deliver medical education in a cost-effective manner, and to demonstrate return on investment for these educational activities. In many cases, it is now a requirement to demonstrate the success of a medical education initiative by assessing outcomes against pre-specified key performance indicators, thereby determining whether the objectives of the initiative have been met, and whether the money has been 'well spent'.

Budget restraints also mean that medical education agencies need to become more creative in the way in which they deliver medical education. In order to spare the expense of flying out physicians to a standalone educational events, as well as reducing the demands on the physicians' time, medical

education is now often delivered online. While virtual meetings will never be able to completely replace face-to-face meetings, as most people get much more out of a real meeting versus a virtual one, they can deliver educational messages to a much wider audience and allow this audience to take control over when and where they learn.

Conclusions

In summary, medical education plays a crucial role in the field of oncology, providing invaluable educational resources that aim to further medical advancement and optimize patient care and outcomes. Effective medical education acknowledges that numerous healthcare professionals are involved in patient care and that, therefore, educational messages need to be delivered to nurses and pharmacists, as well as physicians. It also takes into account the fact that the collaborative working between different medical disciplines is critical to effective patient care, and provides forums for dialogue between these different specialties. Effective medical education also acknowledges that different people like to learn in different ways and therefore attempts to deliver the education in a variety of different format to speak to these differences. It also depends on the delivery of well-thought-out educational messages that speak to the educational needs of the audience and precipitate shifts in thinking that drive forward medical advancement. Effective medical education also acknowledges that many healthcare professionals can no longer attend one-off educational events and want to access educational resources online, wherever they have a spare moment. The challenges posed by tighter restrictions on the way in which medical education is being delivered, and the budgets available, means that it is becoming increasingly important to think creatively when devising medical educational initiatives. They must target the *right* messages to the *right* audience, but should do so in an unbiased and balanced manner. And, most importantly, they must never lose sight of the ultimate goal of medical education – to drive improvements in patient care.

Author information

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Some considerations on the safety evaluation section of clinical study reports for studies with anticancer drugs

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Abstract

The International Conference on Harmonisation (ICH) guideline E3 describes the structure and content of clinical study reports (CSRs). However, this standard structure should be interpreted according to the type of study and data, including modifications to the table of contents and adding, deleting, or rearranging some of the contents defined by the guideline to better display the results and improve the communication of information. One example is the Safety Evaluation section of CSRs for studies with anticancer drugs. A more logical, reader-friendly way of showing data is to reverse the order and numbering of the Safety and Evaluation sections, presenting Safety Evaluation as Section 11 (main endpoints are all of them safety variables) and Efficacy Evaluation as Section 12. In addition, phase I CSRs in oncology require new sections describing results regarding main endpoints: i.e., dose-limiting toxicities, the maximum tolerated dose, and recommended dose for phase II trials. Finally, adverse events that can be measured as laboratory abnormalities (e.g. neutropenia, thrombocytopenia, transaminase increases, etc.) may be underreported if they are only listed based on the adverse events rows of the case report form. Hence, laboratory abnormalities are better reported by objective laboratory results.

Keywords: Clinical study reports, Phase I, Safety, Dose-limiting toxicities, Recommended dose, Oncology

The International Conference on Harmonisation (ICH) guideline E3 describes the structure and content of clinical study reports (CSRs) of studies evaluating therapeutic, prophylactic, or diagnostic agents.[1,2] The guideline has not been revised since it was issued more than 15 years ago. However, in June 2011, the ICH Steering Committee endorsed a concept paper and the establishment of an implementation working group to prepare a question-and-answers (Q&A) document on the guideline.[3] The aims of the Q&A document are to align ICH E3 with requirements of the Common Technical Document (CTD), particularly those for electronic submission, and to clarify other issues encountered since the implementation of the guideline in 1996. One of the aspects being discussed is whether ICH E3 is a guideline or a template. Some companies or sponsors create CSRs that maintain the table of contents and all elements defined by the ICH E3, whereas other companies or sponsors interpret ICH E3 more broadly, including modifications to the table of contents and adding, deleting, or rearranging some of the contents defined by the guideline in order to better display the results and improve the communication of information. In fact, ICH E3 states in its introduction:

> Each report should consider all of the topics described (unless clearly not relevant) although the specific sequence and grouping of topics may be changed if alternatives are more logical for a particular study.

One example where ICH E3 needs to be followed in a more flexible way is the Safety Evaluation section of CSRs for studies with anticancer drugs. The main aim of phase I clinical trials with anticancer agents is to find the maximum tolerated dose (MTD) and recommended dose (RD) for phase II trials, based on a dose escalation design which involves the reporting of dose-limiting toxicities (DLTs).[4] Therefore, the reader of the CSR of a phase I trial in oncology would expect to find first the results about how DLTs, MTD, and RD were found. However, DLTs are part of the safety evaluation and, therefore, according to ICH E3, they

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should be described in Section 12 of the CSR, after the efficacy results have been described. Furthermore, these are dose-escalating trials in which cohorts are based on the toxicity found with dose increments. If efficacy is described first, a lot of cross-references have to be made to the Safety Evaluation section in order to understand the rationale for cohort distribution. Although, the use of electronic PDF submissions with hyperlinked tables of contents may reduce the concern about whether efficacy appears before safety in this type of studies, a more logical and reader-friendly way of showing the data is to reverse the order and numbering of these sections, presenting the Safety Evaluation as Section 11 and the Efficacy Evaluation as Section 12. In these cases, it is useful to add a note at the beginning of the CSR stating the following:

> This report has been written according to the ICH Harmonised Tripartite Guideline E3: 'Structure and Content of Clinical Study Reports' (ICH step 5 version, July 1996). However, Sections 11 (Efficacy Evaluation) and 12 (Safety Evaluation) have been reversed and renumbered in accordance with the primary and secondary objectives of this phase I clinical trial.

This modified structure has been used in several CSRs submitted to the European Medicines Agency (EMA) in marketing authorization applications (MAAs) and has been accepted by the EMA in the validation process.

In addition to the change in the order of the safety and efficacy evaluation sections, phase I CSRs in oncology require a new section with a resumé of results regarding DLTs, MTD, and RD. The ICH E3 guideline does not in fact define this. Table 1 shows an example of a table of contents for a Safety Evaluation section in this type of CSR.

Another issue that affects the safety sections of CSRs in oncology concerns the Clinical Laboratory Evaluation section (Section 11.5 in the example table of contents shown in Table 1). Chemotherapy works by destroying very active cancer cells that grow rapidly. Unfortunately, chemotherapy also affects normal cells that grow rapidly such as blood cells forming in the bone marrow, cells in the hair follicles, or cells in the mouth and intestines. When a patient is undergoing chemotherapy to treat cancer, a lot hinges on the blood test results that precede each intravenous infusion. Low blood counts can indicate serious side-effects, including fatigue, bruising, and vulnerability to infection, and can also mean that treatment must be postponed while the patient's body recovers normal values or the dose has to be reduced in subsequent treatment cycles. Therefore, laboratory findings are of extreme relevance in oncology studies, and hematological and biochemical laboratory abnormalities have to be discussed in separate subsections in the Clinical Laboratory Evaluation section of the CSR.

Table 1: Structure for Safety Evaluation section in a clinical study report of a phase I clinical trial with an antitumor agent

11 Safety Evaluation
11.1 Extent of Exposure
11.1.1 Cycles received
11.1.2 Dose delays
11.1.3. Dose reductions
11.2 Maximum Tolerated Dose And Recommended Dose For Phase II Clinical Trials
11.2.1 Dose level I
11.2.2 Dose level II
…
11.2.x Dose-limiting toxicities (DLTs), maximum tolerated dose (MTD) and recommended dose (RD) for phase II clinical trials
11.3 Adverse Events
11.3.1 Brief summary of adverse events
11.3.2 Display of adverse events
11.3.3 Analysis of adverse events
11.3.3.1 Constitutional adverse events and pain
11.3.3.2 Gastrointestinal adverse events
…
11.3.3.x Other adverse events
11.3.4 Listing of adverse events by patient
11.4 Deaths, Other Serious Adverse Events, And Other Significant Adverse Events
11.4.1 Listing of deaths, other serious adverse events and other significant adverse events
11.4.1.1 Deaths
11.4.1.2 Other serious adverse events
11.4.1.3 Other significant adverse events
11.4.2 Narratives of deaths, other serious adverse events and certain other significant adverse events
11.4.3 Analysis and discussion of deaths, other serious adverse events and other significant adverse events
11.5 Clinical Laboratory Evaluation
11.5.1 Listing of individual laboratory measurements by patient and each abnormal laboratory value
11.5.2 Evaluation of each laboratory parameter
11.5.2.1 Hematological abnormalities
11.5.2.2 Biochemical abnormalities
11.5.2.3 Individual clinically significant laboratory abnormalities
11.6 Vital Signs, Physical Findings And Other Observations Related To Safety
11.7 Safety Conclusions

Please note that we refer to laboratory findings as abnormalities and not as toxicities because patients often have asymptomatic increases or decreases in parameters like neutrophils or transaminases. Adverse events (AEs) are described in a different section (Section 11.3 in this model of CSR), usually in tabulated form as worst grade of toxicity per patient and per cycle of treatment. Toxicity is graded according to the National Cancer Institute-Common Terminology Criteria for Adverse Events (NCI-CTCAE, currently version 4.0). However, AEs that can be measured as laboratory abnormalities (e.g. neutropenia, thrombocytopenia, transaminase increases, hyperbilirubinemia, etc.) may be underreported if they are only listed based on the AE rows of the case report form. This is because reporting depends entirely on the judgment of the investigator and the symptomatic characteristic of the laboratory event. Hence, laboratory abnormalities are better reported by objective laboratory results, also graded using the NCI-CTCAE. Therefore, these laboratory abnormalities should be excluded from AE tables and shown in detail and discussed only in the Clinical Laboratory Evaluation section. Nevertheless, symptomatic AEs due to laboratory abnormalities (e.g. febrile neutropenia) that result in treatment modification (dose reduction or cycle delay) or treatment discontinuation or represent a serious adverse event or lead to death should be described in detail in the respective section.

In conclusion, ICH E3 represents an interesting tool in medical writing, but does not have to be followed rigidly if modifications of the structure are logical and help to tell the history of results in a clear way. Variations of ICH E3 that maintain the goal of harmonized reporting of conduct and results of clinical trials are acceptable, as long as important deviations from the guideline are explained. This article focuses on safety sections, but variations of ICH E3 are also acceptable, for instance, for pharmacokinetic, pharmacodynamic, pharmacogenomic, or quality-of-life data.

References

1. Alfaro V, Cullell-Young M, Tanovic A. Abbreviated clinical study reports with investigational medicinal products for human use: current guidelines and recommendations. Croat Med J 2007;48(6):871–7. Epub 2007/12/13.
2. ICH Topic E 3. Note for Guidance on Structure and Content of Clinical Study Reports (CPMP/ICH/137/95). 1996.
3. Final Concept Paper E3 Q&As. E3: Structure and Content of Clinical Study Reports. Available from: http://wwwichorg/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E3/Concept_papers/E3_Q_As_Final_Concept_Paper_15_June_2011pdf.
4. (CHMP) CfMPfHU. Guideline on the Evaluation of Anticancer Medicinal Products in Man. CPMP/EWP/205/95/Rev.3/Corr. 2005.

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Identifying appropriate journals in which to publish original research on vaccines against human infectious diseases

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Abstract

The most effective way of communicating new research findings is by publishing them in a peer-reviewed journal which is widely read and highly respected. To ensure that important new data are shared with the appropriate audience in a timely manner, a number of important considerations need to be taken into account when choosing a suitable journal. This article provides an analysis of journals which publish original articles describing studies of vaccines against human infectious diseases. A search of PubMed identified over 80 journals which recently published vaccine-related studies. These journals were filtered according to impact factor and number and percentage of vaccine-related studies published from 2006 to 2010, resulting in a core of 32 journals which frequently publish studies of vaccines against human infectious diseases. A survey was then undertaken to gather additional information with respect to acceptance rate, average time needed from manuscript submission to acceptance and from acceptance to publication. This dataset should provide a useful source of metrics which can help ensure that manuscripts are submitted to the most appropriate journal.

Keywords: Vaccine, Infectious diseases, Journal metrics, Impact factor, Acceptance rate

Publishing in a peer-reviewed journal which is widely read and highly respected in the scientific and medical communities is the primary goal when seeking to communicate important new study findings. Readers can expect that data published in a high-quality journal will have undergone rigorous scrutiny and that the study conclusions will be of considerable importance to the field. In practice, however, the vast majority of manuscripts submitted to the top-ranking journals are not accepted for publication. Rejection will mean, in most cases, a requirement to re-structure and re-format the manuscript before it can be submitted to an alternative journal. In the worst case, the manuscript will have undergone a lengthy review process; this delay may result in a loss of data novelty and the context of the manuscript may need substantial revision. Re-writing and updating the manuscript will involve further lost time and this could result in a considerably diminished impact when the article is eventually published. This scenario can be avoided by a more appropriate initial choice of target journal.

The key processes involved in identifying suitable target journals have been recently described as part of a detailed 'Authors' submission toolkit' published by members of the pharmaceutical industry and biomedical journals.[1] Important considerations include matching the focus of your study with that of the journal, assessing whether and how often the journal has published similar types of study in the recent past, restrictions on word, figure and table counts, impact factor (IF), rejection/acceptance rates (ARs), and times between submission, acceptance, and publication. Much of this information can be gathered from journal websites, citation databases and individual publications; however, this is a cumbersome task and would be impracticable to undertake for each new submission. The purpose of this article is to provide a database of journal metrics which will help authors to make informed decisions about where to submit manuscripts which focus on original research in the field of vaccines against human infectious diseases.

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Methods

To identify an initial list of potential target journals suitable for an international audience, an advanced search for English-language vaccine-related original research articles was done on PubMed[2] using the algorithm:

((((((((((((((((((((((("2006"[Publication Date] : "2010"[Publication Date]) NOT "comment" [Publication Type]) NOT "corrected and republished article"[Publication Type]) NOT "duplicate publication"[Publication Type]) NOT "editorial"[Publication Type]) NOT "guideline" [Publication Type]) NOT "historical article"[Publication Type]) NOT "interview" [Publication Type]) NOT "news"[Publication Type]) NOT "published erratum"[Publication Type]) NOT "retracted publication" [Publication Type]) NOT "retraction of publication" [Publication Type]) NOT "review" [Publication Type]) NOT "letter"[Publication Type]) AND vacc*[Title]) NOT vaccini*[Title]) NOT vaccr*[Title]) NOT vacca*[Title]) NOT vaccinol*[Title]) NOT vaccen*[Title]) NOT vaccina[Title]) NOT vaccinal*[Title]) NOT vaccinos*[Title]) AND "english"[Language].

As a second step, the list of retrieved articles was sorted by journal and all journals publishing at least five articles between 2009 and 2010 (i.e. over 2 years) were selected. Next, the PubMed algorithm was extended to include AND 'x' [Journal], where 'x' represents one of the journals identified in step two, to retrieve an estimate of the number of original research articles published on vaccine-related studies over the 5-year period from 2006 to 2010 (V). To estimate the equivalent total number of original research articles published in these journals (T), the following PubMed search algorithm was used to query each journal:

((((((((((((((((((((((("2006"[Publication Date] : "2010"[Publication Date]) NOT "comment" [Publication Type]) NOT "corrected and republished article"[Publication Type]) NOT "duplicate publication"[Publication Type]) NOT "editorial"[Publication Type]) NOT "guideline" [Publication Type]) NOT "historical article"[Publication Type]) NOT "interview" [Publication Type]) NOT "news"[Publication Type]) NOT "published erratum"[Publication Type]) NOT "retracted publication" [Publication Type]) NOT "retraction of publication" [Publication Type]) NOT "review" [Publication Type]) NOT "letter"[Publication Type]) AND "english"[Language].

These data were then used to calculate an estimate for the proportion of vaccine-related studies as a percentage of all original research studies in each journal (%V).

Three different databases which provide a measure of journal and article impact were then mined to extract the following journal metrics: Journal Citation Reports 2010 Impact Factor (IF), 5-year impact factor (5 Yr IF), and Immediacy Index,[3] Eigen Factor Article Influence (EF AI),[4] SCImago Journal Rank (SJR) and Cites/doc (CD).[5] To distill a core of higher ranking journals which regularly publish vaccine-related studies, a ranking filter was utilized with the following cut-off criteria: IF <2.0 OR V < 15 OR %V <0.5% OR (IF < 3.5 AND V < 35 AND %V < 3.0).

The abstracts of articles retrieved for the remaining journals with <25 vaccine articles for 2006–2010 were then manually inspected to remove inappropriate articles such as non-research articles, studies which did not actually investigate vaccines, purely epidemiological studies, case studies, historical studies, opinion, surveys, etc. A final manual inspection removed journals which publish vaccine studies focusing exclusively or almost exclusively on cancer, AIDS, or veterinarian vaccines.

Additional information on the journal such as focus with respect to infectious disease type (general, viral, non-viral, or diseases primarily affecting tropical or developing countries) and research stage (preclinical or clinical) and abridged aims and scope relevant to vaccine studies were gathered from journal websites. To gain information on AR, time from submission to acceptance, time from acceptance to publication, and open access (OA) status/options, a short questionnaire was sent to an email contact on the journal website. To unify reported time units to half week intervals, months were converted to weeks by multiplying by 4.333, days were converted to weeks by dividing by 7, and numbers were rounded up or down accordingly. When a range was reported, the median of this range was used. If there was no response within 1 month, follow-up telephone calls were made. If these data were not available or journals did not respond or were unwilling to supply the data, this was recorded as NA.

Results and discussion

A total of 2 818 596 original research articles were estimated to have been published in the 5-year period between 2006 and 2010, and, of these, 15 230 (approximately 0.5%) were judged to be vaccine related, as defined by the respective PubMed search algorithms. Table 1 describes the journals which met all of the criteria to be included in further analyses after filtering on the basis of IF, number, and percentage of vaccine-related articles published between 2006 and 2010, and the type of study published. A selection of journals which were considered initially but did not qualify for further analysis are listed in the Appendix.

Thirteen journals published in excess of 100 vaccine-related articles within the 5-year analysis period: *Vaccine* (3122), *Clinical and Vaccine Immunology* (287), *Human Vaccines* (271), *Journal of Infectious Diseases* (270), *PLoS ONE* (241), *Infection and Immunity* (232), *Pediatric Infectious Diseases Journal* (227), *Journal of Virology* (221), *Journal of Immunology* (216), *Pediatrics* (166), *Clinical Infectious Diseases* (120), *PNAS USA* (103), and *Virology* (101).

The top 10 ranked journals with respect to the percentage of vaccine-related articles published (%V) were *Human Vaccines* (77%), *Vaccine* (64%), *Influenza and Other Respiratory Viruses* (23%), *Clinical and Vaccine Immunology* (21%), *Pediatric Infectious Diseases* (18%), *Journal of Infectious Diseases* (12%), *Infection and Immunity* (7%), *Clinical Infectious Diseases* (6%), *FEMS Immunology and Medical Microbiology* (6%), and *Microbes and Infection (6%).*

Four of the top five ranked journals with respect to IF were general medical journals (*New England Journal of Medicine*, *The Lancet*, *Journal of the American Medical Association*, *Lancet Infectious Diseases and the British Medical Journal*), which publish exclusively clinical research and reported very low ARs (5–9%). Most other journals reported ARs between 10 and 35%, with no specific relationship between AR and IF for these journals. A small number of journals reported ARs of 50% or higher.

With respect to the average time required from submission to acceptance, and from acceptance to publication, these ranged from 4 to 24 weeks and <1 to 28 weeks, respectively; there was no clear relationship between IF and times required between submission and acceptance and between acceptance and publication.

The majority of the journals had OA options (i.e. these journals usually require payment from readers but the author can pay a fee upfront for the article to be made freely available online) and a small number were online-only journals which only publish OA articles.

This analysis is intended only as guide and there are a number of limitations to the study. The analysis was not sensitive enough to distinguish between all vaccine-related and non-vaccine studies as demonstrated by the %V score of 77 and 64% for *Human Vaccines* and *Vaccines*, respectively, which only publish vaccine-related studies. Particularly the data provided by the journals with respect to average times between submission and acceptance and between acceptance and publication can only be used as guidelines as these are likely to vary to some extent from year to year and at different times of year, for example, it may be difficult to find reviewers during holiday seasons. In most cases, the length of time required from submission to acceptance will be highly dependent on the quality of the manuscript and the time taken for the authors to complete revisions, should they be required. In addition, direct comparisons between ARs and average times from submission to acceptance/acceptance to publication are difficult to make between journals as in most cases journals did not report how these are calculated; there are likely to be a number of differences in this respect, for example, use of mean or median, definition of submission date and acceptance date, definition of publication date, etc. Finally, this study did not include very new journals which have published too few articles to meet the criteria as defined by the PubMed search algorithm and filter or which do not yet have an IF. As an example, the publishers of *Vaccine* have recently announced that they have launched a new journal, *Trials in Vaccinology*, which, as the name suggests, will be specifically dedicated to the publication of vaccine clinical trials.

In summary, the results of the analysis of journal metrics reveal large differences between journals with respect to the number and proportion of vaccine-related studies, published ARs and reported average times required from submission through to publication. Although the dataset has several caveats, it should prove a useful tool to help authors of manuscripts describing studies of vaccines against human infectious diseases to choose the most appropriate target journal for each submission.

Table 1: Peer-reviewed journals which frequently publish studies of vaccines against human infectious diseases

Journal	Publisher	IF 2010	5 Yr IF	Imm. Index	EF AI	SJR	Cites/ doc	V 06–10	T 06–10	%V 06–10	Disease	Stage	AR (%)	S to A (weeks)	A to P (weeks)[a]	OA[b]	Aims/scope relevant to vaccine studies
NEJM	MMS	53.5	52.4	10.7	19.9	4.01	33.9	59	2839	2.1	G	C	<6	22	11	No	Original clinical research
Lancet	Elsevier	33.6	32.5	10.9	10.9	1.65	14.2	57	2288	2.5	G	C	5	NA	NA	No	Any original contribution that advances or illuminates medical science or practice
JAMA	AMA	30.0	29.3	7.2	11.4	2.06	19.2	25	2111	1.2	G	C	9	7.5	5	No	All subjects that relate to the practice of medicine and the betterment of public health worldwide
[c]**Lancet Inf. Dis**	Elsevier	16.1	15.5	3.4	5.2	1.54	15.0	5	163	3.1	G	C	6	NA	NA	No	Any original research contribution that advocates change in or illuminates infectious disease clinical practice
BMJ	BMA	13.5	11.9	6.8	4.2	0.13	3.6	30	2400	1.3	G	C	7	2.5 (D)	9	Yes	Trials asking an original research question that aids doctors' decisions. Priority given to phase III or IV head-to-head effectiveness trials
PNAS USA	PNAS	9.8	10.6	1.9	4.9	2.24	9.5	103	17 824	0.6	G	P/C	19	3 (D)	4.5	O	Cutting-edge research reports. Biological, physical, and social sciences

Continued

Table 1: *Continued*

Journal	Publisher	IF 2010	5 Yr IF	Imm. Index	EF AI	SJR	Cites/ doc	V 06–10	T 06–10	%V 06–10	Disease	Stage	AR (%)	S to A (weeks)	A to P (weeks)[a]	OA[b]	Aims/scope relevant to vaccine studies
PLoS Pathogens	PLoS	9.1	9.7	1.5	4.1	1.58	7.9	27	1496	1.8	G	P	22	18	7	Yes	Articles that significantly advance the understanding of pathogens and how they interact with their host organisms. Topics include rational vaccine design
Clin Infect Dis	IDSA/ OUP	8.2	7.9	2.5	2.6	0.96	8.2	120	2147	5.6	G	C	10	24	12	O	Prevention of infection, the evaluation of current and novel treatments, and the promotion of optimal practices for diagnosis and treatment
Mol Ther	NPG	7.1	6.5	1.9	2.0	1.04	6.6	56	1192	4.7	G	P/C	<33	14	3	O	Vector development and design, vaccine development, safety/ efficacy studies, and clinical trials
J Inf Dis	IDSA/ OUP	6.3	6.1	1.7	2.1	0.97	6.6	270	2347	11.5	G	P/C	17	16	17	O	Microbiology, immunology, pathogenesis, diagnosis, and treatment of infectious diseases
J Immunol	AAI/ HighWire	5.7	5.9	1.0	2.2	1.57	5.6	216	8965	2.4	G	P/(C)	40	5 (D)	<7.5	No	All areas of experimental immunology
Pediatrics	AAP/ HighWire	5.4	5.9	1.0	1.9	0.51	5.6	166	3621	4.6	G	C	13	4	6	No	Original research in the field of pediatrics, as broadly defined

J Virol	ASM	5.2	5.3	1.3	1.6	1.07	5.2	221	6689	3.3	Vi	P	NA	NA	NA	O	The nature of the viruses, virus–cell interactions, cellular responses to infection, gene delivery, viral pathogenesis and immunity, and vaccines
Eur J Immunol	Wiley	4.9	4.7	1.1	1.9	1.32	4.9	44	1675	2.6	G	P	35	3.5 (D)	1	O	Basic immunology research including, cellular immune response, immunity to infection, molecular immunology, clinical immunology, and new technology
[d]**PLOS Negl Trop Dis**	PLoS	4.8	4.8	0.6	1.7	0.47	4.4	16	696	2.3	T	P/C	47	17	8	Yes	Pathobiology, epidemiology, prevention, treatment, and control of neglected tropical diseases
PLoS ONE	PLoS	4.4	4.6	0.5	1.9	0.81	4.1	241	15 111	1.6	G	P/C	64	14	4.5	Yes	Primary research from any scientific discipline
Infection Immunity	ASM	4.1	4.1	0.9	1.3	0.69	4.2	232	3330	7.0	NV	P	NA	NA	NA	O	Mechanisms of host-pathogen interactions. Development of vaccines against nonviral pathogens
[d]**Influenza Other Resp**	Wiley	3.8	3.3	0.6	0.6	0.34	3.5	31	135	23.0	Vi	P/C	50	12	5	O	Exclusively influenza and other respiratory viruses including prevention by vaccines and clinical studies
Vaccine	Elsevier	3.6	3.5	0.7	0.9	0.45	3.6	3122	4902	63.6	G	P/C	NA	NA	NA	O	All areas of vaccine research, vaccination, and vaccinology

Continued

Table 1: *Continued*

Journal	Publisher	IF 2010	5 Yr IF	Imm. Index	EF AI	SJR	Cites/ doc	V 06–10	T 06–10	%V 06–10	Disease	Stage	AR (%)	S to A (weeks)	A to P (weeks)[a]	OA[b]	Aims/scope relevant to vaccine studies
J Gen Virol	SGM/ HighWire	3.6	3.4	0.9	1.0	0.51	3.4	59	1940	3.0	Vi	P	NA	NA	NA	O	All aspects of viruses, molecular biology and immunology, virus–host interactions
Virology	Elsevier	3.3	3.3	0.8	1.6	0.52	3.3	101	2665	3.8	Vi	P	NA	NA	NA	O	Basic research in all branches of virology, molecular biology of virus multiplication, molecular pathogenesis, molecular aspects of the control and prevention of viral infections
Pediatr Inf Dis J	WKH/ LWW	3.1	3.3	0.7	1.0	0.38	3.3	227	1275	17.8	G	C	20	21.5	28	O	Infectious diseases in children, diagnostic techniques, effective therapies and treatment
J Med Virol	Wiley	2.9	2.7	0.5	0.8	0.35	2.9	41	1351	3.0	Vi	P/C	NA	NA	NA	O	Fundamental and applied research concerning viruses affecting humans. Characterization, diagnosis, epidemiology, immunology and pathogenesis of human virus infections
BMC Infect Dis	BMC	2.8	3.0	0.5	0.9	0.31	2.9	53	1046	5.1	G	C	45	6 (D)	2	Yes	All aspects of the prevention, diagnosis and management of infectious diseases in humans

Microbes Infect	Elsevier	2.7	2.9	0.5	1.0	0.43	3.1	48	880	5.5	G	P	NA	NA	NA	All fields of infection and immunity, in particular vaccine development, including novel strategies and adjuvants
Clin Vaccine Immunol	ASM	2.5	2.6	0.4	0.7	0.31	2.5	287	1339	21.4	G	P/C	NA	NA	<1	O	Understanding the immune response in health and disease. Development of vaccines, human and animal immune responses to vaccines, vaccine vectors, adjuvants
Int J Infect Dis	Elsevier	2.5	2.6	0.3	0.7	0.18	2.1	31	696	4.5	Dev	C	NA	NA	NA	O	Treatment and control of infectious diseases with particular emphasis placed on those diseases that are most common in less-developed countries
Immunol Letters	Elsevier	2.5	2.5	0.4	0.9	0.51	2.4	30	598	5.0	G	P	NA	NA	NA	O	All aspects of molecular and cellular immunology
FEMS Imm Med Microbiol	Blackwell	2.5	2.2	0.4	0.7	0.24	2.8	36	638	5.6	NV	P	35	14	4.5	O	Immunology, medical microbiology and cell biology of infectious diseases and the biochemistry, molecular biology and genetics of pathogen

Continued

Table 1: *Continued*

Journal	Publisher	IF 2010	5 Yr IF	Imm. Index	EF AI	SJR	Cites/ doc	V 06–10	T 06–10	%V 06–10	Disease	Stage	AR (%)	S to A (weeks)	A to P (weeks)[a]	OA[b]	Aims/scope relevant to vaccine studies
Virol J	BMC	2.5	n.a.	0.3	1.0	0.30	2.5	30	959	3.1	Vi	P	70	13	3	Yes	All aspects of virology research including molecular aspects of the control and prevention of viral infections with vaccines and the use of viruses as gene therapy vectors
Am J Trop Med Hyg	ASTMH/ HigWire	2.4	2.9	0.5	0.9	0.31	2.3	49	2003	2.5	T	P/C	50	6 (D)	13	O	Emphasis on tropical medicine, parasitology, immunology, infectious diseases, prevention and control methodologies. Topics include molecular biology of vaccine development
[e]**Hum Vaccines**	Landes	2.0	n/a	0.5	0.8	0.24	2.5	271	350	77.4	G	P/C	NA	NA	NA	O	Bacterial or viral diseases. Therapeutic vaccines, immunotherapeutics

[a]If times were reported for both online and print publication, the shorter is used.
[b]Open access refers to journals which publish all articles online free of charge to all readers worldwide. Optional open access refers to journals which provide open access in exchange for an author fee. Some journals also grant open access to users or institutions in developing countries and/or make selected articles or older articles freely available online.
[c]*Lancet Infectious Diseases* has published original research articles since 2010.
[d]Published since 2007.
[e]From January 2012, Human Vaccines and Immunotherapeutics.
IF, Journal Citations Reports (JCR) impact factor; 5 Yr IF, 5-year JCR impact factor; Imm. Index, JCR immediacy index; EF AI, Eigen Factor Article Influence; SJR, SCImago Journal Rank; Cites/doc, SJR citations per document; V, vaccine-related original research articles; T, total original research articles; %V, percentage of total original research articles which are vaccine-related; AR, acceptance rate; S to A, average time from submission to acceptance (A); D, average time to first decision when time to acceptance not available; A to P, average time from acceptance (A) to publication (P) either online (O) or in print (P); OA, open access; O, optional open access; NA, data not available; UO, unedited proof online only. Disease classification: G, general; Vi, viral; T, tropical; NV, non-viral; Dev, primarily affecting developing countries. Stage: C, clinical; P, pre-clinical.

References

1. Chipperfield L, Citrome L, Clark J, David FS, Enck R, Evangelista M, *et al.* Authors' Submission Toolkit: a practical guide to getting your research published. Curr Med Res Opin 2010;26:1967–82.
2. PubMed. NCBI, 2011. Available from: http://www.ncbi.nlm.nih.gov/pubmed
3. JCR. Thomson Reuters, 2011. Available from: http://thomsonreuters.com/products_services/science/science_products/a-z/journal_citation_reports/
4. Eigenfactor. Eigenfactor, 2011. Available from: http://www.eigenfactor.org/
5. SCImago Journal Rank. SCIMAGO, 2011. Available from: http://www.scimagojr.com/journalrank.php

Appendix

Selected journals (with 2010 JCR IF) which were included in the initial analysis and which also publish vaccine-related studies but which were omitted from further analyses due to the filter criteria:

Acta Virologica (0.5), *Advances in Experimental Medicine and Biology* (1.4), *AIDS* (6.3), *AIDS Research and Human Retroviruses* (2.1), *American Journal of Infection Control* (3.0), *American Journal of Preventive Medicine* (4.1), *Antiviral Research* (4.4), *Archives of Virology* (2.2), *Biochemical and Biophysical Research Communications* (2.6), *Biologicals* (1.8), *Clinical and Experimental Immunology* (3.1), *Clinical Immunology* (3.9), *Clinical Therapeutics* (2.6), *Emerging Infectious Diseases* (6.9), *Clinical Microbiology and Infection* (4.8), *Epidemiology and Infection* (2.3), *European Journal of Clinical Microbiology and Infectious Diseases* (2.6), *Gene Therapy* (4.5), *Human Gene Therapy* (4.8), *Immunity* (24.2), *Immunobiology* (4.1), *Infection* (2.2), *Journal of Biological Chemistry* (5.3), *Journal of Clinical Immunology* (3.3), *Journal of Clinical Investigation* (14.1), *Journal of Clinical Microbiology* (4.2), *Journal of Experimental Medicine* (14.8), *Journal of Immunotherapy* (3.6), *Journal of Infection* (3.8), *Journal of Medical Microbiology* (2.4), *Journal of Pediatrics* (4.0), *Journal of Translational Medicine* (3.5), *Microbiology and Immunology* (1.2), *Molecular Immunology* (2.9), *Nature* (36.1), *Nature Biotechnology* (31.1), *Nature Medicine* (25.4), *PLoS Medicine* (15.6), *Scandinavian Journal of Immunology* (1.9), *Scandinavian Journal of Infectious Diseases* (1.6), *Science* (31.4), *Vector Borne Zoonotic Diseases* (2.7), *Viral Immunology* (1.9), *Virus Genes* (1.7), *Virus Research* (2.9), *Viruses* (1.0).

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New myths about English

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Keywords: Myths, English grammar, Terminal prepositions, Table and figure titles, Starting sentences with digits, Writing dates

My first 39 myths about English were published in *The Write Stuff* in a series of articles between January 2006 and January 2008.

The myths are mainly drawn from claims about English made by participants at my training events on the use of English in the scientific and medical context. Participants often tell me: 'An English native speaker told me that there is a rule that …'. And native speakers of English often say: 'I learned that …'. Because the teaching of rules about the use of English has been patchy since the mid-1970s in the two countries with the most native English speakers (the United Kingdom and the USA) – and I suspect also in other major English-speaking countries such as Canada and Australia – I do wonder where these 'rules' were learned.

Some of these 'rules' have remarkable staying power, and fighting against some of them is definitely a lost cause. But one problem with language is that writers seek the security of rules, whether the language they are writing is their first, second, or third language. While some languages have clear rules on grammar and structure, this is one security that English cannot offer. We have rules, of course, but there are many exceptions and unregulated areas. Those with English as a second language often know some of the real rules better than native speakers (e.g. how to use the apostrophe), while those with English as a first language are often unaware that the way they express something naturally is actually following a rule. A further problem is that different resources often contradict one another, both traditional reference works and Internet sites. We just have to live with this in English because of its widespread use in every field.

Myth 40 was published in *TWS* in December 2008; I repeat it here to incorporate it in the series. Myths 40–45 follow.

Myth 40: If you start a sentence with digits, the noun after the digits has to be capitalized.

Before going into this, I refer readers to the March 2006 issue of *TWS*, where I discussed the myth that you must not start a sentence with digits.[1]

If you cannot bring yourself to start a sentence with digits, then you will not be faced with this problem because you will write *One hundred and twenty-one* for the example below.

Do you write: *121 patients were enrolled* or *121 Patients were enrolled*?

My simple answer is that you do not need to capitalize the word *patients* here, nor is there a rule that you must.

Myth 41: There is a rule in English that table titles have to go above tables and that figure titles have to go below figures.

First, this has nothing to do with English. It could just well apply to any other language. Second, who started this one? Many journals follow this pattern. But who says it is a rule? A figure caption could just as well be placed above a figure as below it, and I have often seen table captions below tables to no detriment.

Convention determines that in most publications table captions are above tables, and figure captions are below figures. I have often wondered why this is the case. One reason for putting figure captions below figures may be that they often contain a lot of explanatory information on the figure, such as keys to line styles and symbols, and comments on different parts of a multi-panel figure. This often extends over several lines and might look strange if positioned above the figure. But maybe it would only look strange because we are not used to seeing it above the figure. If you are preparing a publication, do what the target journal does. Regulatory documentation is probably subject to in-house style which should just be followed. Regardless of what you choose to do, be consistent in one document. It does not matter if different reports in a dossier follow different

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conventions, but be consistent throughout the text of your Common Technical Document.

Myth 42: P (as in P-value) has to be italicised.

Respected style guides contradict each other on this one. P, p or *p* – it does not matter one jot, so any time spent discussing this is totally wasted. Do what your author, co-author, statistician, boss, or client wants or what is required by house style or your target journal. Enjoy the luxury of doing what you want if you have your choice – mine is 'p'. And be consistent within one document.

Myth 43: The correct way to write the date is Sunday, April 1st, 2012.

There are many different ways of writing the date and different recommendations. I firmly come out in favour of Sunday 1 April 2012 and not what is in the title of this myth. You can read why in 'Dating made easy' published in *TWS* in 2006.[2] In brief, why complicate your text with two commas and an ordinal suffix when you can convey exactly the same information without?

Myth 44: Colons are always followed by capital letters.

Generally, in flowing text, a colon is followed by an uppercase letter in American English and a lowercase letter in British English. At least that is what we try to do on each side of the Atlantic. Our (the British) attempts often fail, however, and the capital letter after the colon is definitely creeping in. Is this really important? The answer is no. Try to be consistent if you have time. There are more important things in your text – and in life – than ensuring that you always capitalize a word after a colon. If you are not consistent about this in the middle of a sentence or paragraph in regulatory documentation, it is highly unlikely that you will be regarded as a sloppy writer or that your marketing authorization application will be turned down. You should, however, make the effort to be consistent in publications or medical communications documentation.

What probably will be noticed in any type of text – and could brand you as careless – is using introductory phrases for successive paragraphs and not consistently following these with capital or small letters. So do check that you have been consistent for this. For example:

Efficacy results: **O**verall survival was 2.4 ± 1.1 years in Group A and ….

Safety results: **d**ose-limiting toxicity was observed in ….

In publication titles with parts separated by a colon, the word after the colon is usually capitalized whether in British or American English. This is determined by the publisher.

Myth 45: There is a rule that sentences must not end with prepositions.

The one thing that pleased me about this British participant's claim is that he obviously knew what a preposition is! But internally I said 'Oh dear, not again!'. I have dealt with old chestnuts before, and this one will just not go away.

The most popularly quoted objection to this is attributed to Winston Churchill: 'This is the sort of bloody nonsense up with which I shall not put' instead of 'This is the sort of bloody nonsense which I shall not put up with'. As with many much used quotes, there are many variants around (see http://public.wsu.edu/~brians/errors/churchill.html). Note also that the 'undesirable' version that does not avoid the terminal preposition actually finishes with two prepositions in this case (up with), thanks to the abundance of phrasal verbs in English. Such phrasal verbs are used very frequently when speaking or writing informally, and much less in formal writing, which means that they do not very often present a problem in our context. My empirical observation is that this is not something I change often when editing texts. (I nearly said *correct*, but in many cases it would be just *changing* and not *correcting*.)

For a general comment on this, I can do nothing better than quote Jack Lynch:[3] Not ending sentences with prepositions is a

> favourite bugbear of the traditionalists. Whatever the merit of this 'rule' – and both historically and logically, there's not much – there's a substantial body of opinion against end-of-sentence prepositions; if you want to keep the crusty old-timers happy, try to avoid ending written sentences (and clauses) with prepositions, such as *to*, *with*, *from*, *at*, and *in*. Instead of writing 'The topics we want to write on', where the preposition *on* ends the clause, consider 'The topics on which we want to write'. On the other hand – and it's a big other hand – old-timers shouldn't always dictate your writing, and you don't deserve your writing license if you elevate this rough guideline into a superstition. Don't let it make your writing clumsy or obscure; if a sentence is more graceful with a final preposition, let it

stand. For instance, 'He gave the public what it longed for' is clear and idiomatic, even though it ends with a preposition; 'He gave the public that for which it longed' … doesn't look (or sound: AR) like English. A sentence becomes unnecessarily obscure when it's filled with *from whoms and with whiches*.

As with many aspects of the use of English, this is an area where you have to use a bit of common sense. In scientific and medical texts, I think the above is good advice for publications and other non-regulatory documents. See whether you can avoid ending sentences with a preposition, by choosing perhaps a different verb. I appreciate that this is sometimes difficult because of phrasal verbs, but as I said above, these are used much more in informal writing. Regulatory documents (except for SmPCs and patient information leaflets) are different. Obviously they should convey their message clearly, but – as was discussed last year in the medical writing forum in *Linked-In* – if the message is clear, it is not necessary to spend hours searching for the most elegant formulation.

The differences between the spoken word and more formal modes of expression for the same idea are illustrated by the examples below.

What you might say when giving a talk (all sound perfectly good when speaking) or for emails:
[1a] *We were aware that the arthritis study was a project that we would have to do a lot of preparatory work for*.
[1b] *Here is the result we ended up with*.
[1c] *After many attempts, these were the concentrations we eventually made the samples up to*.
[1d] *This is the kind pressure from a government department that we will never give in to.*

More formal when writing:
[2a] *We were aware that the arthritis study was a project for which we would have to do much preparatory work*.
[2b] *We finally obtained this result:* ('with which we ended up' is correct but sounds ridiculous)
[2c] *After many attempts, the concentrations of the samples were eventually made up to the following*:
[2d] *We will never give in to this is the kind pressure from a government department* ('in to which we will never give' is impossible)

Avoidance of terminal prepositions by more extensive reformulation:
[3a] *We were aware that the arthritis study would require much preparatory work* or *We knew we would have to do much preparatory work for the arthritis study*.
[3b] *The final result was as follows*:
[3c] *After many attempts, the final concentrations for the samples were*:
[3d] *We will never bow to this kind of pressure from a government department*.

There are obviously many other variants for [2a–d] and [3a–d]. These simply illustrate the transition from less formal to more formal writing. Note also that [3a–d] are all much shorter than [1a–d] but retain the same message. Shorter is always better if there is no information loss.

References

1. Reeves A. Myths about English. TWS 2006;15(1):22–4.
2. Reeves A. Dating made easy. TWS 2006;15(1):25–6.
3. http://andromeda.rutgers.edu/+jlynch/writing/p.html #prepend [accessed 8 January 2012].

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From researcher in Europe to medical writer in India

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Abstract

This is an article about my returning back to India from Europe and transition from research career to a profession of medical writing. I was introduced to medical writing through European Medical Writers Association (EMWA) while I was in Europe. After a PhD degree and postdoctoral experience in Europe, I returned to India and started anew as a medical writer at a knowledge process outsourcing company. My training period in the company involved introduction to company ethics and policies, different topics of medical writing, and functional approaches. Working on client-specific projects required training in their processes and business rules. In the company, I experienced an open work environment and helpful colleagues. On the projects I was able to use several skills that I learned while in research. I faced a steep learning curve in different therapeutic areas, reports, and client's expectations. Medical writing in India is still developing. The challenges include getting acknowledged for manuscript writing, standardization of rates for work, and for training courses.

Keywords: Medical writing in India, Knowledge process outsourcing, KPO

Genesis of a medical writer

Medical writing was an unknown profession for me until I discovered the European Medical Writers Association (EMWA) website during my PhD tenure in Germany. I took a chance and opted to undertake certification in medical writing with EMWA. The EMWA courses exposed me to the intricacies of drug development, clinical research, and medical writing. They also covered diverse topics including global healthcare facilities, regulatory compliance, and patients' rights and awareness in different countries.

As an Indian I could immediately see the advantages that India has in this field, not only as a big market for global pharmaceutical companies but also as an outsourcing destination, that can provide skilled and relatively inexpensive English-speaking talent for all stages of clinical research and documentation. I observed that there are reservations in Europe about outsourcing this type of work because of concerns related to the quality of the work and the impact of outsourcing on local job availability.

I took up a post as a postdoctoral researcher in the UK after completing my PhD in Germany, and my quest for medical writing continued during my full-time research jobs. However, my wish to shift to medical writing came true only on returning to India, my homeland. Luckily for me an article I wrote for *The Write Stuff* ('Going Home')[1] led me to my present position as a medical writer.

My first job as a 'medical writer'

Armed with research experience in chemistry and a medical writing certificate from EMWA, I started life as a medical writer at Sciformix, India. Sciformix is a knowledge process outsourcing (KPO) company working specifically for global pharmaceutical and biopharmaceutical clients. I found it easy to blend in, as the organization is a close-knit group of about 250 people, from diverse backgrounds. We work in different fields such as biometrics, medical writing, safety and risk management, regulatory affairs, and clinical operations, but we all interact.

The medical writing team here is involved in preparing a range of clinical documents of varying complexity both for local and for global clients as shown in Scheme 1.

My training period

On joining the company I spent a few weeks as a trainee. Along with other new employees, I was given general training on company background and ethics. Senior medical writers provided training on aspects of medical writing ranging from the general (ICH-GCP overview) to the specific (editing and proof reading). Thanks to the EMWA

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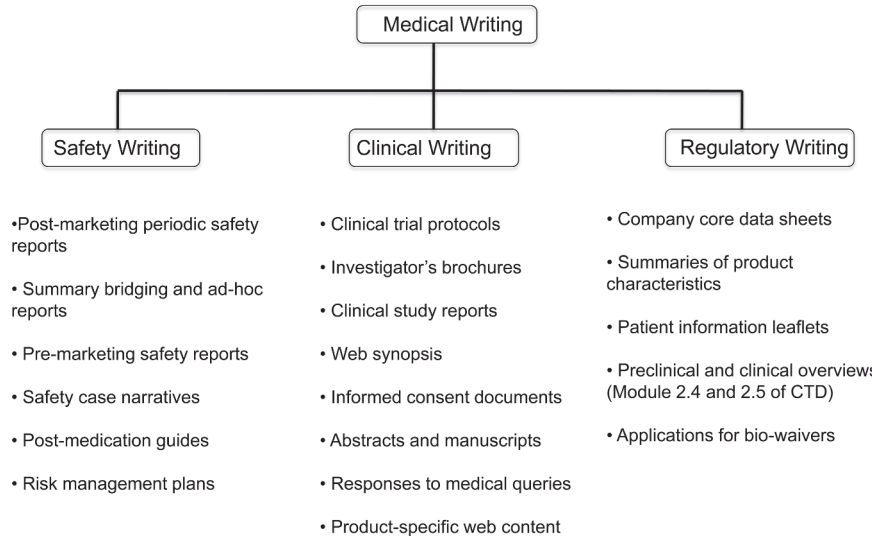

courses, the terminology and processes involved in medical writing were familiar.

First assignment

I was assigned to an ongoing project and was given time to understand the processes before starting production. I had to go through style guides and business rules provided by the client and the references related to the therapeutic area assigned to me. My first draft was carefully reviewed by my project leader and coach. By now, I was getting to know the importance of the client's template, subject content, scientific balance, style guides, and the importance of 'word count'. The document was reviewed by a subject expert who provided the necessary medical input. On incorporation of all the comments and after another level of peer review, my draft went through rigorous editing and proof reading before being sent to the client. As a result of the continuous evolution of the processes involved in medical writing, I can see that external workshops and training at client sites will form part of a continuous learning process.

Work environment and colleagues

I find it helpful that I can approach anyone in the team, just as in Europe, and that extra care is taken to synchronize the interests and knowledge of individual writers with the requirements of a project. Work pressure is evident as maintaining 100% time compliance is a very important criterion for a service provider. Every day I plan my time for expected deliverables but I also need to be open and flexible, especially when contributions from various authors and reviewers are required for regulatory documents. I am learning methods of tracking metrics in real time. Filling up time sheets at the end of each day provides a reality check of how much time is required to prepare a document and how much more goes for communication with the team (internal and external), literature search, planning, etc.

Interacting with colleagues constitutes a major part of working life. I see many colleagues at a time and they come from different backgrounds such as medicine, pharmacy, clinical research, statistics, and software. It is refreshing to work with people who see the world from a different perspective. I find working in a KPO to be truly multifaceted.

Projects coming my way

While working on postmarketing periodic safety reports, company core data sheets and responses to medical information queries, the skills honed during my research career proved helpful – literature searching, analysis, and review of articles on the basis of evidence, sorting out relevant articles, understanding them and their systematic presentation are required in all these projects. An eye for detail (another skill acquired during my research career) is coming in very handy in medical writing. I am also learning to modify my writing according to the target audience, which ranges from regulatory officials and healthcare professionals to the general public.

Learning curve

In a client-servicing company, I often face a steep learning curve in terms of my ability to draft and review complex documents, and to understand the different therapeutic areas. I am keen to develop

my understanding of required therapeutic areas and documents types, and to start contributing to projects as early as possible. I go back to the material and resources from the EMWA courses to refresh the basics before starting each new project.

Working with clients in different time zones who speak with different accents is a common challenge in a KPO. The relationship with the client is primarily based on virtual communication so it is essential to take extra care with email etiquette and accent-free English pronunciation.

Current challenges faced by the pharmaceutical industry compound the challenges faced by the service provider industry due to uncertainty about project scope and timelines. In spite of that, it is important that everyone keeps working diligently and builds a level of confidence and understanding with clients for future projects. Deadlines in a KPO are certainly more stringent than in academia.

Medical writing in India

Medical writing is still maturing as a profession in India. Regulatory writing is primarily done according to client specifications. In the case of manuscript writing, however, authorship roles and acknowledgement of medical writers are still under consideration. EMWA[2] has clear guidelines about the role of a medical writer in a publication. However, the acknowledgement of a medical writer's role in manuscript writing is still a challenge in India. Freelancers, KPOs, and clinical research organisations in India need to come together to start a trend of acknowledgement. A national platform for medical writers was much needed in India to raise questions and solve issues of authorship and standardization of remuneration rates in medical writing. Moreover, training courses for individuals wanting to join the medical writing profession are few and far between, and are sorely needed. Looking at these needs the All India Association of Medical Writers (www.freewebs.com/aimwa/) has been founded recently.

Its development is still at an early stage and international associations like EMWA can share their experience and help this association to give a strong platform for medical writers in India.

Disclaimer

All the views presented in this article solely belong to the author.

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References

1. Pal C. Going home. The Write Stuff 2011;20(2):11–112.
2. Jacobs A, Wager E. European Medical Writers Association (EMWA) guidelines on the role of medical writers in developing peer-reviewed publications. Curr Med Res Opin 2005;21(2):317–21.

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Imaging techniques in oncology

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Identifying and diagnosing cancerous diseases is currently one of the main tasks of today's radiologist. Every year cancer is diagnosed worldwide in over 12 million people. Within a single year, 7 million people die from cancer worldwide.

The most commonly diagnosed cancers are lung, breast, and colorectal cancers. The most common causes of cancer death are lung, stomach, and liver cancers.

Besides identifying primary tumours, it is also very important that radiology identifies possible metastases in other organs such as the liver, bones, brain, etc. at an early stage. Today all this information is gained using imaging techniques. The radiologist thus plays an important part in the treatment of people suffering from cancer.

A further important task of the radiologist using imaging techniques is judging whether oncological treatment of the tumour's course has to be initiated. In this way, the radiologist is able to make a statement as to whether the targeted oncological therapy has achieved its goal or whether in the absence of a response it has to be further adjusted.

The total medical care costs for people with cancer are approximately 20% higher than those for heart or vascular diseases, which are the second leading causes of global health costs. These high costs, however, arise as the result of many different factors such as costs of medication and the various therapy options, nursing care, and a lesser proportion also due to the application of radiological techniques.

The radiologist has many different techniques at his disposal to identify neoplasias within the body.

In principle, there are techniques using or not using X-rays.

Ultrasound

Ultrasound involves emitting sound waves of different wavelengths via a special transducer and a piezoelectric crystal into the body, which are then able to be converted to images. This method is free of X-rays and can be supplemented by special well-tolerated contrast media. The procedure is relatively inexpensive but heavily dependent on how well trained the physician is in using this technique.

X-rays

This is one of the oldest imaging techniques and is based on the use of small doses of X-rays. These penetrate the body and can render images of individual structures of the body's interior. The procedure is relatively inexpensive but, depending on application, of varying sensitivity. In mammography in particular, breast cancers can be discovered relatively well.

Computer tomography

Cross-sections of the body can be used with this method, which show a very high resolution. In addition, the images can be 'reconstructed' using various techniques, which may be very useful in identifying tumours. The procedure is extremely fast and imaging of the human body from head to foot can be completed within a few seconds. These procedures are used extremely often in the diagnosis of oncological diseases. Disadvantages of the procedure are the relatively high costs and a certain degree of exposure to radiation for the patients. Using new radiation-saving techniques, it will, however, be possible to reduce exposure to radiation in the future dramatically.

Magnetic resonance tomography

This procedure is based on hydrogen atoms of the human body being excited electromagnetically with the help of a strong magnet resulting in the generation of a signal. The procedure is very versatile and in addition to medical care of cancer patients is used in practically all areas of medical care (orthopaedics, neurology, paediatrics, etc.). The advantage of this technique is extremely good contrast of soft tissues, with whose help tumours can be imaged and diagnosed very well. Clinical observations of a tumour's course are also perfectly possible using this procedure. No harmful effect of this procedure is known, this being the reason why even unborn

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children in the womb can be examined. The disadvantage, however, is the relatively high cost involved.

Nuclear medicine procedures

In nuclear medicine procedures, among other things, radioactive substances can be injected into the body, which can then accumulate specifically in certain diseased regions. In addition to the diagnosis of various oncological diseases, the procedures can partly be used therapeutically (e.g. in the thyroid). In the meanwhile, nuclear medicine procedures can also be combined with other radiological techniques (e.g. PET/CT).

Summarizing, there are a variety of radiological techniques for the medical care of cancer patients. Without these techniques, oncological medicine would no longer be conceivable today.

Clinical pharmacology series
Does pharmacokinetics have a role in anti-cancer drug development?

It has been estimated by the International Agency for Research on Cancer that the instances of newly diagnosed cancer will more than double from 12 million in 2008 to 27 million in 2030.[1] Furthermore, almost 13% of deaths worldwide are cancer related. Unsurprisingly the pharmaceutical industry is keen to develop novel treatments in this important disease area. In the fiscal year ending 30 September 2011, the FDA approved 35 new medicines, of these 7 provided major advances in cancer chemotherapy.[2] In a similar time period, marketing authorization approval was granted by the European Medicines Authority (EMA) for Zytiga (Abiraterone) and Yervoy (ipilimumab), respectively, indicated for the treatment of metastatic advanced prostate cancer and advanced melanoma.

Abiraterone is a small molecule administered orally as an immediate release tablet. Ipilimumab is a fully human monoclonal antibody (MoAb), given via an intravenous infusion. Nevertheless, examination of the respective EMA assessment reports for this small molecule and biologic indicated that an understanding of pharmacokinetics (PK) was an important consideration in the posology for both drugs.[3,4]

Abiraterone has a mechanism of action that is non-cytotoxic (it is anti-androgenic); hence it was safe to initially investigate the PK of the compound in healthy volunteers. A critical finding from these studies was the influence of food on the systemic exposure of the compound, up to a 10-fold increase in area under the curve was observed with a high fat meal. The summary of Medical Product Characteristics contained the consequent dosing recommendation that abiraterone should be taken at least two hours after eating and no food should be eaten for at least one hour after taking the drug.

The pharmacology of ipilimumab was such that it was not possible to study the PK in healthy volunteers. PK data were generated from patients with advanced melanoma either through extensive sampling in Phase I-type single and multiple dose studies or the use of sparse sampling and population PK methodology in efficacy studies. Population PK data, gathered from 498 patients across four Phase II studies, were instrumental in evaluating the influence of physiologic and demographic factors on ipilimumab concentration–effect relationships. These investigations found that no specific dose adjustment was necessary in patients with mild-to-moderate renal dysfunction; information that was transferred to the final product label.

For both abiraterone and ipilimumab the dose proportionality and systemic drug exposure were assessed in addition to the predictability of multiple dose PK from the single-dose data. Overall, the EMA concluded that the PK of both novel drugs had been adequately studied.

The investigation of the PK properties of anti-cancer medication during development is concurrent with the EMA 'Guideline On The Evaluation Of Anticancer Medicinal Products In Man' (2005).[5] The document outlines the need to investigate PK in vulnerable populations and those with organ impairment. For MoAbs it suggests that understanding the PK provides some guidance for dose-finding as clearance may be related to target saturation.

The development programmes for abiraterone and ipilimumab illustrate two important principles. In cancer, like other disease areas, it is important to understand the factors that can contribute to variability in PK and subsequently pharmacodynamics, as this potentially influences the dose selected. Secondly it is incumbent on the drug developer to investigate such variability, irrespective of whether the anti-cancer agent is a small molecule or a biologic.

References

1. Wilking N, Jönsson B. Cancer and economics: with a special focus on cancer drugs. Oncol News 2011;6:17–9.
2. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm278383.htm.
3. EMA, Committee for Medicinal Products for Human Use (CHMP). Assessment report Zytiga (abiraterone). 21 July 2011. Procedure No.: EMEA/H/C/002321.
4. EMA, Committee for Medicinal Products for Human Use (CHMP). Assessment report Yervoy (ipilimumab). 19 May 2011. Procedure No.: EMEA/H/C/002213.
5. EMA, CHMP, Guideline on the Evaluation of Anticancer Medicinal Products in Man. London: EMA. December 2005.

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Is cancer preventable? A literature review

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Abstract

Despite significant progress in tumour diagnosis and treatment over the last few years, cancer remains a major cause of death worldwide. Cancer prevention through diet and lifestyle changes is gaining importance, as our understanding of the potential of dietary patterns and single foods to avoid carcinogenesis is growing. This review article discusses available evidence for links between nutrition and cancer and summarizes some of the recent findings from observational and interventional studies on the potential of diet and specific nutritional components to reduce cancer risk.

Keywords: Cancer, Risk, Prevention, Diet, Nutrition, Chemopreventive

Substantial progress has been made in the field of oncology over the last few years. Widespread population screening programmes have significantly improved early detection of specific types of cancer (breast, prostate, cervical, and colorectal cancers) and enhanced survival rates. Nevertheless, cancer continues to be a major cause of death worldwide and killed almost 8 million people (13% of all human deaths) in 2008.[1]

Despite the enormous amount of research invested in the last decade, cancer remains a challenge in modern medicine. It is difficult to treat, if not impossible to cure, has a dramatic impact on patient's quality of life, and is lethal, particularly when not diagnosed at an early stage or aggravated by comorbidities. Treatment options (whether surgical removal of the tumours, chemotherapy, or radiation therapy) are limited, expensive, and coupled with adverse effects (e.g. chemotherapy-induced nausea and vomiting, immuno- and myelosuppression, cardio-, hepato-, or nephrotoxicity).

Cancer: a lifestyle disease

Cancer is a complex, multifactorial disease. Only a small percentage of cancer cases, approximately 5–10%, are thought to be entirely hereditary. The remaining proportion results from an interaction between biological or environmental insults and genetic predisposition. Common environmental factors that contribute to cancer death include diet and obesity (30–35%), smoking (25–30%), infections (15–20%), radiation (both ionizing and non-ionizing, up to 10%), stress, lack of physical activity, and environmental pollutants.[2] Hence, most forms of cancer have their roots in the environment and lifestyle and, as such, are preventable. And because cancer is difficult to manage, its prevention is the first and best strategy.

The correlation between lifestyle and cancer is evidenced by the large variation in rates of specific cancers in different countries and by the changes observed in incidence rates when people migrate to other countries.[2,3] Immigrants develop the cancer risk of their new country, often within one generation. Further evidence comes from studies in monozygotic twins, which showed that inherited genetic factors make only a minor contribution to susceptibility to most types of neoplasms.[4] These findings indicate that lifestyle and environmental factors have the principal role in causing sporadic cancer.[5,6]

A comprehensive report compiled by the World Cancer Research Fund and the American Institute for Cancer Research in 2007 presents a clear correlation between lifestyle and cancer risk.[7–9] The 670-page report was concerned with food, nutrition, physical activity, body composition, and the prevention of cancer worldwide. An expert panel composed of over 100 scientists from 30 different countries summarized a 5-year research of all evidence-based sources into eight general and two

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special recommendations. In summary, these are: keeping body weight within the normal range, being physically active, eating mostly foods of plant origin, limiting consumption of energy-dense foods, red meat, processed meat, salt, alcohol, and sugary drinks, and aiming to meet nutritional needs through diet alone rather than using dietary supplements. This sounds easy, does it not? But perhaps for most of us, there are too many items on the list to be followed.

Food-derived carcinogens

The pioneer work pointing to a link between diet and cancer was published 30 years ago by Doll and Peto,[10] in which they estimated that approximately 30–35% of cancer deaths in the USA were linked to diet. It was noted in the 1970s that people in many Western countries had diets high in animal products, fat, and sugar, and high rates of cancers of the colorectum, breast, prostate, endometrium, and lung. In contrast, individuals in developing countries usually had diets that were based on one or two starchy staple foods, with low intake of animal products, fat, and sugar, and low rates of these cancers.[11] Diets that are high in processed or red meats and low in fruits, vegetables, and whole grains have been linked to a number of cancers.[12]

In theory, the link between diet and cancer is simple:

- Sporadic cancer arises from mutations caused by carcinogens or free radicals.
- A major source of carcinogens is food; they come from either the food itself, food contaminants (e.g. aflatoxins, dioxins, pesticides), food additives (e.g. nitrates, nitrites), or from food preparation (frying, barbecueing) at high temperatures (e.g. nitrosamines, heterocyclic amines, polycyclic aromatic hydrocarbons).
- Several food carcinogens have been shown to activate inflammatory pathways such as those involving nuclear factor-kappa B (NF-κB).
- Some nutrients are able to minimize oxidative damage to DNA caused by free radicals. These are basically antioxidants found in fruits, vegetables, cereals, spices, and teas.
- Nutrients interact with other molecules, particularly proteins including enzymes and lipids, within cells; some of these are then able to regulate expression of genes (e.g. oncogenes, tumour suppressor genes) and activity of enzymes that are involved in the control of cell proliferation and differentiation, and programmed cell death.

The extent to which diet contributes to cancer varies greatly depending on the type and anatomical site of the cancer.[3] For instance, diet is thought to account for 70% of colorectal cancer cases. Consumption of red meat, fat, and alcohol is associated with an increased risk of colorectal cancer.[13–15] Heavy consumption of red meat or processed meat (sausages, bacon, and hot dogs) is a risk factor for several cancers, especially for those of the gastrointestinal tract, but also for prostate, bladder, and breast cancers.[2] Epidemiological association studies have linked consumption of grilled meat to an increased risk of oesophagus and stomach cancer,[16] colon cancer,[17] pancreatic cancer,[18] and breast cancer,[19] a phenomenon which could be due to the presence of carcinogens in foods cooked at high temperatures.[20]

Obesity and cancer

According to a prospective cohort study of 900 000 US Americans published in 2003, obesity correlates with increased mortality from various cancers.[21] In both men and women, body mass index (BMI) was significantly associated with higher rates of death due to cancer of the oesophagus, colon and rectum, liver, gallbladder, pancreas, kidney, non-Hodgkin's lymphoma, and multiple myeloma. Significant trends of increasing risk with higher BMI values were observed for death from cancers of the stomach and prostate in men, and for death from cancers of the breast, uterus, cervix, and ovary in women. On the other hand, caloric restriction has been shown to reduce cancer incidence in animals and humans.[2,22]

The correlation between obesity and cancer might have several causes. Obese people usually eat an unhealthy diet rich in processed food, saturated fatty acids, *trans* fatty acids, refined sugar, red meat, and processed meat products, which are a good source of carcinogens. They eat less fruits, vegetables, and grains, and are physically less active. In addition, they present comorbidities such as diabetes and cardiovascular diseases that may contribute to a bad health state, for instance, by activating inflammatory signalling cascades and increasing systemic chronic inflammation parameters.

Studies have shown that common denominators between obesity and cancer include neurochemicals, hormones (such as insulin-like growth factor 1, insulin, and leptin), sex steroids, inflammation, and insulin resistance.[23] Hyperglycaemia, for instance, has been shown to activate NF-κB.[24] Likewise, several cytokines produced by adipocytes, such as leptin, tumour necrosis factor, and

interleukin-1, are also known to activate NF-κB.[25] The mammalian target of rapamycin (mTOR), a protein kinase which is activated by high cellular nutrient and energy levels, is another possible link between obesity and cancer.[22] The mTOR protein regulates growth, proliferation, motility, and survival of cells. mTOR activity is enhanced in obese and overweight people, and this state is thought to increase the probability of carcinogenesis. The counteractor of mTOR, adenosine monophosphate-activated protein kinase (AMPK), is implicated in the prevention of metabolic disorders. Decreased AMPK activity has been associated with an increased risk of carcinogenesis, and treatment with the AMPK activator metformin reduces cancer incidence in type 2 diabetes patients.[26] AMPK is emerging as an interesting metabolic tumour suppressor and a promising target for cancer prevention and therapy.

The anti-cancer diet

A presumable 'anti-cancer diet' has been extensively discussed in the last years. The topic crossed the boundary of the scientific environment and reached the lay community, fostered by the publication of several books. A few examples are *Foods that fight cancer* (by Richard Béliveau and Denis Gingras, and another one written by Patricia Hausman), *Beating cancer with nutrition* (Patrick and Noreen Quillen), *The cancer-fighting kitchen* (Rebecca Katz and Mat Edelson), *The everything cancer-fighting cookbook* (Carolyn Katzin), *Beyond the magic bullet – the anti-cancer cocktail* (Raymond Chang).

Diets rich in fruits, vegetables, whole grains, and spices have been linked to reduced risks of cancers of the colon, rectum, stomach, liver, oral cavity, pharynx, and other sites, including breast and prostate. A list of 100 fruits, vegetables, cereals, and spices with the potential to prevent cancer is provided in an expert review by Preetha Anand *et al.*[2] from the Cytokine Research Laboratory of the University of Texas, USA. According to this review, the protective role of fruits and vegetables against cancers that occur in various anatomical sites is now well supported, with more than 25 000 different phytochemicals identified that may have anti-cancer activity. They include beta-carotene, lycopene, resveratrol, quercetin, silymarin, indole-3-carbinol, and sulphoraphane from fruits and vegetables, as well as catechins, curcumin, diallyl disulphide, capsaicin, gingerol, anethol, and eugenol from spices and teas. Although most of the evidence of the chemopreventive efficacy of these compounds has come from cell and animal studies, they have advantages in comparison with synthetic drugs because they are regarded as safe and usually target multiple cell signalling pathways.[27]

For instance, catechins interact with more than 10 genes involved in the cellular response to oxidative stress.[28] They are 100 times more powerful than vitamin C and 25 times more powerful than vitamin E in their antioxidant/growth inhibitor potential.[29] Not only tea drinkers but also coffee lovers may enjoy the hot cup. Coffee has been reported to inversely correlate with liver cancer.[30]

Another important source of anti-carcinogens is whole grains. Besides being rich in dietary fibres, they contain chemopreventive antioxidants such as tocotrienols, phenolic acids, lignans, and phytic acid.[2] Whole-grain intake was found to reduce the risk of several cancers, including carcinomas from different sites, lymphomas, and leukaemias, by 30–70%.[31] The most evident correlation between dietary fibre intake and reduced cancer risk has been observed for colorectal cancer.[32,33] A meta-analysis involving 25 prospective cohort and case–control studies published in November 2011 confirmed the protective effect of dietary fibre on colorectal cancer incidence but also revealed that the risk reduction varies among different types of fibres, with the greatest benefits seen for legume fibre (relative risk/RR = 0.62) and cereal fibre (RR = 0.90).[34] Whole grains contain less antioxidants than some berries, but more than common fruits or vegetables.[35] However, the refining process used in most industrialized countries reduces their content of nutrients by removing the outer layers.[36]

Some isoflavones (genistein, daidzein, equol) have been linked to a lower incidence of breast cancer. However, there is also controversy on whether isoflavones, as phytoestrogens, might rather contribute to hormone-dependent cancers.[37] The effects of isoflavones on early breast cancer markers differ between pre- and post-menopausal women. Human and animal studies have yielded conflicting results with regard to the effect of soy isoflavones on breast cancer risk. As recently shown, this may be due to differences in isoflavone metabolism between humans and rodents.[38]

The most important class of phytoestrogens in the Western diet are lignans (found in flaxseeds, sesame seeds, rye bran). They are transformed by the intestinal microflora into enterodiol, and enterolactone. Lignans are capable of binding to oestrogen receptors and interfering with the cancer-promoting effects of oestrogen on breast tissue. In a meta-analysis, high lignan intake was shown to be associated

with a significantly reduced risk of breast cancer in post-menopausal women,[39] but this finding was not confirmed in an epidemiological study.[40] Among women (but not men), colorectal cancer risk was inversely associated with enterolactone and total enterolignans.[40] On the other hand, enterolignan intake positively correlated with prostate cancer risk, but this correlation was attenuated after adjustment for dairy intake.

Fruits and vegetables: the value of a good reputation

The few examples given above stress how complex the influence of diet and specific nutrients on the risk of various cancers is. Despite the currently available body of evidence from *in vitro*, animal and human studies for the chemopreventive effect of a healthy diet, some observational studies have found that consuming lots of fruits and vegetables has little or no effect on preventing cancer. The European Prospective Investigation into Cancer and Nutrition (EPIC) study, for instance, only detected a very small inverse association between the intake of total fruits and vegetables and cancer risk (hazard ratio/HR = 0.97 for 200 g/day increased intake of fruits and vegetables combined).[41] The reduced risk of cancer associated with high vegetable intake was restricted to women (HR = 0.98). Stratification by alcohol intake suggested a stronger risk reduction in heavy drinkers and was confined to cancers caused by smoking and alcohol. Similar results were published in another report from the EPIC study, which showed that a high intake of fruits and vegetables was associated with a decreased risk of lung cancer in current smokers.[33] A Mediterranean dietary pattern exerted similar protective effects against smoking-related cancers in the EPIC cohort.[42]

Lifestyle issues are powerful confounding factors when investigating the effect of fruits, vegetables, and dietary fibre on health.[22] For instance, smoking and alcohol are usually associated with low intake of fruits and vegetables, whereas people who consume large amounts of fruits and vegetables are less likely to smoke or drink alcohol.[43]

The polemic findings of the EPIC study are discussed by Walter Willett from the Harvard School of Public Health in an editorial of the *Journal of the National Cancer Institute*.[44] He argued that the evidence for a large preventive effect of fruits and vegetables against cancer has come primarily from case–control studies, which can be biased by differences in recall of past diets. Even more problematic is a selective participation (as control subjects) of more health-conscious people who have a healthier diet and lifestyle compared with those who do not participate. These biases are avoided in prospective cohort studies, and this type of study has shown that the results of case–control studies were overly optimistic and that any association of intake of fruits and vegetables with risk of cancer is weak at best. Nevertheless, Willett remarked that a very weak or undetectable association between total fruits and vegetables and risk of cancer does not exclude the possibility that one or a small group of fruits or vegetables, or a specific substance in some of these foods has an important protective effect.

Not only case–control and cohort studies have yielded conflicting results, but also and most notably epidemiological studies and randomized clinical trials (RCTs). This topic is discussed by Todd Gibson *et al.*[45] from the National Cancer Institute, USA. The authors listed several sources of discrepancy, including differences in study populations, dose and timing of the exposure, compliance, length of follow-up, and the primary endpoint. They agree with Willett in that null findings in RCTs do not necessarily indicate a lack of effect of the tested compound, as RCTs can only test a specific intervention in a certain population over a relatively short period of time. They believe that some nutrients may have chemopreventive effects if given to the right subjects at the right time and in the right dose. Furthermore, they postulate that dietary benefits against cancer arise from a combination of factors rather than single components acting in isolation. Two limitations inherent to RCTs are (1) the difficulty in testing combinations of nutrients and other bioactive food components in their natural context and (2) the need to intervene in older subjects to achieve sufficient statistical power. Both aspects are crucial when analysing the impact of diet on cancer risk.

The magic bullet

Although foods containing certain nutrients have been shown to be beneficial against cancer, intake of isolated nutrients has failed to confer the same benefits. Quite the contrary, harmful effects have been reported with supplementation of certain compounds. For instance, an *increased* risk of lung cancer among smokers who took beta-carotene supplements was reported in the Alpha Tocopherol, Beta-carotene Cancer Prevention (ATBC) trial[46] and in the Beta-Carotene and Retinol Efficiency Trial (CARET)[47] (20 and 30 mg of beta-carotene

supplementation, respectively). In the ATBC study, beta-carotene had little or no effect on the incidence of cancer other than lung cancer. However, total mortality was 8% higher among participants who received beta-carotene than among those who did not, primarily due to more deaths from lung cancer and ischaemic heart disease.[46] The effect is specific to the supplementation dose, as no lung damage was detected in those who were exposed to cigarette smoke and who ingested a physiological dose of beta-carotene (6 mg), in contrast to high pharmacological doses (20–30 mg).[48] The harmful effect also seems to be specific to smoke exposure.

The initial report of the Selenium and Vitamin E Cancer Prevention Trial (SELECT) found no reduction in the risk of prostate cancer with either selenium (200 μg/day from L-selenomethionine) or vitamin E (400 IU/day of all rac-alpha-tocopheryl acetate) supplements, but a statistically non-significant increase in prostate cancer risk with vitamin E.[49] Follow-up (7–12 years) data published in October 2011 provided further evidence that dietary supplementation with vitamin E significantly *increased* the risk (HR = 1.17, $P = 0.008$) of prostate cancer among healthy men.[50] The vitamin E dose used in SELECT was 12 times higher than the recommended intake, which is 33 IU daily.

For vitamin C supplementation, the scenario is even more unclear. Three RCTs performed at the Mayo Clinic using oral vitamin C for cancer patients were negative.[51] It has been controversially debated whether or not vitamin C has any clinically significant antitumour activity.

Conclusions

Many cases of sporadic cancer are preventable. Cancer prevention based on dietary and lifestyle changes remains a hot research topic because of the potential of an effective intervention to decrease cancer incidence at low cost and with a high positive impact on health economics globally. However, conflicting results obtained from epidemiological studies versus clinical trials underscore the need for improving study designs.

Effective cancer prevention involves smoking cessation; minimal consumption of fat, red meat, and processed meat; increased ingestion of fruits, vegetables, and whole grains; avoidance of alcohol; caloric restriction; physical activity; avoidance of prolonged exposure to sunlight; vaccinations; and regular check-ups.[2] Increased consumption of fat, red meat, and processed meat has been clearly associated with increased cancer risk. However, the key link between diet and cancer seems to be obesity, a condition fostered by diets based on high-fat meat products.

Inconsistent results from many studies have not been able to conclusively establish an inverse association between fruit and vegetable intake and overall cancer risk.[41] It has been claimed that fruits, vegetables, and dietary fibre *per se* have a very marginal, if any, effect on cancer incidence,[22] except for cancers caused by smoking and alcohol, and this effect might be due to residual confounding by these factors.[43] Nevertheless, negative results from RCTs of individual compounds do not preclude that single foods or whole dietary patterns have chemopreventive effects in settings different from those that can be investigated within RCTs.

A diet rich in fruits and vegetables helps avoid the risk of obesity, metabolic syndrome, and cardiovascular diseases.[52,53] In addition, it provides valuable sources of antioxidants and other phytochemicals with chemopreventive activity. Evidence is accumulating that active phytochemicals have synergetic effects that cannot be achieved with mono-supplementation of isolated compounds. The use of nutritional supplements in well-nourished individuals is not supported by current evidence. Not all substances present in fruits, vegetables, spices, and teas have been studied, and there are certainly many of them not yet identified. Taking this into account, future research should focus on whole dietary patterns and other lifestyle factors.

As pointed out by Gibson *et al.*,[45] future efforts need to recognize the integrative nature of dietary exposures and attempt to study nutrients in the larger context of the foods and diets in which they are consumed. Given the limitations of RCTs, we may need to rely more on observational evidence. Therefore, it is of paramount importance to improve the methodology for conducting high-quality, conclusive observational studies and, most importantly, to translate their results into meaningful benefits in cancer prevention.

References

1. Jemal A, Bray F, Center MM, *et al.* Global cancer statistics. CA Cancer J Clin 2011;61:69–90.
2. Anand P, Kunnumakkara AB, Sundaram C, *et al.* Cancer is a preventable disease that requires major lifestyle changes. Pharm Res 2008;25:2097–116.
3. Willett WC. Diet and cancer. Oncologist 2000;5: 393–404.
4. Lichtenstein P, Holm NV, Verkasalo PK, *et al.* Environmental and heritable factors in the causation of cancer – analyses of cohorts of twins from Sweden, Denmark, and Finland. N Engl J Med 2000; 343:78–85.

5. Irigaray P, Newby JA, Clapp R, *et al.* Lifestyle-related factors and environmental agents causing cancer: an overview. Biomed Pharmacother 2007;61:640–58.
6. Mucci LA, Wedren S, Tamimi RM, *et al.* The role of gene-environment interaction in the aetiology of human cancer: examples from cancers of the large bowel, lung and breast. J Intern Med 2001;249:477–93.
7. American Institute for Cancer Research and World Cancer Research Fund. Food, nutrition, physical activity, and the prevention of cancer: a global perspective. 2007. ISBN-13: 978–0972252225.
8. World Cancer Research Fund and American Institute for Cancer Research. Food, nutrition, physical activity and the prevention of cancer: a global perspective. Available from: http://www.dietandcancerreport.org/?p=about_the_report.
9. World Cancer Research Fund and American Institute for Cancer Research. Food, nutrition, physical activity and the prevention of cancer: a global perspective. Available from: http://en.wikipedia.org/wiki/Food,_Nutrition,_Physical_Activity_and_the_Prevention_of_Cancer:_a_Global_Perspective.
10. Doll R, Peto R. The causes of cancer: quantitative estimates of avoidable risks of cancer in the United States today. J Natl Cancer Inst 1981;66:1191–308.
11. Key TJ, Allen NE, Spencer EA, *et al.* The effect of diet on risk of cancer. Lancet 2002;360:861–8.
12. Kushi LH, Byers T, Doyle C, *et al.* American Cancer Society guidelines on nutrition and physical activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity. CA Cancer J Clin 2006;56:254–81.
13. Watson AJ, Collins PD. Colon cancer: a civilization disorder. Dig Dis 2011;29:222–8.
14. Gingras D, Béliveau R. Colorectal cancer prevention through dietary and lifestyle modifications. Cancer Microenviron 2011;4:133–9.
15. Chao A, Thun MJ, Connell CJ, *et al.* Meat consumption and risk of colorectal cancer. JAMA 2005;293:172–82.
16. Ward MH, Sinha R, Heineman EF, *et al.* Risk of adenocarcinoma of the stomach and esophagus with meat cooking method and doneness preference. Int J Cancer 1997;71:14–9.
17. Sinha R, Peters U, Cross AJ, *et al.* Meat, meat cooking methods and preservation, and risk for colorectal adenoma. Cancer Res 2005;65:8034–41.
18. Anderson KE, Kadlubar FF, Kulldorff M, *et al.* Dietary intake of heterocyclic amines and benzo(a)pyrene: associations with pancreatic cancer. Cancer Epidemiol Biomarkers Prev 2005;14:2261–5.
19. Steck SE, Gaudet MM, Eng SM, *et al.* Cooked meat and risk of breast cancer – lifetime versus recent dietary intake. Epidemiology 2007;18:373–82.
20. Zheng W, Lee SA. Well-done meat intake, heterocyclic amine exposure, and cancer risk. Nutr Cancer 2009;61:437–46.
21. Calle EE, Rodriguez C, Walker-Thurmond K, *et al.* Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. N Engl J Med 2003;348:1625–38.
22. Wicki A, Hagmann J. Diet and cancer. Swiss Med Wkly 2011;141:w13250. DOI: 10.4414/smw.2011.13250.
23. Hursting SD, Lashinger LM, Colbert LH, *et al.* Energy balance and carcinogenesis: underlying pathways and targets for intervention. Curr Cancer Drug Targets 2007;7:484–91.
24. Nareika A, Im YB, Game BA, *et al.* High glucose enhances lipopolysaccharide-stimulated CD14 expression in U937 mononuclear cells by increasing nuclear factor kappaB and AP-1 activities. J Endocrinol 2008;196:45–55.
25. Tang CH, Chiu YC, Tan TW, *et al.* Adiponectin enhances IL-6 production in human synovial fibroblast via an AdipoR1 receptor, AMPK, p38, and NF-kappa B pathway. J Immunol 2007;179:5483–92.
26. Luo Z, Zang M, Guo W. AMPK as a metabolic tumor suppressor: control of metabolism and cell growth. Future Oncol 2010;6:457–70.
27. Aggarwal BB, Shishodia S. Molecular targets of dietary agents for prevention and therapy of cancer. Biochem Pharmacol 2006;71:1397–421.
28. Comparative Toxicogenomics Database. Catechin. Available from: http://ctdbase.org/detail.go? type=chem&acc=D002392.
29. Abdulla M, Gruber P. Role of diet modification in cancer prevention. Biofactors 2000;12:45–51.
30. Larsson SC, Wolk A. Coffee consumption and risk of liver cancer: a meta-analysis. Gastroenterology 2007;132:1740–5.
31. Marquart L, Wiemer KL, Jones JM, *et al.* Whole grains health claims in the USA and other efforts to increase whole-grain consumption. Proc Nutr Soc 2003;62:151–60.
32. Bingham SA, Day NE, Luben R, *et al.* Dietary fibre in food and protection against colorectal cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC): an observational study. Lancet 2003;361:1496–501.
33. Gonzalez CA, Riboli E. Diet and cancer prevention: contributions from the European Prospective Investigation into Cancer and Nutrition (EPIC) study. Eur J Cancer 2010;46:2555–62.
34. Aune D, Chan DS, Lau R, *et al.* Dietary fibre, whole grains, and risk of colorectal cancer: systematic review and dose-response meta-analysis of prospective studies. BMJ 2011;343:d6617. DOI: 10.1136/bmj.d6617.
35. Miller HE, Rigelhof F, Marquart L, *et al.* Antioxidant content of whole grain breakfast cereals, fruits and vegetables. J Am Coll Nutr 2000;19(3 Suppl.):312S–9S.
36. Slavin JL, Jacobs D, Marquart L. Grain processing and nutrition. Crit Rev Food Sci Nutr 2000;40:309–26.
37. Bondesson M, Gustafsson JA. Does consuming isoflavones reduce or increase breast cancer risk? Genome Med 2010;2:90.
38. Setchell KD, Brown NM, Zhao X, *et al.* Soy isoflavone phase II metabolism differs between rodents and humans: implications for the effect on breast cancer risk. Am J Clin Nutr 2011;94:1284–94.
39. Buck K, Zaineddin AK, Vrieling A, *et al.* Meta-analyses of lignans and enterolignans in relation to breast cancer risk. Am J Clin Nutr 2010;92:141–53.
40. Ward HA, Kuhnle GG, Mulligan AA, *et al.* Breast, colorectal, and prostate cancer risk in the European Prospective Investigation into Cancer and Nutrition-Norfolk in relation to phytoestrogen intake derived from an improved database. Am J Clin Nutr 2010;91:440–8.
41. Boffetta P, Couto E, Wichmann J, *et al.* Fruit and vegetable intake and overall cancer risk in the European Prospective Investigation into Cancer and Nutrition (EPIC). J Natl Cancer Inst 2010;102:529–37.
42. Couto E, Boffetta P, Lagiou P, *et al.* Mediterranean dietary pattern and cancer risk in the EPIC cohort. Br J Cancer 2011;104:1493–9.

43. Key TJ. Fruit and vegetables and cancer risk. Br J Cancer 2011;104:6–11.
44. Willett WC. Fruits, vegetables, and cancer prevention: turmoil in the produce section. J Natl Cancer Inst 2010;102:510–1.
45. Gibson TM, Ferrucci LM, Tangrea JA, *et al.* Epidemiological and clinical studies of nutrition. Semin Oncol 2010;37:282–96.
46. The Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group. The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. N Engl J Med 1994;330:1029–35.
47. Omenn GS, Goodman G, Thornquist M, *et al.* The beta-carotene and retinol efficacy trial (CARET) for chemoprevention of lung cancer in high risk populations: smokers and asbestos-exposed workers. Cancer Res 1994;54(7 Suppl.):2038s–43s.
48. Russell RM. Beta-carotene and lung cancer. Pure Appl Chem 2002;74:1461–7.
49. Lippman SM, Klein EA, Goodman PJ, *et al.* Effect of selenium and vitamin E on risk of prostate cancer and other cancers: the Selenium and Vitamin E Cancer Prevention Trial (SELECT). JAMA 2009;301:39–51.
50. Klein EA, Thompson IM Jr, Tangen CM, *et al.* Vitamin E and the risk of prostate cancer: the Selenium and Vitamin E Cancer Prevention Trial (SELECT). JAMA 2011;306:1549–56.
51. Cabanillas F. Vitamin C and cancer: what can we conclude – 1609 patients and 33 years later? P R Health Sci J 2010;29:215–7.
52. Hung HC, Joshipura KJ, Jiang R, *et al.* Fruit and vegetable intake and risk of major chronic disease. J Natl Cancer Inst 2004;96:1577–84.
53. World Health Organisation. Diet, nutrition and the prevention of chronic diseases. Technical Report Series 2003.

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A rising tide: Hospitals and social media

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Abstract

The advent of social media has changed the face of healthcare communications. More and more hospitals are recognizing this fact and seeking to integrate tools like Twitter® and Facebook® into their own communications strategies. This article gives an overview of the challenges clinics are facing vis-à-vis social media, and of the benefits they reap when the new tools are used effectively. Trends in social media use by hospitals in North America and Europe are highlighted and a range of best practice examples given. These include brand and crisis management, patient and physician education, fundraising, community building, and recruitment. Finally, the shifting role of medical writers and communicators toward social media management is explained.

Keywords: Hospitals, Social media, Healthcare, Medical communications, Medical writing, Patient experience

Many players in the field of healthcare have been integrating social media channels such as Twitter®, Facebook®, and YouTube™ and Co. into their communications strategies.[1] Although most hospitals have not been 'early adopters' of these new tools, the last 2–3 years have seen a significant increase in the number of clinics using social media.[2] Although a hospital whose 'bottom line' should continue to be restoring health to patients is not the same thing as a profit-oriented corporation, many of the problems and chances hospitals are confronted with when using social media are similar to those that companies face. However, some clinics are rising to the challenge and there are already a range of best practice examples where hospitals are using social media to their advantage.

Challenges and chances of social media for hospitals

Many of the restraints holding hospitals back from using social media are the same as those in other institutions: ignorance of the new tools, insecurity about how to use them, and organizational barriers, insufficient resources and/or a lack of strategy and guidelines on social media use. When the first three issues have been addressed and a clinic decides to enter the world of social media, the latter issues quickly come to the fore.

Social media should be integrated into the overarching communications strategy of a hospital and focused towards achieving clearly defined goals. In addition, its unique potential for interacting with audiences needs to be recognized and implemented accordingly. Some hospitals – as indeed some companies – have not yet fully grasped the Web 2.0 paradigm shift and are continuing to just 'push' information at audiences, instead of trying to engage in a conversation with them.[3] Having a conversation with the many people who are likely to engage with a hospital's social media presence is a great deal of work. The Mayo Clinic in the USA, arguably one of the leaders of the pack when it comes to social media use by a hospital, started out with limited personnel but now employs a full-time staff of nine to monitor and feed the hospital's social media channels.[4]

The conjunction of social media and healthcare automatically opens up ethical questions on what is allowed in a hospital setting. Hospitals need to address these and work out a binding social media policy for all players within the organization to avoid embarrassing gaffes or full-blown crises. A case in point is the so-called 'Placenta Incident', where nursing students faced disciplinary measures after posting a picture of a placenta on Facebook® after a training session.[5] Social media trailblazers like the University of Maryland Medical Center and the Mayo Clinic have been exemplary in implementing such guidelines and making them openly accessible.[6,7]

On the face of it, social media might seem to some hospital administrators to be a huge drain on resources without any return. However, as best

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practice examples show, when used strategically social media does reap significant benefits. Hospitals are getting back at least as much as they are giving, be it money through fundraising schemes, qualified personnel through recruitment efforts, or unfiltered information by listening to what people are saying about them. As never before, social media offer clinics the chance to improve their policies and processes based on patient and/or community feedback. Given that there is always room for improvement when it comes to the patient experience,[8] social media can be an invaluable sounding board for what their 'customers' really think. That being said, a positive social media experience can allow hospitals to build and strengthen their own patient communities.

North American hospitals leading the way

So which hospitals are already employing social media? In general, clinics in North America seem to be further along than their European counterparts when it comes to using the new channels of communication. Approximately one in five American hospitals (21%) uses Facebook®, Twitter®, and/or YouTube™ [9] – a figure which is similar in Canada.[10] This level of usage is yet to be reached by European clinics: Of Germany's approximately 2000 hospitals,[11] almost 200 were present on Facebook® in 2011,[12] i.e. about 10%. Data from 2010 suggest that hospitals in some Scandinavian countries (e.g. Sweden and Norway) are very active on LinkedIn, but significantly less so on social media channels like Facebook®.[13,14] LinkedIn usage is also high in the Netherlands (<50%) and in UK hospitals (<40%).[15] A 2010 study found that 40% of British NHS Primary Care Trusts use at least one social media channel.[16]

Whether or not a hospital is able or willing to engage in social media depends on a range of factors. A 2011 study showed that US hospitals that were large, urban or part of a health system were statistically more likely to use social media; they were also more likely to treat children or be involved with graduate medical education.[9] What is encouraging is the creative way in which some clinics are experimenting with social media, be it to strengthen their brand, educate patients and doctors, engage in fundraising, recruit qualified personnel, or manage critical situations. Hospitals that have quickly embraced the new technologies can be expected to have a significant edge over their non-networking competitors in the approaching years.

Expanding a brand

The Mayo Clinic in the USA was one of the world's first hospitals to start using social media. It favored a learning-by-doing approach, dovetailing existing resources with the new tools, and growing its social media platform incrementally. The hospital has by now successfully expanded its brand into the social media world and currently has more than 60 000 Facebook® fans, 260 000 Twitter® followers, and its own YouTube™ channel. Mayo's media strategists saw social media as an extension of the 'word-of-mouth' principle that has always contributed to the hospital's success. Hence, the clinic stays tightly focused on its core strategy – helping people with issues concerning their health and well-being – and trusting that satisfied patients and family members will also act as multipliers on the new channels.[4] The hospital has created its own online community that allows people to access health-related information and connect with one another on specific topics.[17]

Informing patients

Hospitals are using diverse social media platforms to inform and educate their patients and/or the general public. Some are using videocasts, whether integrated into their own websites or promoted via proprietary YouTube™ channels, as a particularly effective medium for explaining complex medical procedures. The University Hospitals Birmingham in the UK have done this particularly well: They produced an

animated videocast explaining radiotherapy treatment to children in collaboration with Aardman animation (the makers of the 'Wallace and Gromit' films).[18] Videocasts are also a means of humanizing hospitals by giving visual access to the people 'behind the scenes' and by storytelling. Clinics use their YouTube™ channels to show interviews with specialists on specific conditions[19] or feature patients explaining how they experience and cope with illness.[20]

Blogs are also an excellent means of keeping patients up to date on medical issues. The Wellington Hospital in the UK curates an extensive blog that can be searched for everything from 'Breast Care' to 'Urology'.[21] The Klinkum Essen-Mitte in Germany used its patient magazine as the starting point for a multimedia information campaign that integrates print, video, and social media. Parts of the print magazine have been converted into videocasts[22] and the different platforms promote each other. The print magazine points readers toward online offerings, and vice versa, users can order the magazine via Facebook®.[23]

Raising funds

San Francisco Medical Center in the USA significantly stepped up fundraising results by employing social media. Its 'Challenge for the Children' competition initially wanted to raise funds for a new children's hospital by pitting individual teams against each other. One of the teams used the popular internet gaming platform Farmville to generate more than $800 000 in donations from 162 544 donors – an amount that far exceeded the hospital's projected goal of $100 000. Players were able to buy seeds for peppermint sticks and then received a teddy bear for their virtual Farmville farm, with all of the proceeds from the candy going to the donation fund.[24] St. Jude's Research Hospital in the USA has almost half a million Facebook® fans and almost 100 000 Twitter® followers. The hospital consistently uses its social media platforms to raise funds for ongoing research into childhood cancer.[25]

Building healthy communities

The South Coast Health System, a non-profit health delivery system encompassing three regional hospitals in the USA does not have a flashy social media presence, but is much geared toward the needs of its specific community. As a result it has developed an iPhone app called MyHealth to help patients and caregivers manage their healthcare environment (prescriptions, appointments, etc.).[26] Other hospitals are discovering how to use Twitter®, which is a powerful tool for connecting with patients and which some experts say is still not being used to its full potential in healthcare settings.[27] That being said, the NHS Nottingham City in the UK uses Twitter® to alert patients to the need for getting a flu jab and offers web resources to direct patients to their nearest hospital or healthcare provider.[28] Birmingham's Heartlands Hospital in the UK hosted a two week Twitter®-o-thon to educate patients on diabetes and obesity.[29] And a Twitter® session by a Mayo Clinic specialist led to a patient seeking help from the hospital on a condition she had been told was untreatable.[30]

Managing crises

The South Coast Health System (SCHS) in the USA also used Twitter® during an environmental crisis to keep people updated on an ongoing basis. After a large chemical spill, numerous people were taken to local hospitals for treatment. The SCHS kept up a continuous live stream of information on patient admittances and releases, treatment progression, and on what the media was reporting about the accident.[31] Hospitals might do well to explore further uses for Twitter® in an emergency care setting, i.e. in triage situations or in the management of emergency response teams. Texas Health Resources, a 13-hospital system, used Yammer (a kind of internal Twitter® for companies) when one of the system's hospital emergency departments was overcrowded with flu patients. The Chief Nursing Officer sent a message on Yammer about the problem, whereupon another hospital offered to share its resources to help meet the emergency.[32]

Educating doctors

Social media can be used not just to inform and educate patients, but healthcare professionals too. Johns Hopkins Medicine is using Twitter® to tweet live during seminars, upping its re-tweet rate, and own popularity among followers.[33] The University of Buffalo is encouraging its surgeons to tweet during surgery, hoping to accelerate and enhance the flow of information for medical training purposes.[34] Several US hospitals have employed Twitter® during live surgery, not just to educate doctors, but also to inform patients and the general public about specialized procedures.[35]

Recruiting talent

After having trouble recruiting gastroenterologists via medical journals and direct mail, Geisinger Health System in the USA decided to shift their

focus to social media channels. They launched a Facebook® page with pictures, information on recruiting events and links to their own website which proved to be substantially more successful in attracting candidates and filling vacant positions than the conventional channels had been.[36] Many hospitals like the Children's Hospital of Philadelphia are using videocasts to describe what their medical employees do on a daily basis and to attract people who may be looking into a career such as nursing.[37,38]

Role of medical writers and communicators

With the proliferation of communications platforms and the speed of change driving the communications process, the role of medical writers and/or communicators active in a clinic environment is subtly shifting and broadening. Writers will not just have to stay abreast of current developments online, they will need to expand their qualifications to include formats like pod- and videocasts, whose effective use still hinges on the conceptualization skills necessary for good writing, but whose storytelling approach is different. In addition to communicating with external target groups directly, writers will need to extend their role within the organization, i.e. by identifying and recruiting individuals willing and able to engage with the new tools, by teaching staff how to use social media platforms, and by encouraging them to find their own writing 'voice'. In effect, writers and/or communicators are becoming what is termed as 'social media managers' or 'community managers' – flexible enablers capable of getting messages across by intelligently fusing old and new communications tools.

Conclusion

After a slow start, hospitals in the Western world are increasingly using social media channels to connect with different audiences. Clinics in North America have a head start over their European counterparts as to the frequency of usage, but there are best practice examples on both sides of the Atlantic that show how social media can be used to benefit the players involved. Social media not only offers hospitals the chance of connecting directly with their communities and receiving valuable feedback on their services, but can be used for a range of other activities like brand and crisis management, patient and physician education, fundraising, and recruitment. The role of medical writers and communicators within this environment is evolving into that of a social media manager responsible for integrating old and new tools and using them strategically to the best effect.

References

1. U Schoenberg. Tricky terrain: healthcare and social media, The Write Stuff/J Eur Med Writers Assoc 2011;20(4):240–243.
2. http://ebennett.org/hsnl/data
3. http://verasoni.com/ahha3/2216
4. http://www.emarketer.com/blog/index.php/case-study-mayo-clinic-supports-patients-social-media
5. http://healthland.time.com/2011/01/05/placentas-on-facebook-nursing-school-says-no-way
6. http://www.umm.edu/resources/web_comments_policy.htm
7. http://sharing.mayoclinic.org/guidelines/for-mayo-clinic-employees
8. http://www.nejm.org/doi/full/10.1056/NEJMsa0804116#t=articleTop
9. Thaker SI, Nowacki AS, Mehta NB, Edwards AR. How U.S. hospitals use social media. Ann Intern Med 2011;154:707–708.
10. http://www.smich.ca/?page_id=12
11. http://de.statista.com/statistik/daten/studie/2617/umfrage/anzahl-der-krankenhaeuser-in-deutschland-seit-2000
12. http://gesundheitswirt.posterous.com/liste-der-deutschen-krankenhauser-kliniken-be
13. http://hospitalseu.wordpress.com/2011/01/10/use-of-social-media-by-hospitals-in-sweden-part-2
14. http://hospitalseu.wordpress.com/2011/01/28/use-of-some-by-hospitals-in-norway-part-2
15. http://aci.schattauer.de/en/news-archive/aci-news/single-news-from-aci/newsDate/2010/november/24/newsArticle/increasing-numbers-of-hospitals-using-social-media.html
16. Hawker MD. Social networking in the National Health Service in England: a quantitative analysis of the online identities of 152 primary care trusts. Stud Health Technol Inform 2010;160(1):356–360. Hospital Social Network List (updated 19 October, 2010).
17. http://connect.mayoclinic.org
18. http://www.youtube.com/user/uhbvideos#p/u/5/8pBjobqdtrc
19. http://www.youtube.com/user/ChildrensHospital#p/u/21/B4xtpZj8uLw
20. http://www.youtube.com/user/ummcvideos#p/u/12/p2eizLHg-kg
21. http://blog.thewellingtonhospital.com
22. http://www.pulsschlag.tv
23. http://de-de.facebook.com/KlinikenEssenMitte
24. http://www.ucsf.edu/news/2010/11/5843/challenge-children-fundraising-competition-heats
25. http://www.stjude.org
26. http://www.southcoast.org/myhealthapp
27. http://www.slideshare.net/philbaumann/140-health-care-uses-for-twitter-presentation
28. https://twitter.com/#!/NHSNottingham
29. http://nhslocal.nhs.uk/story/heartlands-hospital-first-uk-health-organisation-give-advice-social-media
30. http://www.youtube.com/watch?v=1tWmfRSGoMc&feature=relmfu
31. http://twitter09.wordpress.com/the-book/case-study-hospitals
32. http://www.aha.org/about/membership/constituency/hcs/texashlthcase.html
33. http://gracemediainc.com/tag/healthcare
34. http://www.buffalo.edu/news/12925
35. http://www.launchyourmovement.com/2010/04/10-hospital-social-media-success-stories

36. http://www.healthleadersmedia.com/content/239450/topic/WE_HLM2_MAR/Health-System-Uses-Social-Media-to-Recruit-Physicians.html
37. http://www.youtube.com/watch?v=c2iCWXyRb5g
38. http://www.youtube.com/watch?v=hGiLZ_thNdA&feature=related

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Media coverage of cancer

Beyond the oncology clinical study reports and the medical manuscripts that we medical writers prepare is a body of literature on cancer that targets the lay audience. And these may actually paint a completely different picture of the disease than what we see in tables, figures, and listings.

Two studies investigated how the media cover cancer research in two countries. In one study, American researchers conducted a content analysis of cancer news reporting by US newspapers ($n = 8$) and magazines ($n = 5$) between 2005 and 2007. Their results showed that of the 436 randomly sampled articles analysed, 32.1% focused on survivorship and only 7.6% on mortality. The majority of the articles covered aggressive cancer treatments (57.1%), but only 13.1% reported that these treatments can fail. The topic of end-of-life palliative care for cancer patients is very rarely discussed (2 of the 436 articles). The authors criticized the American media for misleading the public by giving an 'inappropriately optimistic view of cancer treatment, outcomes, and prognosis'.[1]

Another study analysed stories by the world's largest broadcasting organization, the UK-based BBC, on cancer research from July 1998 to June 2006. Innovations in cancer treatment are a favourite topic (20%) followed by lifestyle choices (12%), genetics (9%) and nutrition (e.g. food and beverage; 8%). Most of the stories cited as sources articles published in peer-reviewed journals but with a bias towards UK (40%) and US (36%) research papers. In fact, the British papers were overcited by a factor of about 6 relative to research papers from the rest of the world. The sources were dominated by *The Lancet*, *British Journal of Cancer*, and *British Medical Journal*, journals with high impact factors. The authors concluded that 'media reporting of cancer research by the BBC is, relative to global cancer research activity and outputs (publications), narrow'.

Both studies reported breast cancer as the cancer type most covered by the media (>30% of all the BBC stories), which was actually over-reported relative to its cancer disease burden of 13%.[2] Preference for the 'pink' cancer may be due to its high survival rate which gives lots of happy-ending material. However, survivorship of young, beautiful celebrities (e.g. Kylie Minogue, Christina Applegate) also 'glams' the malignancy and keeps the paparazzi busy.

Statistics estimate that one in two men and one in three women will have cancer during their lifetime.[1] Everybody knows at least one person diagnosed with cancer. Sad as it may sound, cancer is so widespread it has almost become a household word. All the more reason why a balanced and less hyped media reporting on cancer is needed.

References

1. Lewison G, Tootell S, Roe P, Sullivan R. How do the media report cancer research? A study of the UK's BBC website. Br J Cancer 2008;99(4):569–76.
2. Fishman J, Ten Have T, Casarett D. Cancer and the media: how does the news report on treatment and outcomes? Arch Intern Med 2010;170(6):515–8.

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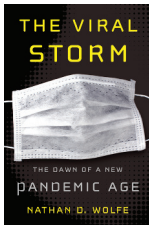
In the Bookstores



The Viral Storm: The Dawn of a New Pandemic Age
by Nathan D. Wolfe; Macmillan, 2011.
ISBN-13: 978-1846142987. 14.99 GBP. 320 pages.

All you ever wanted to know about pandemics – and then some

A warning, for those with a nervous disposition this is not a book for you; if you have an obsessive compulsive nature and go around cleaning door handles after others have touched them, then this is also not the book for you.

Pandemic originates from the Greek *pan* meaning all and demos meaning *people*. Whether or not a disease is labelled as a pandemic is not related to how many people it manages to kill, but by how much it can spread. The ideal candidate has the ability to spread easily from person to person as well as harm and kill those it infects. The author defines pandemic as 'a new infectious agent that has spread to individuals on all continents' (except Antarctica) and tries to answer how and why pandemics start, and what can be done to prevent them.

Using the spread of HIV as the template for other potential pandemics, he attempts to explain how our evolution from small isolated hunter-gather communities into city-dwelling, high-density populations, who globe-trot around the world has allowed us to create the conditions for a viral 'perfect storm'. Viral sequencing has enabled scientists to trace HIV evolution back to the late nineteenth or early twentieth century when it is presumed that a hybrid Simian immunodeficiency virus jumped from chimpanzees to humans via hunters catching and butchering infected animals. From this beginning, the virus remained unobserved and unrecognized in small isolated communities in Africa, 50 years before we had ever heard of it, and often following evolutionary 'dead-end' pathways. At some point, an HIV isolate obtained the necessary capacities to allow it to spread more easily and by capitalizing on our modern lifestyles involving urbanization and global travel it has spread into every corner of the world. In the way that HIV has gone global, are there other viruses waiting in the wings that will evolve in a similar way and are as yet undiscovered?

As I read the first part of the book, I found myself thinking 'we're doomed;' however, we are left with some hope. The ability to stop pandemics is dependent on the dedication of the author, alongside that of several other teams of equally committed individuals across the globe. Self-styled as virus hunters, and reminiscent of storm chasers, Nathan Wolfe and his colleagues provide 'listening posts' at 'hot spots' around the globe with the objective of stopping potential pandemics in their tracks before they are able to take hold and spread. By harnessing modern, cutting-edge technology they are monitoring global 'viral chatter.' One eventual hope is that we will soon have the ability to recognize 'early unusual clusters of health complaints that might signal the beginning of an epidemic,' otherwise known as 'digital epidemiology'.

Written in a very accessible style, the book makes a compelling read. As well as highlighting areas of modern-day medical virology relevant to halting the spread of a potential pandemic, it is an anthropological study of the interaction of people and viruses. The author examines our ancestry from a viral perspective and helps to explain the natural evolution of pandemics without bamboozling the reader with science. Well worth a read – but maybe not when you have flu-like symptoms or a cough.

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Impact of protocol amendments, bias and quality in industry-funded trials, and rethinking authorship criteria

Impact of protocol amendments

Amendments to clinical trial protocols are widespread, but can result in increased costs and delays in study implementation. Little is known about the nature and impact of protocol amendments; therefore, the Tufts Center for the Study of Drug Development (Tufts CSDD) in the USA conducted a study, in collaboration with 17 midsize to large pharmaceutical and biotechnology companies, to measure the incidence, causes, and repercussions of protocol amendments.[1] Protocols approved between January 2006 and December 2008 and across a range of therapeutic areas and developmental phases were examined, and data were collected on the protocol design characteristics; the number, nature, and causes of amendments; and the time and costs to implement these amendments. A total of 3410 protocols were submitted providing data on 3596 amendments: 54% were phase I studies, 18% phase II, 13% phase III, and 15% phase IIIb/IV.

Across all study phases, 58.8% of completed protocols had at least one amendment; 43% were amended before the first subject first visit. Each amended protocol had an average of 2.3 amendments and required an average of 6.9 changes to the protocol; later stage phase II and III protocols had a slightly higher average number of amendments (2.7 and 3.5, respectively). The therapeutic areas that had the highest number of amendments and changes were cardiovascular and gastrointestinal diseases. Larger studies and studies involving longer treatment durations were significantly positively correlated with more amendments ($P < 0.001$ using Spearman's rho correlational analysis). The most common protocol amendment adjustments made were to the population description (including inclusion and exclusion criteria; 16%) and to the safety assessments (12%). The most common causes of protocol amendments were: the availability of new safety information about the drug (19.5%), requests from regulatory agencies to amend the study (18.6%), and changes in the study strategy (18.4%); design flaws and difficulty recruiting were also commonly cited reasons. One-third of amendments were considered 'somewhat or completely avoidable'. Each amended protocol resulted in an average of 4 months of incremental time to put into action; approximately half of this time was spent determining what changes needed to be made. The average cost per amendment was substantial ($453 932); but this figure should be viewed cautiously as the available sample size for this calculation was small at only 20 amendments. The authors thought it important to emphasize that protocol amendments are often necessary, particularly when they impact patient safety, but suggested that their results offer insights into ways some amendments can be avoided leading to possible time and cost savings.

Quality of industry-funded versus non-industry-funded trials

In a short Current Medical Research and Opinion (CMRO) commentary, Angelo Del Parigi discussed the differences in the quality of industry-funded clinical trials compared with non-industry-funded trials.[2] Concerns about industry-funded trials often arise, particularly relating to fears that the commercial goals and interests of pharmaceutical companies can overrule the design, execution, analysis, and interpretation of trial results. Few researchers however have attempted to compare the quality of industry versus non-industry-funded trials objectively. The evidence so far suggests that the quality of industry-funded trials is, on average, higher than non-industry-funded trials. Del Parigi gave a few examples, such as an analysis of randomized controlled trials in a number of disease areas from a sample of Cochrane reviews that found that while conclusions tended to favour the experimental drug in industry-funded studies, they were also more likely to have larger sample sizes, more complete recording of adverse events, more frequent use of placebos or no treatment controls and double blinding, and were more likely to be published in high-impact journals compared with non-industry-funded trials.[3] Other examples included a paper on long-term randomized controlled trials in obesity that found that the quality of reporting was

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significantly higher for industry-funded trials and a systematic review showing that industry-funded trials had 'more complete reporting' of safety data compared with non-industry-funded trials.[4,5]

Del Parigi pointed out that evidence of the higher quality of industry-funded studies does not excuse the presence of publication biases (e.g. selective reporting or downplaying negative outcomes) or of cases of alleged or real misconduct in industry-funded research. Del Parigi appreciated that industry-funded trials may be submitted to multiple levels of scrutiny often by external bodies, which may in part be responsible for the high-quality clinical and reporting practices associated with these trials. However, he also argued that there is still room for improvement and suggests that a first step would be to make data sets publicly available to encourage multiple independent data interpretations.

More on defining authorship

In a short *BMJ* Personal View piece, David Shaw, a lecturer in ethics at the University of Glasgow, expressed his concerns over the current and widely adhered to definition of publication authorship from the International Committee of Medical Journal Editors (ICMJE).[6] To recap, according to the ICMJE, 'authorship credit should be based on (1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; and (3) final approval of the version to be published. Authors should meet conditions 1, 2, and 3'. Using a hypothetical example of three researchers each contributing to the design, implementation, and reporting of the study in different ways, Shaw showed that none of the researchers met all three of the ICMJE criteria for authorship. Shaw took the idea further and suggested that the ICMJE criteria were unethical and should be changed because 'Having a great idea and sharing it with colleagues and approving what they do with it is clearly to cowrite a paper. Gathering and analysing data is to cowrite a paper. And redrafting and reviewing a paper is to cowrite a paper'. He suggests that the ICMJE criteria would be more sensible if they considered that meeting one of the three criteria was sufficient for legitimate authorship.

References

1. Getz KA, Zuckerman R, Cropp AB, Hindle AL, Krauss R, Kaitin KI. Measuring the incidence, causes, and repercussions of protocol amendments. Drug Inf J 2011;45(03):265–75.
2. Del Parigi A. Industry funded clinical trials: bias and quality. Curr Med Res Opin 2012;28(1):1–3.
3. Als-Nielsen B, Chen W, Gluud C, Kjaergard LL. Association of funding and conclusions in randomized drug trials: a reflection of treatment effect or adverse events? JAMA 2003;290(7):921–8.
4. Thomas O, Thabane L, Douketis J, Chu R, Westfall AO, Allison DB. Industry funding and the reporting quality of large long-term weight loss trials. Int J Obes (Lond) 2008;32(10):1531–6.
5. Golder S, Loke YK. Is there evidence for biased reporting of published adverse effects data in pharmaceutical industry-funded studies? Br J Clin Pharmacol 2008; 66(6):767–73.
6. Shaw D. The ICMJE's definition of authorship is illogical and unethical. BMJ 2011;343:bmj.d7192.

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Why won't you give me your data?

In 2005, Dutch researcher Jelte Wicherts and his colleagues contacted the corresponding authors of 141 papers published in four high-ranking psychology journals requesting their datasets to assess the impact of outliers on statistical outcomes.[1] Although all the authors had signed statements confirming that they would share their data with others to allow verification, 73% failed to do so. Why?

To answer this and other questions, Wicherts and his colleagues conducted a new study, recently published in *PLoS One*,[2] in which they tested whether there is a link between willingness to share data and the strength and accuracy of statistical results. Does unwillingness to share data stem from fear that reanalysis will expose errors and challenge the authors' conclusions?

Wicherts *et al.* took a sample of 49 papers from their original study and used the information they contained – reported test statistics (t, F, and χ^2), degrees of freedom and P values – to test whether (1) accuracy of statistical reporting and (2) sizes of

P values varied according to whether or not the corresponding author had supplied the dataset.

Of the 49 reporting errors they found, a whopping 96% involved reported *P* values that were smaller than the recalculated ones. A significant majority (73%) occurred in papers whose authors had failed to provide data, while none of the corresponding authors of the seven papers in which supposedly significant *P* values were in fact found to be non-significant had given Wicherts and his colleagues their data.

In a second recent study,[3] Wicherts and his colleague Marjan Bakker analysed 281 psychology papers and found that 15% of them incorrectly assigned statistical significance or non-significance to at least one result.

Further analysis in the *PLoS One* study[2] showed that *P* values were, on average, higher in papers whose data had not been shared. But does authors' fear of their work being undermined, of *P* values losing their significance explain these findings?

By Wicherts and his colleagues' own admission, this is not the only possible explanation. Could it instead be the case that researchers who analyse their data with more rigour also archive them better and thus have an easier job of retrieving them on request?

Irrespective of what lies behind it, something must be done about the seemingly widespread failure to share data. According to Wicherts, what we need is for journals and other bodies to implement mandatory archiving policies. Making it impossible to publish papers without depositing the data in a web archive would surely alleviate the problem.

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How short can an abstract be?

Biomedical journals specify word limits for abstracts in the articles they publish. The upper limit is usually in the range of 100–250 words. Sometimes it is difficult to keep within these limits. However, it seems that not all authors have this problem. The abstract below appeared on the physics preprint server arXiv and was sent to *Medical Writing* by Jim Hartley (j.hartley@psy.keele.ac.uk).

Can apparent superluminal neutrino speeds be explained as a quantum weak measurement?

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Abstract
Probably not.

Keywords: Quantum measurement, interference, neutrino oscillations
Source: http://arxiv.org/abs/1110.2832

Conflicts of interest: what do peer reviewers think?

Whether or not industry sponsorship causes bias in scientific papers has been much debated. On the other hand, until now, no one has looked at whether conflicts of interest influence how peer reviewers view and review manuscripts.

To explore peer reviewers' feelings about financial conflicts of interest, Suzanne Lippert and her colleagues sent a 29-question web-based survey to 410 active reviewers for *Annals of Emergency Medicine*, one of the many journals that now require authors to make statements regarding their conflicts of interest.

Most of the 218 reviewers who provided complete responses to the survey felt that authors were influenced by their financial ties to industry.[1] However, this did not clearly translate into changes in the way they evaluate manuscripts.

While a majority of reviewers claimed that they would read more carefully papers whose authors had conflicts of interest, and felt that the credibility of such papers would be reduced, considerably fewer would change their recommendations to the editor.

In their responses to one particular question, three-quarters of reviewers expressed doubt as to whether authors of industry-sponsored articles have full access to data. Meanwhile, a small majority (54%) believed that an honorarium of any size biases an author's judgement, which does not exactly lend support to Lippert *et al.*'s proposal that authors divulge the *sizes* of the payments they have received from companies.

Interestingly, a smaller proportion of reviewers who themselves had received such payments considered that they cause bias. Do the experiences of these reviewers not square with the suspicions of those who have never consulted for pharmaceutical companies? Are academics who do not believe that honoraria cause bias more likely to accept them? We can but speculate.

Lippert *et al.* further suggest that authors confirm that they had full access to the study data, while acknowledging that this is already covered by ICMJE guidelines.[2] Their third key proposal—that peer reviewers themselves disclose industry payments—is, and has long been, a stipulation of the journal whose reviewers they surveyed.[3,4]

In other conflict-of-interest news, David Isaacs, Editor-in-Chief of the *Journal of Paediatrics and Child Health*, has written an editorial warning of the dangers of financial conflicts of interest and refuting the notion that declaring them does anything to prevent bias.[5]

References

1. Lippert S, Callaham ML, Lo B. Perceptions of conflict of interest disclosures among peer reviewers. PLoS One 2011;6(11):e26900.
2. International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals: writing and editing for biomedical publication. [cited 30 November 2011]. Available from: http://www.icmje.org/urm_full.pdf.
3. Callaham ML. Journal policy on ethics in scientific publication. Ann Emerg Med 2003;41(1):82–9.
4. Annals of Emergency Medicine. Annals conflict of interest policy for editors and reviewers. [cited 1 December 2011]. Available from: http://www.annemergmed.com/content/instauth#conflict.
5. Isaacs D. Conflict of interest: no such thing as a free lunch. J Paediatr Child Health 2011;47(10):679–80.

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Cannabinoids in oncology: more than a palliative

Usually you have chemotherapeutics and biologicals in mind when you are talking about oncology. Would you have thought of cannabinoids? I don't think so but for decades, cannabinoids have been known to exert palliative effects in cancer patients including appetite stimulation and pain relief.[1,2] Δ^9-Tetrahydrocannabinol (Unimed Pharmaceuticals, THC, Marinol®) and its synthetic analogue nabilone (Valeant Pharmaceuticals International, Cesamet®) are approved for the treatment of chemotherapy-induced nausea and emesis. Sativex® (Unimed Pharmaceuticals), a mucosal spray containing cannabis extract, licensed for multiple sclerosis spasticity, is currently under development for cancer pain (Phase III stage). In Canada, Sativex® has already been approved as an adjunctive analgesic treatment in adult patients with advanced cancer. And apart from the established use in palliative care, you might be astonished to hear that cannabinoids are regarded as possible anti-tumour agents with a low-toxicity profile.

However, firstly we need to step back a little. What are cannabinoids? The hemp plant *Cannabis sativa* produces approximately 60 unique compounds known as cannabinoids, of which THC is the most studied owing to its high potency and abundance. THC is mainly responsible for the desired effects in the recreational use of cannabis and marijuana. Cannabinoids exert a wide array of effects within the central nervous system (CNS) as well as in the periphery such as immune, cardiovascular, digestive, reproductive, and ocular functions. Most of these effects are mediated via two cannabinoid-specific receptors, CB_1 and CB_2. The CB_1 receptor is particularly abundant in the CNS, whereas the CB_2 receptor is predominantly expressed by peripheral immune cells. The most important endogenous ligands on these receptors are anandamide and 2-arachidonylglycerol, which together with the respective receptors and specific processes of synthesis, uptake and degradation constitute the endogenous cannabinoid system. As the isolation of anandamide and 2-arachidonylglycerol, further endocannabinoids have been identified like noladin ether and virodhamine, the latter having been identified as the first endogenously occurring CB_1 receptor antagonist.[3]

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Cannabinoids might directly inhibit cancer growth via complex mechanisms. Actually, the antiproliferative properties of cannabis compounds were first reported 30 years ago by Munson *et al.*,[4] who showed that THC inhibits lung adenocarcinoma cell growth *in vitro* and after oral administration in mice. Although these observations were promising, further studies in this area were not carried out until the late 1990s. Various cannabinoids, including plant-derived, synthetic, and endocannabinoids have now been shown to block cancer cell proliferation and to induce apoptosis of cancer cells both *in vitro*[5,6] and *in vivo*.[7,8] Cannabinoids also possess promising anti-angiogenic, anti-invasive, and anti-metastatic potential. This is, for example, associated with a reduced expression of vascular endothelial growth factor[9] and other pro-angiogenic cytokines as well as modulation of expression of matrix metalloproteinases and their inhibitors. Matrix metalloproteinases are proteolytic enzymes that allow tissue breakdown and remodelling during angiogenesis and metastasis.[10–12]

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The endocannabinoid system is activated in several cancer tissues and malignant cells, and *in vivo* and *in vitro* studies indicated that this upregulation might be involved in the tonical control of tumour growth.[13] Endocannabinoids possess anti-tumourigenic potential via inhibition of proliferation,[14] induction of apoptosis,[15] and inhibition of angiogenesis.[16] Manipulation of the endogenous cannabinoid system may represent a means to combat tumour development. Table 1 gives an overview of findings regarding cannabinoid-based cancer therapy.

Despite promising evidence from *in vitro* and *in vivo* studies, clinical data are still very rare. The first study could not prove a benefit of cannabinoid treatment in glioma patients, but at least provides the basis for further clinical investigation.[17] Clinicaltrials.gov reveals no further cannabinoid studies in cancer apart from palliative use. Limitations for cannabinoids and endocannabinoids as cancer therapeutics may be their psychotropic activity and modulation of the immune response, which will need to be circumvented.

The following websites will give you a comprehensive picture of the possibilities of the use of cannabinoids in medicine in general and specifically as an anti-tumour treatment:

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2697681/?tool=pubmed
http://pharmrev.aspetjournals.org/content/58/3/389.long

These are reviews on CB receptor agonists as therapeutic options by Pertwee,[19] one of the leading working groups in cannabinoid research, and Pacher *et al.*[3]

http://jpet.aspetjournals.org/content/332/2/336.long
http://herb.com/guzman.pdf[18]

Further reading on the anti-tumourigenic properties of cannabinoids for those of you who want to gain deeper mechanistic insights.

http://cancer.about.com/od/chemotherapysideeffects/a/Marinol.htm

Dronabinol is another name used for THC and it is the active ingredient of Marinol®. Whether medical marijuana or Marinol® is the better choice is a matter of debate. Here you can find a collection of articles around this debate. However, a clear answer is still outstanding.

http://www.gwpharm.com/Sativex.aspx

Sativex® is a quite interesting medication. On the one hand, because of its route of administration (i.e. mucosal spray), on the other hand because of its active ingredient, which is an extract of cannabis that is standardized for the content of THC and cannabidiol. The manufacturer's website on Sativex® offers a lot of information around this special product and the development of it.

http://www.cannabis-med.org/index.php?lng=en

The use of cannabis, its ingredients or derivates is not only a medical question, it is to a great extent a

Table 1: Applications, mechanisms, and pros and cons of cannabimimetics in cancer therapy

	CB_1 agonists/activators	CB_2 agonists/activators	Endocannabinoids	Endocannabinoid analogs
Possible application	Mammary, prostate, thyroid, cervical and colon carcinoma, neuroblastoma, glioma, lung cancer	Cervical carcinoma, glioma, lung cancer	Mammary, prostate, and thyroid carcinoma	Glioma, cervical carcinoma
Mechanisms	Inhibition of mitogen-induced stimulation of the G_0/G_1–S phase of cell cycle – inhibition of metastasis, cancer cell invasion, migration, angiogenesis	Apoptosis, inhibition of cancer cell invasion	Inhibition of mitogen-induced stimulation of the G_0/G_1–S phase of cell cycle	Apoptosis receptor independent
Advantages	Little or no toxicity, little or no suppression of the immune system	No psychotropic effects, little or no toxicity	Little or no toxicity	Metabolically stable
Disadvantages	Psychotropic effects, possible dependence	Interference with the immune response	Little efficacy due to metabolic instability	Toxicity not yet assessed

Adapted and updated from[20] and[21].

political one. It is restricted in its use by the narcotic laws and therefore the use of medicinal cannabis and its components are closely connected to a debate about legalization of the use of cannabis. The International Association of Cannabis in Medicines fights for the medical use of cannabis, and it is indeed a fight, with law and politics, as you can read from their website. Apart from these aspects, the website is a great source for up-to-date information on what is going on in the world of cannabis research.

http://www.youtube.com/watch?v=8Md2WNqqxTQ&feature=fvst

Medical Cannabis explained… If you prefer listening and watching instead of reading, here you go! This video covers the medical aspects and also provides a short excursion on the political aspects and the history of cannabis use.

If you have any further questions or you have any other comments or suggestions, please email me.

References

1. Glare P, Miller J, Nikolova T, Tickoo R. Treating nausea and vomiting in palliative care: a review. Clin Interv Aging 2011;6:243–59.
2. Farquhar-Smith WP. Do cannabinoids have a role in cancer pain management? Curr Opin Support Palliat Care 2009;3:7–13.
3. Pacher P, Batkai S, Kunos G. The endocannabinoid system as an emerging target of pharmacotherapy. Pharmacol Rev 2006;58:389–462.
4. Munson A, Harris L, Friedman M, Dewey W, Carchman R. Antineoplastic activity of cannabinoids. J Natl Cancer Inst 1975;55:597–602.
5. Sanchez C, Galve-Roperh I, Canova C, Brachet P, Guzman M. Δ9-tetrahydrocannabinol induces apoptosis in C6 glioma cells. FEBS Lett 1998;436:6–10.
6. Jacobsson S, Wallin T, Fowler C. Inhibition of rat C6 glioma cell proliferation by endogenous and synthetic cannabinoids. relative involvement of cannabinoid and vanilloid receptors. J Pharmacol Exp Ther 2001;299:951–9.
7. Galve-Roperh I, Sanchez C, Cortes M, del Pulgar T, Izquierdo M, Guzman M. Anti-tumoral action of cannabinoids: involvement of sustained ceramide accumulation and extracellular signal-regulated kinase activation. Nat Med 2000;6:313–9.
8. Casanova M, Blazquez C, Martinez-Palacio J, Villanueva C, Fernandez-Acenero M, Huffman J, *et al.* Inhibition of skin tumor growth and angiogenesis in vivo by activation of cannabinoid receptors. J Clin Invest 2003;111:43–50.
9. Blazquez C, Gonzalez-Feria L, Alvarez L, Haro A, Casanova M, Guzman M. Cannabinoids inhibit the vascular endothelial growth factor pathway in gliomas. Cancer Res 2004;64:5617–23.
10. Blazquez C, Casanova M, Planas A, Pulgar TD, Villanueva C, Fernandez-Acenero M, *et al.* Inhibition of tumor angiogenesis by cannabinoids. FASEB J 2003;17:529–31.
11. Ramer R, Hinz B. Inhibition of cancer cell invasion by cannabinoids via increased expression of tissue inhibitor of matrix metalloproteinases-1. J Natl Cancer Inst 2008;100:59–69.
12. Ramer R, Merkord J, Rohde H, Hinz B. Cannabidiol inhibits cancer cell invasion via upregulation of tissue inhibitor of matrix metalloproteinases-1. Biochem Pharmacol 2010;79:955–66.
13. Bifulco M, Laezza C, Valenti M, Ligresti A, Portella G, DiMarzo V. A new strategy to block tumor growth by inhibiting endocannabinoid inactivation. FASEB J 2004;18:1606–8.
14. Petrocellis LD, Melck D, Palmisano A, Bisogno T, Laezza C, Bifulco M, *et al.* The endogenous cannabinoid anandamide inhibits human breast cancer cell proliferation. Proc Natl Acad Sci USA 1998;95:8375–80.
15. Sarker K, Maruyama I. Anandamide induces cell death independently of cannabinoid receptors or vanilloid receptor 1: possible involvement of lipid rafts. Cell Mol Life Sci 2003;60:1200–8.
16. Portella G, Laezza C, Laccetti P, Petrocellis LD, Marzo VD, Bifulco M. Inhibitory effects of cannabinoid CB1 receptor stimulation on tumor growth and metastatic spreading: actions on signals involved in angiogenesis and metastasis. FASEB J 2003;17:1771–3.
17. Guzman M, Duarte M, Blazquez C, Ravina J, Rosa M, Galve-Roperh I, *et al.* A pilot clinical study of Δ9-tetrahydrocannabinol in patients with recurrent glioblastoma multiforme. Br J Cancer 2006;95:197–203.
18. Guzman M. Cannabinoids: potential anticancer agents. Nat Rev Cancer 2003;3:745–55.
19. Pertwee RG. Emerging strategies for exploiting cannabinoid receptor agonists as medicines. Br J Pharmacol 2009;156:397–411.
20. Bifulco M, DiMarzo V. Targeting the endocannabinoid system in cancer therapy: a call for further research. Nat Med 2002;8:547–50.
21. Freimuth N, Ramer R, Hinz B. Antitumorigenic effects of cannabinoids beyond apoptosis. J Pharmacol Exp Ther 2010;332:336–44.

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Communication needs of cancer patients

Cancer patients have a need to access easily understandable information about the disease, treatments, side effects, and outcomes as quickly as possible. This article reviews the many facets of the special and changing communication requirements of oncology patients and provides some relevant ULRs.

Why the need for secondary resources, you might ask. Aren't these patients getting the information they need from their doctors? Some are not, and there are several possible explanations for this. Research has shown that while some patients are willing to trust in their physician's knowledge and therefore are unlikely to seek out extra information, others are reluctant to take up too much of a doctor's time, aware of the limited time they then have for other patients.[1,2] If cancer patients do not get the answers they want from their doctor's surgery, the Internet is an obvious port of call but the information they find there might not be easily understandable. One study, for example, found that 'information regarding breast cancer prevention obtained from the National Cancer Institute's web site is written at far too high of a level'.[3]

A study conducted among 269 cancer patients in the UK in the mid-1990s found that 79% of them wanted as much information as possible.[4] However, particularly in the case of cancer, all issues stemming from an accurately conveyed and understood diagnosis may be difficult to correctly identify, particularly as some doctors do not reveal the actual diagnosis to the patient – 'in many cases even when the patient asked to be told the truth'.[5] An online survey of cancer patients conducted in Israel in November 2011 found that 35% defined the information they received from their doctors about their disease and possible treatments as insufficient, 28% regarded it as incomplete, and 21% said it was unclear.[6]

In the UK, the NHS Cancer Plan (2000)[7] sets out the importance of cancer patients having access to high-quality, accurate information, whereas in the US, the National Comprehensive Cancer Network (NCCN), which provides clinical practice guidelines for physicians, has recently created patient-friendly versions to provide state of the art cancer treatment information in easy-to-understand language. The rationale is to help patients with cancer speak with their treating oncologist about their best treatment options (see box).

It is also important to realize that cancer patients are not a homogeneous group. Research has shown that their information needs are fluid, liable to change as their disease progresses. Various studies have found that patients at certain times during their treatment avoided potentially negative information as part of a coping mechanism.[1,8]

With better prevention, early diagnostics, and ever-improving treatments, more patients survive and new issues concerning them have surfaced, making the survivor another important stakeholder in the field of cancer communication.

Originally the term 'cancer survivor' referred to family members who had lost a loved one to the disease. However, by the 1960s physicians began to refer to 'cancer survivors' as those who had survived 5 years past their diagnosis or treatment, when the risk of a recurrent cancer had diminished substantially. These days there are still differing views as to what constitutes a survivor, but the National Coalition for Cancer Survivorship and the NCI Office of Cancer Survivorship consider a person to be a cancer survivor from the time of cancer diagnosis through the balance of his or her life.[9]

The rise in survivor rates reflects big strides in cancer detection and treatment and the effect of an aging population. For example, nearly 12 million people in the USA, almost four times as many as 40 years ago, are survivors.[10] In the UK, there are over 2 million survivors, predicted to rise to 4 million by 2030.[11]

As you can imagine, there has also been an accompanying rise in the number of survivor narratives available (see box, for an example). These survivors, like many patients are usually well informed and particularly motivated to transmit the knowledge they gained during their treatment to fellow patients. For example, some 70% claim they would volunteer to assist in survivorship activities.[12]

This patient group is now very visible on most information sites. The website of the American Society of Clinical Oncology (ASCO) even has its own section dedicated to survivors (see box). Survivors' quest for information and involvement in oncology issues may not lessen once treatment for cancer has ended because many of them face a lifetime of side effects caused by their treatments. In one study of over 1000 survivors, 53% of respondents reported secondary health problems and 49% that non-medical cancer-related needs were unmet.[11]

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References

1. Leydon GM, Moynihan C, Boulton M, Mossman J, Boudioni M, McPherson K. Cancer patients' information needs and information seeking behaviour: in depth interview study. BMJ 2000;320:909–13.
2. McKenzie J. Similar study had similar findings. Letters to the editor. BMJ 2000;321:632.
3. Hoppe IC. Readability of patient information regarding breast cancer prevention from the Web site of the National Cancer Institute. J Cancer Educ 2010;25(4): 490–2.
4. Meredith C, Symonds P, Webster L, Lamont D, Pyper E, Gillis CR, *et al.* Information needs of cancer patients in west Scotland: cross sectional survey of patients' views. BMJ 1996;313(7059):724–6.
5. Thomsen OO, Wulff HR, Martin A, Singer PA. What do gastroenterologists in Europe tell cancer patients? Lancet 1993;341(8843):473–6.
6. Evan D. Survey: Israeli doctors withhold information from cancer patients. Haaretz 2011;92(28148):1–2.
7. The NHS Cancer plan: a plan for investment, a plan for reform. Department of Health. 2000. Available from: http://www.cancerinfo.nhs.uk/images/stories/docs/cancer_plan_2000.pdf.
8. Mayer DK, Terrin NC, Kreps GL, Menon U, McCance K, Parsons SK, *et al.* Cancer survivors information seeking behaviors: a comparison of survivors who do and do not seek information about cancer. Patient Educ Couns 2007;65(3):342–50.
9. Hewitt M, Greenfield S, Stovall E, (eds.) From cancer patient to cancer survivor: lost in transition. Committee on Cancer Survivorship: Improving Care and Quality of Life, Institute of Medicine and National Research Council. 2006. Washington D.C., USA: National Academies Press. Available from: http://www.nap.edu/catalog/11468.html.
10. Centers for Disease Control and Prevention (CDC). Cancer survivors—United States, 2007. MMWR. 2011;60(9):269–272.
11. Glaser A. Introduction: a new approach. Health Serv J 2011;2(supplement). Available from: http://www.ncsi.org.uk/wp-content/uploads/HSJ_survivorship_supplement.pdf.
12. Wolf SN, Nichols C, Ulman D, *et al.* Survivorship: an unmet need of the patient with cancer—implications of a survey of the Lance Armstrong Foundation (abstract). J Clin Oncol 2005 ASCO Annual Meeting Proceedings; 23(16S), Part I of II (June 1 Supplement): 6032. Accessible from: http://www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst_detail_view&confID=34&abstractID=31848.

A selection of websites relevant for cancer patients

Website of the American Society of Clinical Oncology (ASCO):
http://www.asco.org/

ASCO's website for patients/section for survivors:
www.cancer.net/www.cancer.net/patient/Survivorship/

National Cancer Institute (NCI):
www.cancer.gov/cancertopics

National Comprehensive Cancer Network (NCCN) Guidelines for Patients™:
www.nccn.org/patients/default.asp.

A medical education website for oncology clinicians:
http://www.researchtopractice.com/

Free individualized survivor care plan:
http://www.oncolink.com/oncolife/

An example of a survivor narrative:
http://www.nccn.com/component/content/article/67/848-elizabeth-edwards-and-sam-donaldson-discuss-cancer.html

A cancer survivor networking/dating site:
http://www.cancermatch.com/

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What are the most common reasons for a manuscript to be rejected (and how can they be avoided)?

In their article on handling manuscript rejection, Woolley and Barron[1] offer the following soothing advice:

> Authors, particularly inexperienced authors, may take comfort in knowing that manuscript rejection is common.

The rejection rate for many journals is over 50%, and for top-tier journals, it can be over 90%.[2–6] Some of the reasons for these rejections are under the control of the medical writer, whereas others are not. Regardless, medical writers should be aware of the main reasons to minimize their occurrence and to be able to give practical advice to the authors and other contributors.

1 Lack of new or useful information

The most common reason for rejection of a manuscript is that it does not add to the current literature or that it lacks originality.[2,7,8] As a manuscript writer, there is not always a lot that you can do to avoid this problem. However, you should be familiar and up to date with the literature so that you can advise the contributors when you have a concern about the novelty or importance of the results. In some cases, you can encourage the contributors to include or to focus on data that are novel or especially interesting.

2 Study design and methodology problems

Whether the study has an appropriate, rigorous, and comprehensive design is cited as the most or second-most important factor deciding the fate of a manuscript.[2,7,9–12] Main problems in this regard include:

- a fundamentally weak hypothesis or question;
- poor methodology;
- inadequate description of methods, including study design and technical methods;
- results not addressing the hypothesis, question, or stated objectives;
- questionable results due to inappropriate methods or statistical analysis.

As a medical writer, you cannot do much about poor study design or methodology, but you should ensure that the hypothesis/question, objective, study design, and technical methods are easy to find, complete, clear, and consistent with the experimental findings. Pay particular attention to the methods because this is where mistakes most often occur and because it is the section most often responsible for rejection of a manuscript.[9]

Table 1 lists guidelines that can help ensure that the study design is fully described and that the technical methods are complete.

Table 1: Available guidelines for study designs

Guideline	Applies to	Checklist included?	Reference
ICMJE	All manuscripts	No	13
CONSORT	Randomized clinical trials	Yes	14
STROBE	Observational studies	Yes	15
PRISMA	Systematic reviews and meta-analyses	Yes	16
TREND	Non-randomized evaluations of behavioral and public health interventions	Yes	17

3 Logic problems

After study novelty and study design/methodology, the most important aspect determining a manuscript's fate is whether it is logical and well written.[2,7,9,10] How the study design, results, and

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conclusion are interconnected is of utmost importance to peer reviewers when commenting on a manuscript and deciding its fate.[7,8] In addition, inadequate reporting of results and excessive enthusiasm about their implications can be major reasons for rejection.[18]

Your most important job as a manuscript writer is to logically tell the story of what happened in the study. Present the study problem and gradually take the reader through the study, its results, and its implications. Following are some tips to help ensure a logical flow.

- *Consider the following questions*:
  Why did you start (introduction)?
  What did you do (methods)?
  What did you find (results)?
  What does it mean (discussion)?
- *Break the writing into manageable pieces*: break the methods and results into subsections. Maintain one idea per paragraph and one thought per sentence. If a sentence or paragraph gets too long, break it into smaller parts.
- *Present the appropriate information in each section of the manuscript*:
  Introduction: give the background, describe the problem and finish with the question/hypothesis and study objective(s).
  Methods: include the study design, patient selection, treatments, measures, technical methods, and statistical methods. Do not present any data.
  Results: present results that address the study question/hypothesis, and stated objectives. Progress logically from subject demographics/disposition through the results. You may summarize but do not discuss the meaning of the results.
  Discussion: discuss the main results and move gradually through them. Compare the results with the scientific literature. Include limitations, applications, and implications. Make conclusions based on the results and linked to the study design and the study problem, question, or hypothesis. Do not repeat yourself and do not present any new data.

4 Language problems

Common language problems identified by editors and reviewers include excessive wordiness, poor syntax, poor grammar, redundancy, and deliberately complicated writing.[2,9,18] Language problems are not usually an important reason for rejection of manuscripts, but reviewers may become critical of a study when the manuscript contains too many language errors.[7]

It is your job as a professional medical writer to write well. Language problems should definitely not be a limitation to the acceptance of a manuscript you have written. Your writing should be clear and concise, and use good English spelling, grammar, and syntax. Most importantly, you should write for the reader: information should be easy to find and easy to understand. Manuscripts are not a place to demonstrate your ability to write poetically or with big words. If a reader, editor, or reviewer misunderstands something or finds the manuscript hard to read, it is *your* fault, not theirs!

Always run a spelling and grammar check before submitting a manuscript, and always have a colleague proofread the article. Do not expect that the authors will catch language problems. If writing in English and not a native-English speaker, if possible, have your manuscript read and corrected by someone who is a native English speaker. If you are a native-English speaker, have the courage to correct the writing of non-native speakers, even if they are well-known or experienced researchers.

5 Wrong journal

Content irrelevant to the journal is an important reason that editors reject manuscripts.[10] Journal editors usually have limited space and must select articles according to their priority, which is based on whether the article is appropriate for their journal and readership and whether it is sufficiently novel and interesting according to the journal's standing. Sometimes, contributors will feel that the manuscript deserves a premier journal, but these can have rejection rates over 90%.[4–6] Detailed advice on selecting an appropriate journal was the subject of the previous manuscript writers' corner.[19]

6 Badly written abstract

A confusing or boring abstract can cause an article to be rejected without entering the review process.[20] Take the time to put together a good abstract that captures the reader's attention. Guidance for writing a successful abstract was provided in a previous article in *The Write Stuff*.[21]

7 Not formatted according to the instructions for authors

Although few manuscripts are rejected because they do not perfectly meet the instructions for authors, they have to comply with the instructions to be published. Getting this right at the beginning puts the

manuscript in a good light and will help ease its acceptance.

References

1. Woolley KL, Barron JP. Handling manuscript rejection: insights from evidence and experience. Chest 2009;135:573–7.
2. Wyness T, McGhee C, Patel DV. Manuscript rejection in ophthalmology and visual science journals: identifying and avoiding the common pitfalls. Clin Exp Ophthalmol 2009;37:864–7.
3. Armstrong AW, Idriss SZ, Kimball AB, Bernhard JD. Fate of manuscripts declined by the Journal of the American Academy of Dermatology. J Am Acad Dermatol 2008;58:632–5.
4. Lancet Information for Authors. [cited 2011 October 7]. Available from: http://download.thelancet.com/flatcontentassets/authors/lancet-information-for-authors.pdf.
5. JAMA Instructions for Authors. [cited 2011 October 7]. Available from: http://jama.ama-assn.org/site/misc/ifora.xhtml.
6. Welcome to Resources for Authors. [cited 2011 October 7]. Available from: http://resources.bmj.com/bmj/authors.
7. Ehara S, Takahashi K. Reasons for rejection of manuscripts submitted to AJR by international authors. AJR Am J Roentgenol 2007;188:W113–6.
8. Shakiba B, Salmasian H, Yousefi-Nooraie R, Rohanizadegan M. Factors influencing editors' decision on acceptance or rejection of manuscripts: the authors' perspective. Arch Iran Med 2008;11:257–62.
9. Byrne DW. Common reasons for rejecting manuscripts at medical journals: a survey of editors and peer reviewers. Sci Ed 2000;23:39–44.
10. Northam S, Yarbrough S, Haas B, Duke G. Journal editor survey: information to help authors publish. Nurse Educ 2010;35:29–36.
11. Turcotte C, Drolet P, Girard M. Study design, originality and overall consistency influence acceptance or rejection of manuscripts submitted to the Journal. Can J Anaesth 2004;51:549–56.
12. Lee KP, Boyd EA, Holroyd-Leduc JM, Bacchetti P, Bero LA. Predictors of publication: characteristics of submitted manuscripts associated with acceptance at major biomedical journals. Med J Aust 2006;184:621–6.
13. Uniform requirements for manuscripts submitted to biomedical journals: Writing and editing for biomedical publication. [cited 2011 October 7]. Available from: http://www.icmje.org/urm_full.pdf.
14. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. PLoS Med 2010;7:e1000251.
15. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol 2008;61:344–9.
16. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol 2009;62:1006–12.
17. Des Jarlais DC, Lyles C, Crepaz N. Improving the reporting quality of nonrandomized evaluations of behavioral and public health interventions: the TREND statement. Am J Public Health 2004;94:361–6.
18. Pierson DJ. The top 10 reasons why manuscripts are not accepted for publication. Respir Care 2004;49:1246–52.
19. Leventhal PS. How do I select a target journal for a manuscript? TWS 2011;20:268–269.
20. Bernhard JD. No further studies are required: additional notes on avoiding manuscript rejection. J Am Acad Dermatol 2001;44:541–2.
21. Ohri M, Dawes K. Successful abstract writing: an essential skill for medical writers. TWS 2009;18:27–8.

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Writing first sentences

The *New Statesman* magazine runs a weekly competition. There are recurring favourites, such as the one for opening sentences of novels so awful that the reader will read no further. Some medical opening sentences are likely to have the same effect. Here is the first sentence of a chapter on renal blood flow, from a book about specialized cardiovascular physiology.

> The kidneys are bilateral, bean shaped organs, which lie in a retroperitonal position on either side of the vertebral column beneath the diaphragm.

This curious mixture of *Reader's Digest* and anatomical detail is unnecessary for even a second year medical student, let alone someone reading a specialized textbook. (It is also inaccurate, because the kidneys are on each side, not either side, of the vertebral column.) A presentation on how to write papers (accessible via medicine.yale.edu) advises, 'Grab the reader, drawing them immediately to the crucial issue that your paper addresses'. Too many papers start with information that can only be described as banal, the written equivalent of clearing the throat. Sometimes, a paper is improved instantly by just deleting the first sentence and starting with the second; sometimes a banal first sentence is an indication that a paper's introduction

needs rewriting, often because the authors have fallen into the trap of thinking that the introduction should be a general review of the topic. While appropriate for a thesis, a general review is unnecessary – and boring – in a research paper that asks and answers a circumscribed question.

I found a paper in the journal *Chest*, which is the official journal of the American College of Chest Physicians. It is ranked 3rd of 46 respiratory journals on its impact factor, so it is a leading journal. The paper was titled: 'Significance of pulmonary arterial pressure and diffusion capacity of the lung as prognosticator in patients with idiopathic pulmonary fibrosis'. (Some may find the single word prognosticator better than the phrase prognostic factor. I do not, and think rather that a prognosticator is a person who makes prognoses.) The opening sentence of the paper was 'Idiopathic pulmonary fibrosis is a relatively common interstitial lung disease', surely unnecessary for readers of *Chest*. Of the paper's 34 references, 29 were available as full text on the internet. Twelve of these had opening sentences that were little improvement, being variations on 'Idiopathic pulmonary fibrosis is a progressive interstitial lung disease of unknown etiology and with a poor prognosis'. Just two papers had focused opening sentences that told readers what was coming next: 'In idiopathic pulmonary fibrosis, there is an unmet need for an accurate noninvasive measure of disease severity' and 'Idiopathic pulmonary fibrosis has undergone important redefinition in the last several years, based largely on revised histopathologic classification criteria'.

I think the best – or worst – example I found in my search was the opener to 'The search for an ideal method of abdominal fascial closure: a meta-analysis'. With blinding insight, the authors had written, 'The ideal suture for closing abdominal fascia has yet to be determined'.

You can usually rely on orthopaedic surgeons to be straightforward. The opening sentence to 'Dislocations after total hip-replacement arthroplasties' was not waffle about hip replacements being an increasingly common weapon in the orthopaedic surgeon's armamentarium but, 'Between January 1972 and June 1975, 300 total hip-replacement procedures were performed by five surgeons on the orthopaedic service of the Northwestern Memorial Hospital'; and right away we were in there with the surgeons looking at their results.

It is not a novel, and it is not a medical paper, but my favourite opening sentence is from one of my favourite books by one of my favourite authors, an author who has written a number of books about words: Bill Bryson. The best of his travel books is *The lost continent*. Its opening sentence – actually, its opening two sentences, its opening paragraph: but there are only eight words in all, and two of them are the name of a town – is a brilliant book, and I was unable to put the book down once I had read them:

'I come from Des Moines. Somebody had to'.

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The European Medicines Agency looks to the future

At the end of 2010, the European Medicines Agency (EMA) published a road map that laid out a 'strategic vision for the operation of the European Medicines Agency' from 2011 to 2015.[1] According to this document, there are three strategic areas where much of their effort will be spent in the coming years: addressing public health needs, facilitating access to medicines, and optimizing the safe and rational use of medicines. As a follow-up to the road map, the EMA has published a document explaining how it will go about achieving its goals in each of the strategic areas mentioned above.[2] Interestingly, there is the candid recognition that we are living through a difficult economic situation, and this will have an impact on the availability of resources and the achievement of the stated goals. Below, I discuss a couple of aspects that most caught my eye.

The efficacy–effectiveness gap

The EMA seems to be increasingly aware that there is a difference between 'efficacy', that is, how well a drug works in the controlled setting of a clinical trial, and 'effectiveness', that is, how it does in a clinical practice setting. There are many reasons for this so-called efficacy–effectiveness gap, but perhaps the most important are differences in clinical trial populations and the ultimate target population (the former are usually free of factors such as multimedication and comorbidities that might blur the results of a trial) and poor adherence to treatment in real life (a drug will not work if you do not take it, and adherence is usually much better in clinical trials, which are often designed to obtain good adherence).[3]

The remit of the regulators is to generally assess efficacy, even though patients and national health authorities may be more interested in whether the drug will actually work in the clinic. With a broader regulatory remit, sponsors could, in principle, be forced to design clinical trials that better reflect real life.[3] However, even as it stands, the health authorities are privy to information that could be useful to health authorities and other payers to make their decisions, and that information could be made more readily available without redesigning the whole process. Indeed, according to the road map, the EMA does aim to 'focus on increasing the role of the Agency as an information provider and on greater collaboration with health technology assessment processes [that is, the bodies responsible for determining cost-effectiveness, such as the National Institute of Clinical Excellence in the UK]'. In addition, there is a commitment to improve the 'focus on the needs of geriatric patients', which is recognition that patients over 65 years are often excluded from clinical trials (for example, because they are multimedicated) when such patients will form a sizeable portion of users of many drugs (for example, hypertension therapies). Such changes, if they occur, will bring the regulatory approval closer to real life.

The menace of antibiotic resistance

The road map also mentions antibiotic resistance. This problem is by no means new. For example, in 1992, in an article titled 'The crisis of antibiotic resistance', Neu[4] outlined how some of the microbes that cause conditions such as diarrhea, urinary infection, and sepsis are now 'resistant to virtually all of the older antibiotics', largely due to inappropriate use of antibiotics. Is the current situation really any worse than it was 20 years ago?

This time round, there are perhaps more causes for pessimism than before. In this more globalized world, outbreaks of infection have the potential to travel faster. In addition, the increasingly widespread use of antibiotics makes it harder to properly control their use and so avoid resistance. This is compounded by the lack of new antibiotics and, importantly, fewer first-in-class antibiotics coming through the pipeline than before. The reasons for this are partly commercial – developing antibiotics that will be used generally for a few days does not seem as attractive as developing, say, a lipid-lowering compound that will be taken for life. Bacteria might also quickly develop resistance to the antibiotic leading to a potentially short useful lifecycle.

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It may also be that there are only a finite number of viable molecular targets for drug development, and many of the most useful ones have already been exploited, leaving only the more difficult (and less effective) ones for development.

These reasons aside, there are also certain regulatory hurdles that can hinder approval and deter development. For example, the regulatory requirement to demonstrate that an antibiotic is equivalent to what is already on the market is difficult in that the epidemiology of bacterial resistance varies from place to place and over time. So even though an antibiotic might be inferior to another in most situations, this might not always be the case. Often, the clinician is interested in having a range of options from which to choose according to susceptibility testing or epidemiology.

The EMA will encourage pharmaceutical companies by 'Reviewing existing options to promote development of new antibiotics to treat multi-resistant bacteria including adaptation of clinical guidance documents, consideration of the balance between the amount of prior data needed with enhancing post-marketing surveillance, use of orphan legislation, etc'. Although somewhat vague, the general idea seems to be one of reconsidering the burden of proof prior to approval (as is the case with orphan products), while paying close attention to the drug once it is on the market. It is not clear to me whether the reference to orphan legislation also includes the financial incentives associated with these products (access to scientific advice, exclusivity, etc.). Like the EMA road map, the Generating Antibiotic Incentives Now (GAIN) Act, introduced in the US in 2011, also intends to tweak the regulatory approval process. In this case, the act also explicitly recognizes that there is little financial incentive to develop new antibiotics and proposes ways to make development of antibiotics more profitable, in the form of favourable licensing conditions (for example, extensions of exclusivity) rather than actually spending tax dollars. It remains to be seen how much of an impact these measures will have, particularly as the potentially short lifetime of these products will render any extended exclusivity effectively useless.

References

1. Road map to 2015: The European Medicines Agency's contribution to science, medicines and health. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Report/2011/01/WC500101373.pdf.
2. Implementing the European Medicines Agency's Road map to 2015: The Agency's contribution to Science, Medicines, Health 'From Vision to Reality'. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Other/2011/10/WC500115960.pdf.
3. Eichler HG, Abadie E, Breckenridge A, Flamion B, Gustafsson LL, Leufkens H, *et al.* Bridging the efficacy–effectiveness gap: a regulator's perspective on addressing variability of drug response. Nat Rev Drug Discov 2011;10:495–506.
4. Neu HC. The crisis in antibiotic resistance. Science 1992;257:1064–73.

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Good Writing Practice

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The Good Writing Practice initiative was launched in the December 2010 issue of *TWS*[1] by Alistair Reeves and Wendy Kingdom. The aim is to go beyond the classic style guide and provide advice on practical aspects of writing that make texts easier to read – and write, of course. An initial list of topics to be covered was put together by a small group of European Medical Writers Association (EMWA) members, some of whom have already contributed.[1] This project is, however, open to anyone who wishes to contribute advice on writing in our field that is not found in published style guides and that they feel would be useful to their colleagues. The advice may also contradict classic style guides – which is no surprise, since they often contradict one another.

The aim is to keep contributions short so that a variety of topics can be covered in each issue. 'Short' means about 400–500 words, sometimes up to a page. Topics that need more space can be spread across successive issues. So far, we have covered abbreviations, the benefits of using a language dictionary, pleasing the reader, overwriting, using checklists when writing, and writing for specific audiences.

If you have ideas or wish to agree or disagree with any of the advice or add new aspects, do not hold back: send a contribution to Wendy Kingdom or Alistair Reeves, however long or short. Maybe you have a question that you have not found an answer to elsewhere. We have plenty of experts in EMWA who should be able to answer most questions about writing.

Finally, we hope to bring everything together in an EMWA publication. Help us to make this a success!

Reference

1. Reeves A, Kingdom W. Good writing practice. TWS 2010;19(4):281.

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Cultural awareness in medical writing

A different language is a different vision of life.
Federico Fellini

In today's globalized environment, using English as the *lingua franca* is thought to ensure comprehensibility across audiences with different linguistic backgrounds. But is it really that simple? Even if you, as an author, use English as the agreed-upon common language, your writing will be influenced by the cultural and linguistic experiences you have been brought up with. And the same is true for your audience. They will read your text against the background of their own personal cultural experience and culturally shaped ideas, which may be very different from yours. So while you may use the same words, they may mean different things to you and your audience.[1] Talking to my French teacher, I learned that a 'liver crisis' ('crise de foie') in France has little to do with the liver, but refers to a general state of malaise, often after having had a heavy meal (and too much wine) the night before. If someone from Germany complains of 'circulatory problems' ('Kreislaufprobleme'), she is suffering from *low* blood pressure, dizziness, and general malaise. In the UK, low blood pressure is considered as a sign of good health and 'bad circulation' basically means cold hands and feet. Although some of these peculiarities are anecdotal, others can indeed lead to communication problems if the author is not aware of them.

In this introductory article and further, more detailed articles on the subject, I will outline relevant cultural and language issues and suggest ways to address them.

Jargon: Jargon not only heavily relies on context and common background knowledge, but is also highly culture-specific. Stay away from it when you write for a multilingual audience. In our context, 'jargon' often comes in the form of

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'doctor's speak', readily understood only by someone who has worked in an English-speaking healthcare environment (also bear in mind that American and British jargon differ considerably). Examples include terms like 'X-plant clinic' (transplant clinic), Ox4 ('oriented times four', meaning oriented in regard to person, place, time, and situation), and 'the patient coded' (the patient suffered cardiac arrest). If you want to read more about hospital jargon in the United States, the notorious book by Samuel Sham *The House of God*[2] offers abundant examples. As a rule of thumb, see whether you can find the relevant term in a (medical) dictionary. If not, try to find a more general term that is comprehensible to an average non-English reader. Jargon can also, however, refer to 'common speak' like 'pill' for tablets or capsules (!), or a 'strep throat' when simply referring to a sore throat. By the way, it is recommended to always write out angina *pectoris* when you refer to the cardiac condition, since 'angina' (without the 'pectoris') means 'tonsillitis' in German and other languages.

Which brings us to **ambiguous terms:** What I refer to here are terms that can easily be misinterpreted either because they have a double meaning or because of interference from other languages. Here are some examples: the term 'alternative treatment' for 'other treatment' may easily be misinterpreted in languages where 'alternative' (medicine, therapy, and treatment) refers to non-standard interventions like herbal medication or homeopathy. So choose 'other' treatment if that is what you want to say. The use of 'should' has been discussed elsewhere in *TWS*.[3] You may not be aware of this, but even the simple instruction 'Always take the tablets with your dinner' is ambiguous because depending on their cultural background and usage, people (in the UK) may have their dinner at lunchtime or in the evening. To be on the safer side, use 'evening meal', even if it sounds less idiomatic. And last but not least, my pet example: while the use of 'Caucasian' to mean 'White' has become so formalized in our contexts that little ambiguity remains, you should still be aware that in some countries, including Russia, 'Caucasian' refers to a dark-skinned person.

To broaden our experience as medical writers in the area of jargon and potentially ambiguous terms, it would certainly make sense to start collecting similar examples from the EMWA readership. Anyone who wants to contribute on this is very welcome.

References

1. Geercken S. Challenges of (medical) writing for the multilingual audience. TWS 2006;15(2):45–7.
2. Sham Samuel. The House of God. New York, N.Y.: Delta Trade Paperbacks, 2003.
3. Reeves A. Some comments on the 'Compilation of QRD decisions on stylistic matters in product information' from the EMA. TWS 2010;19(3):217–8.

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Use of active and passive voice

Much has been written about this, both on paper and in the Internet, and a few misconceptions and supposed 'rules' have had an enormous effect on how people write in our context.

First, a warning: beware of any recommendations that reduce this issue to simple statements like 'make more use of the active voice' or 'avoid the passive voice', or even 'don't mix the active and passive voices'. Useless advice of this sort – at least for us medical writers and editors – is given in one of the most (not really understandably) revered style guides for the English language, *The Elements of Style*, commonly referred to as Strunk and White.[1] The advice they give is especially bad because the five examples they give of use of the passive voice are not in the passive voice. What is obvious when you sit down and read these recommendations is that they are not intended for people writing the huge range of different types of texts in the life-science field. Also, they have been indiscriminately reproduced over the past 50 years in recommendations and style guides from all sorts of other sources.

Whether you use the active or passive voice is not just a 'high-level' consideration and it is not possible to give blanket advice on when one or the other should be used. Different sections of a document, for example a publication or a study report, may require different approaches. If it is unimportant whether the reader needs to know who performed a certain action – and when reporting on results in a publication or investigations in a case report, this

is usually the case – then the passive is usually the best choice. If you want to bring immediacy and directness to a controversial discussion in an editorial – where 'who said what' is important, you will probably use the active voice to achieve this.

We shall therefore be giving guidance on this, with examples from our types of text, in future issues of *Medical Writing*. Readers are invited to send in any typical examples of problems with the active and passive voice so that we can use these to illustrate our recommendations. Or perhaps you would like to contribute a commentary of your own.

Reference

1. Reeves A. Braving the elements. TWS 2009;18(2):89–92.

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Consistency

Using different terms does not necessarily mean being inconsistent

The word 'inconsistent' means not staying the same throughout a text. It also means acting at variance with one's own principles or former behaviour. In medical writing, the first definition means simply that two (or more) terms used to describe the same concept are not the same, or that different styles of presentation are used for the same elements. The second definition implies that the author has been careless, unprofessional, sloppy, and unthinking. The two definitions of inconsistent are distinct and do not necessarily apply both at the same time.

Consistency is, without doubt, very important. It is important for clarity, where use of a variety of terms is often confusing, and it is important for the professional appearance of a document. Consistency is not, however, the most important point under all circumstances, particularly in documents for regulatory use. As for many other aspects of writing, common sense and not pandering to prescriptivists should prevail.

Many examples of circumstances under which it is helpful to the reader if a rule is not applied on every occasion are similar to the rule of writing out an abbreviated term in full on the first occasion of use, providing the abbreviation in brackets, and using the abbreviation thereafter.[1] There are numerous examples where this rule can and should be broken and we have described some of these previously.[1,2] In addition, if an abbreviated term is written out in full on page 5 but the abbreviation is not used again until page 42, it is reasonable to explain the abbreviation for a second time if it is important to remind the reader what the abbreviation stands for.

If a statistician has produced a table using summary data to a mathematically correct but clinically meaningless number of decimal places (e.g. diastolic blood pressure 84.23 mmHg), presenting the data in text as 84.2 mmHg is a reasonable and sensible thing to do. One can argue that 0.2 mmHg is also clinically meaningless, however, it is reasonable to present a clinical value to one decimal place more than the measured value for summary purposes. Presenting data to more than one decimal place above the measured value will not convince anyone that the drug is effective. Clearly, the number of decimal places to which the variable is described must be the same in an in-text table and in the narrative description in the text. The point is that if the data in the statistical output tables are not sensible and the source tables will not be amended because that is too much bother, presenting rounded values in the text does not mean that the author has been inconsistent.

Similarly, if the wording in a study protocol is ambiguous or unclear, editing the wording for clarity in the study report does not mean that the report is inconsistent with the protocol. It does not make sense to reproduce words that cause confusion. However, the wording of the objectives in a protocol should not be changed no matter how badly they are written – this is going too far.

Medical terms that have been coded according to the Medical Dictionary for Regulatory Activities* are written in catalogue format. It is daft to write the terms in the text exactly as they appear in the source table because we believe that consistency is the only thing that matters. Anyone who is familiar with MedDRA will know that this is like writing about pies apple or jam raspberry because this is how you would find them in the index of a recipe book. If the coded term is 'bundle branch block

*MedDRA; I would have included the abbreviated term here even if MedDRA has been written only once because most readers of this journal will be more familiar with MedDRA than with Medical Dictionary for Regulatory Activities. Not explaining the abbreviation MedDRA would be perfectly acceptable in a text aimed solely at regulatory and pharmacovigilance professionals

right', it is common sense to refer to it in the text as right bundle branch block. A further 'problem' with MedDRA is that companies in Europe have often bought the British English version but have American English as their company language. This means that the spelling of their statistical output and text differs. In such a case, it is ridiculous to alter all supportive and in-text tables manually so that they also use American spelling. A general comment should, however, be made that the spelling is different in different types of table and that alphabetization is therefore different, for example esophageal cancer and oesophageal cancer in a table or list.

Drug names are coded and the decoded terms often include the salt. There are few instances when what follows the drug name is of some relevance (e.g. isosorbide mononitrate and isosorbide dinitrate). However, in most cases, the salt is irrelevant to the pharmacology of the drug. If the document is for marketing purposes, the marketing department will be very keen to preserve brand images and trademarks and so the salt may well be included, no matter how much that irritates the reader. In, a regulatory document, with obvious exceptions such as a study comparing two salts with the same active moiety, or text in a non-clinical section on physical properties, the reader will derive the same information from reading about enalapril, as they will from reading about enalapril maleate – the latter just takes up more space. If clients, co-authors, or bosses are worried about consistency, a footnote at first mention that 'maleate' has been dropped should suffice.

In patient information, whether the explanatory term is given before the technical term, or vice versa, might vary according to what is being written and why. If we just want to ensure that the patient understands a technical but common term, we might write, for example nausea (feeling sick). If we are explaining something they probably would not understand, it might be better to write it the other way round, for example pain in the joints (arthralgia). This is not to say that consistency does not matter in patient information, but that there are times when an alternative approach might be better than slavishly following a rule.

'Inconsistency' should not be the trump card that forces writers to follow 'rules' even when they are not helpful for the reader. Common sense or empathy with the reader might lead the medical writer to do something differently in many cases if this is justified by circumstances. We shall be exploring further examples of this in future issues.

References

1. Anon. Good writing practice: abbreviations (1). TWS 2011;20(1):48.
2. Anon. Good writing practice: abbreviations (2). TWS 2011;20(2):118.

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Lost in abbreviation: an *E. coli* is an *EHEC* is an *STEC* ...

'Could you put a hold on the current article you are working on and produce the following one? "E Coli (sic) Outbreaks in Europe?"'

This email, received from a US client in June 2011, started my quest of unravelling those jumbles of letters associated with a bacterium that infected thousands and killed dozens in Germany. The table below summarizes the most commonly used abbreviations in write-ups about the outbreak:

Abbreviation	What it stands for
EC	*Escherichia coli or E. coli*
EHEC	Enterohaemorrhagic *E. coli*
STEC	Shiga toxin-producing *E. coli*
VTEC	Verotoxin-producing *E. coli*
HUS	Haemolytic-uremic syndrome, which refers to the range of symptoms caused by the bacterium, including haemolytic anaemia, thrombocytopaenia, and renal failure[1]
HUSEC	Haemolytic-uremic syndrome-associated *E. coli*
HUS STEC	Haemolytic-uremic syndrome-associated Shiga toxin-producing *E. coli*
STEC HUS	Shiga toxin-producing *E. coli*-associated haemolytic-uremic syndrome

EHEC vs. STEC

According to the Oxford Textbook of Medicine:

> There is an important epidemiological distinction between the terms 'EHEC' and 'STEC'. The former refers to STEC associated with a distinctive clinical syndrome haemorrhagic colitis, most commonly due to serotype O157:H7. Yet, other STEC can produce a range of diarrhoeal illnesses that do not fit this description. Thus, all EHEC are STEC, but only some STEC are EHEC, and STEC is a more comprehensive term.[2]

STEC vs. VTEC

Because Shiga (named after scientist Kiyoshi Shiga, thus capitalized) toxin is synonymous with verotoxin or verocytoxin, STEC is synonymous with VTEC. However, the aforementioned dictionary states STEC is 'more correct as it is named for the gene designation for the prototype Shiga toxin from *Shigella dysenteriae* type 1'.[2]

HUSEC, HUS STEC/HUS–STEC, and STEC HUS/STEC–HUS

HUS STEC is more specific than HUSEC. In its website, the European Centre for Disease Prevention and Control (ECDC) distinguishes between HUS STEC and non-HUS STEC cases, depending on symptom manifestation. Sometimes HUS STEC is interchangeably used with STEC HUS and I am sure the linguistics experts have a lot to say about this. It all depends on whether we are writing about the symptoms (HUS) or the pathogen (STEC). But where do the hyphens come in?

So how should we call it?

ECDC refers to it as STEC or HUS STEC. The German federal agency Robert Koch Institute which detected the first case refers to it as EHEC or EHEC O104:H4,[3] the numbers being the serotype. The group of scientists who published a possible treatment calls the bug STEC and the illness STEC–HUS.[4] The US Centers for Disease Control and Prevention (CDC) calls it STEC O104:H4[5] to distinguish it from STEC O157:H7 that caused outbreaks in the United States in the 1990s and is under close surveillance by the CDC.

From my perspective, using the serotype is the most unambiguous way of naming this bug.

And no, I do not want to start deciphering those numbers in the serotypes. I will take the geneticists' word for it.

But whatever term you use for this bacterium, do not forget the medical writer's rule of thumb: define the abbreviation at first use and be consistent throughout the document.

Sigh. I hope I have been consistent in this text.

References

1. ECDC. EU case definition: HUS caused by epidemic strain Shiga toxin 2 producing *Escherichia coli*. Available from http://www.ecdc.europa.eu/en/healthtopics/escherichia_coli/epidemiological_data/Pages/EU_case_definition.asp [Accessed 21 June 2011].
2. Warrell DA, Cox TM, Firth JD, eds. Oxford Textbook of Medicine. Vol. 1. 4th ed. Oxford University Press, UK. 2005.
3. Robert Koch Institute. Information update on EHEC outbreak. Available from http://www.rki.de/cln_169/nn_217400/EN/Home/PM082011.html [Accessed 21 June 2011].
4. Lapeyraque AL, Malina M, Fremeaux-Bacchi V, Boppel T, Kirschfink M, Oualha M, *et al.* Complement Blockade in Severe Shiga-Toxin-Associated HUS. N Engl J Med. 2011 May 25. Advanced publication. Available from http://www. nejm.org/doi/full/10.1056/NEJMc1100859 [Accessed on 21 June 2011].
5. Centers for Disease Control and Prevention. Investigation Update: Outbreak of Shiga toxin-producing E. coli O104 (STEC O104:H4) infections associated with travel to Germany. 15 June 2011. Available from http://www.cdc.gov/ecoli/2011/ecoliO104/ [Accessed on 21 June 2011].

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England as the home of English – time for a rethink?

With people who speak English as a second language greatly outnumbering native speakers, where is its true home? Does it even have one?

In an article that a couple of right-leaning British newspapers picked up on,[1,2] Dr Mario Saraceni, Principal Lecturer in English Language and Linguistics at the University of Portsmouth, UK, looks to cast doubt on much of the dogma relating to the English language.[3]

Although many observers would link the rise of English to factors such as colonisation by the British and the ubiquity of US culture, Saraceni questions whether English can really be said to have spread from England. On what grounds? That (i) its beginnings cannot be traced to a particular place or point in time and (ii) the distinctions between languages are artificial. That is to say, there are no languages, only language.

He implicitly rejects the notion that Western English-speaking countries such as the UK and the USA should act as protectors of English, quoting fellow linguistics scholar Henry Widdowson[4]: 'How English develops in the world is no business of native speakers in England, or the United States, or anywhere else'.

But if the UK and the USA do not own English, who does? Potentially, everyone. According to Saraceni, assigning ownership of language is not the business of academics, but rather the personal choice of individual users.

Going one step further, he describes the very concept of the native speaker as 'flawed and misleading', repeating Sri Lankan linguist George Braine's definition of what people perceive distinguishes native and non-native speakers[5] as 'country of origin, names, ethnicity, skin colour, and accent'. In other words, exclusively non-linguistic factors.

In my experience, what counts most is country of origin. This was the reason given by one potential client for rejecting an application for freelance editing assignments from my wife, who is from Sweden but (or should that be and) speaks perfect English without a hint of a Swedish accent.

Saraceni bemoans the fact that the Anglo-centric view of English has prevented other World Englishes such as Indian English and Malaysian English from gaining acceptance. The perception that it is a bastardization of *true* English is, he believes, to blame for the negativity of Malaysian English speakers towards Malaysian English.

For Asian, African, and other forms of English to acquire widespread recognition, he argues, the deferential ties to the supposed mother tongue(s) need to be cut. The forum for this 'de-Anglicization of English' must, in his opinion, be the classroom, and he devotes the second part of his article to the teaching of English.

Not altogether happy that native English speakers with no teaching qualifications can walk into TESOL (teaching English to speakers of other languages) jobs, Saraceni cites Andy Kirkpatrick of Griffith University in Australia.

Writing in 2006,[6] Prof. Kirkpatrick criticized the practice of employing unqualified monolingual native English speakers as teachers in Japan and Korea. Mocking the assumption that they speak some form of *Standard* English, he contested that whatever form of English a teacher does speak may, in a country where English is not the first language, be less appropriate than the local variant.

Both Dr Saraceni and Prof. Kirkpatrick identify the use of British/American cultural reference points as a barrier to the optimal targeting of English teaching to the needs of learners. As Saraceni neatly puts it, 'The Houses of Parliament, red double-decker buses or post-boxes, or Manhattan skylines should be confined to the realms of postcards'.

What they both fail to address is the widely held misconception that all native English speakers speak English well (according to traditional definitions). When trying to sell my own language abilities, I am always at pains to point out that am I not only a native speaker, but also an able one.

But, then, perhaps the very concept of an able native speaker is a fallacy.

References

1. Allen E. Don't teach the 'Queen's English' to foreign language students, linguist urges. Mail Online, 2 November 2011. Available from http://www.dailymail.co.uk/news/article-2056444/Dont-teach-Queens-English-foreign-language-students-linguist-urges.html#ixzz1drRVtAVk [Accessed on 16 November 2011].
2. Howse C. If the English don't speak English, who does? The Telegraph, 2 November 2011. Available from http://www.telegraph.co.uk/culture/culturenews/8865125/If-the-English-dont-speak-English-who-does.html [Accessed on 16 November 2011].
3. Saraceni M. Reflections on the rhetorics on the (re-)location of English. Changing Engl 2011;18(3):277–85.
4. Widdowson HG. The ownership of English. TESOL Quart 1994;28(2):377–89.
5. Braine G. Nonnative Speaker English Teachers. London: Routledge; 2010. p. 9–10.

6. Kirkpatrick A. No experience necessary? Guardian Weekly, 20 January 2006. Available from http://www.guardian.co.uk/education/2006/jan/20/tefl3 [Accessed on 16 November 2011].

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Starting sentences with prepositional phrases and clauses

Authors often create problems for themselves – or just ungainly sentences – by starting sentences with prepositional phrases or clauses where this is not necessary. Sometimes this is because they have not thought enough about the best way to express their idea, but often language interference is the culprit.

By language interference here, I mean that speakers of continental north-west European languages naturally start sentences with prepositional phrases and clauses more frequently than native English speakers – and do the same in English. Starting successive sentences with prepositional phrases and clauses often sounds rather clumsy because native English writers do this less frequently. When they do, it is often to create emphasis, as in the first sentence in this paragraph. Sometimes it is done to add variety, but much less frequently than in other languages.

The simple example below illustrates this:

> [1] In an official Dutch government report issued last year (14), it is stated that 50% of inmates in preventive detention have the ICD-10 diagnosis of DPD.

Nobody will misunderstand this sentence. But was there any need to start it with *in*? And what is the consequence of starting with *in*?

With [1], we have a sentence with two clauses that starts with the subordinate (or dependent) clause. Starting with a prepositional subordinate clause often forces the author to use a dummy subject for the main clause – in this case *it*, but *there* is also frequently used. So the subject of the main clause is the dummy subject *it* in the middle of the sentence. The construction with *it* forces the clause into the passive because it is reporting on a result, which often makes sentences with dummy subjects sound clumsy.

A slight change results in sentence [2] that says exactly the same:

> [2] An official Dutch government report issued last year states (stated) that 50% of inmates in preventive detention have the ICD-10 diagnosis of DPD (14).

With [2], we still have two clauses, but we have an immediately identifiable subject at the beginning of the sentence (*An official Dutch government report*) and have avoided the dummy subject construction by simplifying the structure of the sentence.

Another way of avoiding the prepositional phrase and dummy subject is shown in example [3]:

> [3] According to an official Dutch government report issued last year, 50% of inmates in preventive detention have the ICD-10 diagnosis of DPD (14).

Here, we start with a participial phrase rather than a prepositional phrase (which should also not be overused), but the result is that it is much more likely that the author will spontaneously avoid the use of a dummy subject for the main clause and use a 'real' subject for the reader (*50% of inmates in preventive detention*) combined with the active voice.

If you start a sentence with a prepositional or participial phrase or clause, a comma is needed after the phrase or clause. As [2] shows, you avoid this by starting the sentence with the subject of one of the clauses. You also avoid this by not starting with a participial phrase or clause as in [4]:

> [4] 50% of inmates in preventive detention have the ICD-10 diagnosis of DPD according to an official Dutch government report issued last year (14).

If you avoid starting sentences with prepositions, you will almost always have a simpler sentence. This does not mean that you should always avoid it. But if English is not your first language, you may do this more frequently than the reader of English expects, and it may just not *sound right*.

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Dictionaries have their uses

Looking back on another year of editing scientific text, I can offer a little advice to authors in 2012 – seeking out new words to brighten up your text is commendable but without first checking in a dictionary you do so at your peril. For instance, taking a noun and making an adjective out of it can lead to a dramatic change in meaning as in the following case where the work on synthesis becomes a fake:

> The basis for the measurement of functionally active A1PI was laid by the synthetic work of Bieth *et al*. who described the synthesis of the convenient and water-soluble chromogenic substrate.

In another example the author muddled the expression 'object/target of affection' with the verb 'affect':

> Nonetheless, it remains entirely possible that quantitative differences exist between mice and humans in terms of target organ affection.

Sometimes even dictionaries can't help. Neville Goodman (see page 68) told me that he came across the following when he was idly looking at the *BMJ* on line:

> Professor Malcolm Green thinks the cases that have come to light are 'likely the tip of a much larger iceberg'.

He had thought it was just the point that the tip was from a much larger iceberg, rather than a much smaller one.

Here is a word I read which you will not (yet) find in a dictionary; 'sellness'. I came across it in the following advertisement:

Katschberg ski holidays in luxury apartment

In addition, your rental apartment includes:

- child care services;
- sellness and spa areas;
- cleaning services;
- the use of the hotel restaurant and much more.

Brightening up dull days with English

For those days when you need a laugh tonic, I can recommend a website which *The Guardian* in its Internet picks of the week on 23 October 2011 described as like a British version of *The Onion* crossed with *Private Eye*. The site, *The Poke* (http://www.thepoke.co.uk/2011/12/23/English-pronunciation/), describes itself as the product of a collective of up-and-coming comedy writers, photoshop wizards, and video mixologists – and is the fastest growing humour site in the UK. It aims to 'deliver an ultimate antidote to the daily grind' by 'publishing original spoof news stories, satirical mash-ups, and brilliant photoshoppery plus the funniest stuff on the web'. Medical writers might be interested to read the English Pronunciation poem by G. Nolst Trenité which claims that 'If you can pronounce correctly every word in this poem, you will be speaking English better than 90% of the native English speakers in the world. After trying the verses, a Frenchman said he'd prefer six months of hard labour to reading six lines aloud'.

Allie Brosh's Hyperbole and a half blog is a great example of not only good but good humourous writing, added to which the blog is copiously illustrated with delightful graphics. The home page muses over depression, the type we all get sometimes for no reason. Medical writers will appreciate the 'Alot is Better Than You at Everything' article about the tricks Allie, a grammatically conscientious person, uses to cope with frequently met irritating grammar mistakes. For example, when 'you', is written 'u' instead of getting mad, the economy of letters can be rationalized by imagining the person writing only has one finger on each hand. Remaining calm when 'a lot' is written 'alot' seems to be particularly difficult for Allie who has created an imaginary creature that looks like a cross between a bear, a yak, and a pug. This creature, an alot, is effective in restraining a compulsive need to correct other people's grammar to the extent that it has become almost fun for Allie to encounter the 'a lot' in texts. I will leave you to look at the blog yourself to see how the creature reacts to caring alot, charging alot, alot more dangerous, or liking one thing alot more than another (http://hyperbolean-dahalf.blogspot.com/2010/04/a lot-is-better-than-you-at-everything.html).

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Freelance Section

Welcome to the first OOOO of 2012.

Let us start with Tool Box where Julia Powell gives us a review of Toggl, a handy desktop time tracking tool to help us measure our productivity.

Then, Anu brings us another brain-teasing medical writing jumble.

The May 2012 Cyprus Freelance Business Forum (FBF), attended by 30 members, and reflecting the slightly reduced overall conference registration, was non-the-less as lively as ever. We were delighted to welcome Susan Bhatti, our President, who sat in, listened and advised that she would follow-up to check on responsibility for policing the EMWA LinkedIn page, which despite restrictions relating to the content of posts, frequently has job adverts posted. A request for assistance with writing up the 2012 Freelance Business Survey report for publication in Medical Writing (MEW) Journal later this year, was generously responded to with offers of help from Anne McDonough and Marie Helene Hayles. With a little encouragement, we had a ten entries for the handwriting competition but with only five getting two matches correct, there is no outright winner, but well done and thanks to everyone for joining in anyway. Full FBF meeting minutes are available on the EMWA website in the Freelance Resource Centre (FRC).

Medical Writing Jumble # 2

1. Rearrange the jumbled letters to get a meaningful word related to medical writing.
2. Next, take the circled letters from each word and make a new word(s) that will answer the riddle in the cartoon. Hint: The answer is probably a pun.
3. Use British English.

THARE

GEARN

DAMIEN

TERRPO

The news that the latest contraceptive formulation had failed was greeted with a ____ silence.

Answer:

by Anuradha Alahari | Illustration: Anders Holmqvist

See page 81 for the answers.

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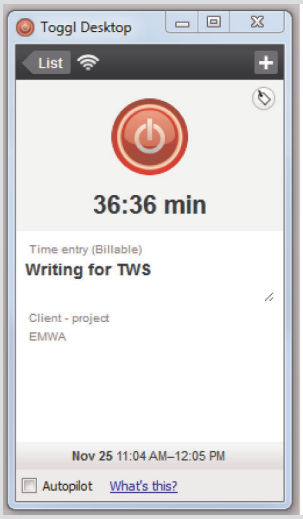
The tool box

Toggl, a desktop time tracking tool

I use a handy desktop timer tool called Toggl to help me keep track of how long tasks and overall projects take. I first came across Toggl by chance when I started out as a freelancer and was searching on the internet for a free tool to help me do this. Initially I was looking for a spreadsheet to save me having to create one, but discovered Toggl instead and have never looked back. It is so easy to use that even a non-techie like me can cope with it.

You start by creating a Toggl account (www.toggl.com) with the option of the basic free plan (located in small text under 'pricing' tab) or you can sign up for a free trial followed by a monthly fee. I find the free plan sufficient for my needs, but the paid-for option does have some useful extra features.

You can either track time on the web page or you can download a desktop timer (from the 'Extras' page), choosing the 'nano' as shown in Figure 1 or the slightly larger 'classic' timer. Both timer styles have a big red stop/start button that you can put wherever you like on your desktop (and handy to pin to your taskbar in Windows 7).



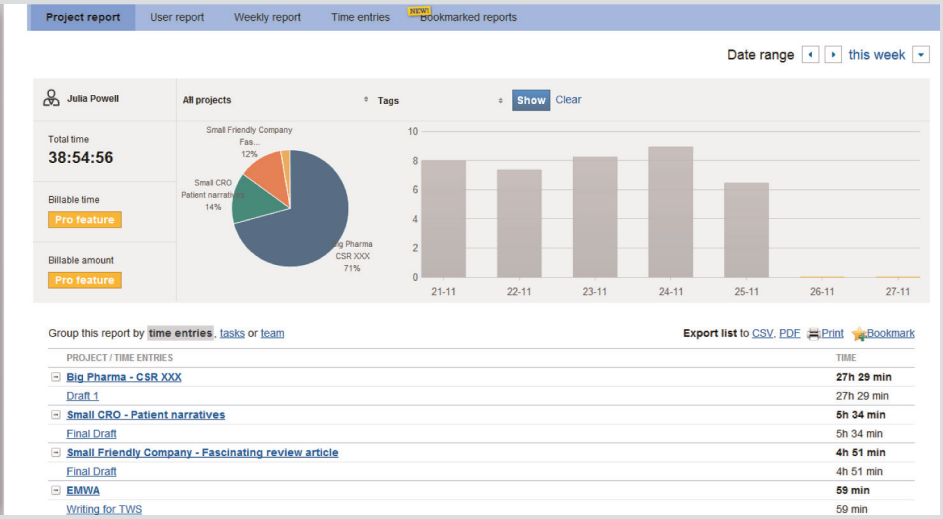


Figure 1.: (left) The 'nano' desktop timer. Figure 2.: (right) A sample project report.

Entries for clients and projects can be set up on the desktop timer or in your account on the Toggl web page and they are automatically synchronized across both. To start timing a project you simply click on the button to turn it from grey to red and the timing starts, and then click on it again to stop. If you start it again the timer continues counting from where it had stopped. You can easily swap between different clients/projects, creating multiple entries for each day if you need to.

Toggl is not only useful if you charge by the hour, but also great for building up a picture of how long things realistically take as you can produce a variety of different reports by client or project broken down by task. Reports can be viewed on the screen as bar charts, line graphs, pie charts, or lists and exported into PDF or CSV format. I have used the reports occasionally to support an invoice, although I should point out that you can edit all aspects of the results and even add/delete entries posthoc if you want to (such as in the report for a totally fictitious week's work in Figure 2).

Toggl also helps provide more accurate 'evidence-based' estimates for future work. Whether you choose to press the stop button on Toggl when having a coffee break, answering a non-related phone call or email or nipping out to the post office, or just leave it running throughout the working day is up to you, but you would be amazed at the difference it makes and it gives you an idea of how productive you really are.

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For a full explanation of how to set up Toggl, go to:
http://support.toggl.com/kb/general/getting-started-toggl-basics

Editor's note: Readers might also be interested in the open-source time-tracking software called Rachota (http://rachota.sourceforge.net), which Pamela Waltl wrote about in *The Write Stuff* 20(2): 91 and 20(4): 228

Answers to Medical Writing Jumble #2:
HEART, RANGE, MEDIAN, REPORT and PREGNANT

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Gained in translation: science at the multilingual crossroads

The spectre of translation quality – Part I

Quality matters in medical translation

In recent years, 'translation quality' has become a buzzword in the translation industry. Particularly since the introduction of European standard EN 15038[1] in 2006 and the certification process that has come with it, many translation service providers (TSPs) have been advertising their proprietary quality management methodologies as a guarantee for success.

But what is EN 15038, and – perhaps equally important from the point of view of quality assurance – what is it not?

In brief, EN 15038 regulates the requirements for translation services and creates a general framework for the interaction between clients and service providers in terms of each party's rights and obligations. Thus, the standard is exclusively concerned with setting up a standardized translation process and implementing measures designed to create a sustainable working environment. Importantly, however, EN 15038 is silent as to how to actually assess the quality of the end product arising from the translation process, i.e. the translated text.

While having a sound process in place is certainly an important prerequisite for delivering high-quality output, it is not in itself already a measure, let alone guarantee, for product quality. Alongside EN 15038, therefore, some TSPs have developed proprietary quality-assessment metrics designed to measure the quality of translated text. Some of these metrics are reportedly based on SAE J24502, the only standard so far available for rating the quality of translation deliverables. Overall, however, such metrics, while spotting the more obvious shortcomings in a text, such as wrong meaning or terminology, omissions, additions, or punctuation errors, fall short in assessing a translated text for style or register, making them 'unsuitable for evaluations of material in which style is important'.[2]

But more on these standards later. Let us first consider some of the reasons why quality in medical translation – as indeed the quality of any text written in a field as sensitive as medicine – is important at all.

Quality matters because…

I see three main reasons for why quality in medical translation matters. First, the requirements for medical texts are that they be error-free. If they are not, they have the potential to cause serious harm or even death. Second, scientific texts should be easily readable and unequivocal. If they are not, they may confuse or mislead. Finally, translated scientific texts should mimic the style characteristics of the text genre in question in order not to make the text sound awkward, thereby undermining the credibility of the author of the source text.

… translation errors in medicine can be dangerous

Accurate and readable instructions for drugs or medical devices may be as important a safety issue as adequate hygiene in the operating theatre.[3] While statistics about how often translation errors actually do cause harm are not available, some reports suggest that the danger is real.

In 2004, Mead Johnson Nutritionals had to recall two different baby food products because the instructions on how the products were to be prepared had been incorrectly translated from English to Spanish. Both the 16-ounce powder infant formula and the 32-ounce ready-to-use infant formula had dangerous preparation instructions, according to the US Food and Drug Administration (FDA). It reported that, if the baby food were prepared according to the incorrect Spanish instructions, the formula could cause seizures, irregular heartbeat, renal failure, and death.[4]

The importance of translated product labelling was also highlighted by a much publicized case from

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Berlin, where 47 patients having had knee replacement in 2006 and 2007 had to undergo re-operation because physicians had implanted the knee prostheses without applying the necessary bone cement.[5] The manufacturer had shipped the device without German instructions for use. Because the English phrase 'non-modular cemented' on the package of non-modifiable prostheses requiring cementing had been taken to mean 'not requiring cementing', hospital staff had sorted the cemented prostheses into the shelf for cement-free prostheses, and patients received prostheses that should have been cemented but were not. The error was not noticed until the US manufacturer started shipping the product with German-language stickers on the outer carton.

A 2007 literature review performed to identify papers on translating clinical and medical research documents identified only 44 relevant articles.[6] Ten of the 44 articles described error types arising during translation, with an inability to obtain cultural equivalence and oversimplification of crucial information the most frequently mentioned sources of error. Unfortunately, the documents reviewed said nothing about the frequency of errors in medical translation, and many, in fact, dealt with interpreting rather than translating.[7]

It is likely that only a fraction of translation errors ever become public. For example, I once coordinated the translation of the Summary of Product Characteristics (SPC) for a medicinal product authorized via the centralized procedure. Requiring translation into multiple languages, the project was outsourced to a major TSP specialized in medical and medical device translation. The product in question was a solution designed for subcutaneous injection. The German translation returned by the TSP, instead of translating 'administering' or 'injecting' the solution as *verabreichen*, *anwenden*, or *injizieren*, used *einnehmen* throughout the entire text, suggesting that the drug be 'swallowed' or 'taken orally'. This (and other, similar, errors) were spotted early enough in the review process to not actually cause confusion or harm – but I was surprised that such an error could occur at all, considering that the TSP reportedly not only employed expert translators but also had rigorous quality assurance (QA) procedures in place.

Alternatively, errors that do not get caught in time may go unnoticed because they are mentally amended by the reader who, even though faced with a text that contains an error or is equivocal, corrects it to mean what he or she knows (or thinks) it should mean.

From the few reports that do get publicized, it is difficult to determine where a translation error actually originated.

There are what may be referred to as 'intrinsic factors'[6] influencing the quality of a translation, referring mainly to the qualification and subject-matter knowledge of the translator. Thus, errors may arise from a lack of proficiency and medical background knowledge of the translator. They may also be due to instances of oversight by the experienced expert translator – an error category which, just as human failure in other areas of life, will be difficult to eliminate altogether. In medicine, inadvertently misplacing a comma can have disastrous consequences.

Then there are a number of 'extrinsic factors' influencing the quality of medical translation. As the examples above illustrate, these include a lack of awareness on the part of the manufacturer or marketer of the importance of making documents in a client's native language available, with either no translation provided at all, the translator not given enough time or resources to do a proper job, or some other process-related shortcoming that precludes even a proficient translator from delivering a high-quality product.

Overall, a combination of well-versed translators and vigorous QA procedures, including an effective review process, may be expected to reduce the number of 'critical' translation errors, i.e. errors potentially leading to patient harm, to a minimum. However, there may be other sources of confusion or misunderstanding resulting from poorly written, imprecise, or misleading phrasing.

… *readability is a* sine qua non *in medical communication*

No matter how technical or non-technical a document may be, it does not serve its audience unless it is easily understandable, i.e. readable. Writing is not readily comprehensible when it is impossible or difficult to interpret, takes too long to make the point, or uses imprecise language. For sentences to be readable, they should use correct grammar, punctuation, and spelling. However, correctness alone is not a guarantee for readability.

In general terms, our writing style depends on the words we choose, the length of our sentences, the way we connect them, and our tone and register. A readable text is consistent, i.e. it uses the same key terms for key concepts and the same spelling and other linguistic and typographic conventions throughout. A readable piece of writing is clear, i.e. any one sentence requires no more than a single reading. A readable text uses exact wording, i.e. words and phrases that communicate rather than obfuscate. A readable text is concise, i.e. it conveys the most information in the fewest words without omitting details. It is fluent, i.e. easy to

read because of clear connections, variety, and emphasis. And it is 'graceful'.[8–10]

The readability of health-related texts has been given some scrutiny in the scientific literature. For example, a US study published in *Pediatrics* in 2003 found that installation instructions for child safety seats generally exceed the reading skills of most consumers, leading to improper installation.[11] Motor vehicle collisions, the authors explain, are a leading cause of death in infants and children, and the single strongest risk factor for injury in car accidents is the non-use of a restraint.

A study on the readability of patient information regarding breast cancer prevention from the website of the US National Cancer Institute also found that the information was written at far too high of a reading level.[12] Also, it has been shown that patients considering to participate in a clinical study may often not be able to give valid consent because they do not understand the study as a result of the low level of readability of the information material they are given.[13]

According to current legislation, the information in package leaflets for medicinal products must be easy for patients to read and understand. A Spanish study analysed the readability of the package leaflets of medicinal products through application of the Flesch formula, selecting the 30 medicinal products most widely consumed and the 30 which generated the highest expenditure during 2005 in Spain. Only five documents obtained an acceptable Flesch score, i.e. a score of 10, while 18 scored 0 and half of the documents had values below 2.[14] Poor readability has been shown to lead to patients becoming fatigued and discouraged, which may affect compliance.

Inefficient or inadequate style makes readers work harder than they should. Writing a clear text is the author's responsibility. The reader's job is merely to follow the author's thinking and – depending on the text type – agree or disagree; the reader's job is not to 'decode the text'.[15]

If these aspects are common requirements for readable text, one would expect the same principles to apply to translated text. There is a close relationship between translation and writing. Translation 'may be looked upon as framed writing, obeying the same rules within a specific framework defined by the original'.[16] As Didaoui has noted,[16] 'rules governing translation as a text-producing exercise are basically the same as original textualisation', taking into consideration any shifts required as one language is transposed into another. Didouai even goes so far as to state that "the word 'translation' may even be substituted with 'text-producing in the target language.'"[16]

The consequences of bad writing can be grave: at its worst, the writing can become unethical, namely when it confuses or misleads. At the very least, it can become less powerful or persuasive. Or, in the case of medicinal products, it may delay marketing authorization. In 2009, according to the record of a telephone conversation between FDA and GlaxoSmithKline (GSK) Biologicals regarding a new submission of one of the company's vaccines, FDA's Center for Biologics Evaluation and Research (CBER) requested a number of Standard Operating Procedures (SOPs) to be submitted by the applicant and that these be made available 'within 2–3 weeks'. GSK stated that the SOPs would have to be translated into English, but that the translations should be available to CBER 'within several days'. SOPs are highly complex documents that portray a company's entire research & development and QA process and that usually take a long time to compile and finalize, and the initiated translator will wonder how any such documents could be translated within a matter of 'several days'. Indeed, in the telephone report, CBER states that there 'appear to be a number of translation errors. The SOP instructions are not clearly written'.[17]

Revising or correcting translated texts that lack clarity and readability can range from simple to tedious. Some sections can be improved by simple editing, as the following sentence with an ambiguous referent shows:

> Treatment of infections with dermatophytes with terbinafine is a good option in transplant recipients.

Turning 'dermatophyte' into an adjective improves the readability rather effortlessly:

> Treatment of dermatophyte infections with terbinafine is a good option in transplant recipients.

In the next example, the rather long list of nominal groups may require a second reading:

> Patients were eligible for inclusion into the study if they required treatment with prothrombin for acute bleeding, overdose of coumarin or coumarin derivates or prophylaxis.

With a comma of separation added before the last noun, one reading will suffice:

> Patients were eligible for inclusion into the study if they required treatment with

> prothrombin for acute bleeding, overdose of coumarin or coumarin derivates, or prophylaxis.

The next sentence is derived from the German translation of the SPC of a centrally approved vaccine.

> Die erste Dosis kann ab Vollendung der 6. Lebenswoche, sollte jedoch nicht später als vor Vollendung der 12. Lebenswoche verabreicht werden.*

Whereas the first part of the German sentence is unequivocal, the phrase *nicht später als vor Vollendung der 12. Lebenswoche*, a sort of literal translation from English, leaves the reader puzzled. Both readability and accuracy are enhanced by simply deleting the words *nicht später als*:

> Die erste Dosis kann ab Vollendung der 6. Lebenswoche, sollte jedoch vor Vollendung der 12. Lebenswoche verabreicht werden.

Sometimes, however, simple editing may not be enough to improve readability, and not all QA procedures appear to consider readability an important textual feature. The next sentence is again derived from the German translation of the vaccine SPC introduced above:

> Bei 5.673 geimpften Säuglingen (2.834 Säuglinge erhielten den Impfstoff) wurde die Wirksamkeit anhand der Abnahme der Inzidenz RV-bedingter Gastroenteritis durch die Impfstoff-G-Serotypen (G1 bis G4), die frühestens 14 Tage nach Gabe der dritten Dosis [des Impfstoffs] auftraten, über die gesamte erste Rotavirus-Saison nach Impfung gemessen.**

With complex sentences such as these, simple editing is unlikely to enhance readability. The phrase would have to be recast in German, departing from the syntax of the English source and disentangling the nested sentence structure, such as in:

> Bei 5673 geimpften Säuglingen, von denen 2834 der Impfstoffgruppe zugewiesen worden waren, wurde die Schutzwirkung anhand der Abnahme der Inzidenz Rotavirus (RV)-bedingter Gastroenteritiden durch die Impfstoff-Serotypen G1–G4 erhoben. Der Beobachtungszeitraum erstreckte sich dabei von Tag 15 nach Gabe der dritten Dosis [des Impfstoffs] über die gesamte erste Rotavirus-Saison nach Impfung.

*English original: 'The first dose may be administered from the age of six weeks and not later than the age of 12 weeks.'

**English original: 'In 5,673 vaccinated infants (2,834 in the vaccine group) protective efficacy was measured as a reduction in the incidence of rotavirus (RV) gastroenteritis caused by vaccine G serotypes (G1-G4) that occurred at least 14 days after the third dose of vaccine through the first full rotavirus season after vaccination.'

…inadequate translation undermines credibility

If a translated text is neither wrong nor misleading, it may still sound awkward. This may be less of a practical danger, but it is potentially harmful to the author's reputation. When the writing, or the translation, is sloppy – what reason does the reader have to believe that the quality of the research the text describes is not?

> *[…] the medical profession (particularly clinical medicine) is full of jargon and idiosyncratic phrases which sound unusual, to say the least, in the context of everyday speech or writing. […] The temptation may be great to change or omit these often awkward-sounding phrases, but they are so much a part of the professional language that the translator who does so is actually making a radical change in the register of the text; and to medical ears, the text becomes jarring and sounds 'less professional' without these familiar phrases. Not only does this make it more difficult for the medical professional end-user to quickly grasp the substance of the communication, but I believe it also has the undesirable effect of undermining the scientific credibility of the article or text (even if only subliminally).*[18]

Biomedical communication does have a distinct style – or, rather, distinct styles – and these should be mimicked in translation, requiring an immersion into a particular discipline to appropriate its language.

Specialized language serves a specific purpose that cannot be accomplished either by the use of general language or by the specialized language of another discipline.[19,20] Therefore, with writing being bound by the conventions of a particular genre 'one writing doesn't fit all'.[21] These insights are far from new. The Roman rhetorician Quintilian said that every piece of writing requires 'a different and distinct style. […] Every species of writing has its own prescribed law, each its own appropriate dress'.[22]

Scientific language is intricately linked with the way scientific knowledge is generated, and this may be different in different areas of scientific

research and at different points in time. In this context, Thielmann[23] mentions two aspects that Ehlich has shown as characterizing scientific communication, namely that scientific texts are designed for a communicative situation in which any new finding is *a priori* considered controversial and has yet to be ratified by scientific peers. Also, the linguistic inventory of the language of science cannot be grasped on the basis of a purely terminology-oriented analysis, with many of the phrases used in science communication reflecting individual aspects of the cognitive process prevailing in science (e.g., *einen Grundsatz ableiten, eine Erkenntnis setzt sich durch*).[23]

Therefore, translators will have to analyse the language and style of the source text and find an equivalent in their target language. The challenge of translating is not only to transpose scientific content but also to adapt the source-language 'dress code' to conform with the conventions expected by the target-language reader.

Translation: industry or craft?

Translation requirements are increasing worldwide, probably as a direct consequence of globalization. Neither the drive towards globalization nor the need for translation is new. For centuries, societies have striven to expand their spheres of influence through colonization or conquest, marrying and giving in marriage*, buying and selling. And throughout history, translation has been a loyal companion facilitating international communication.

What is different today is the speed globalization has gathered in the past two decades, largely as a result of technological advances that have compressed, or 'annilihated', space and distance.[24] Today, global companies bring their products to multiple markets at virtually the same time. Translation is a vital prerequisite for industrial internationalization and, aided by numerous software tools and applications and involving diverse experts from project and terminology managers to computer programmers, editors, graphics designers, and desk-top publishing specialists, has itself become an industry. At the same time, however, translation proper – the process of transferring a text across culture barriers – continues to be an intellectual activity that defies industrialization and requires know-how, expertise, and a human brain capable of anatomizing a source-language text and sewing it back together in the target language. Keeping this in mind, it becomes clear that even the most robust translation process, unless relying on expert translators who master their craft, will not necessarily bring forth a target text that is error-free, readable, and, may I say, graceful – concepts which, admittedly, have yet to be defined.

*Referring to the motto of the Habsburgs to have their members marry into other royal families to forge alliances: Bella gerant alii, tu, felix Austria, nube. 'Let others wage wars, but you, happy Austria, marry'.

References

1. Deutsches Institut für Normung [DIN]. Translation services – Service requirements; English version of DIN EN 15038:2006–08. Berlin, Germany: Beuth Verlag GmbH; 2006.
2. SAE J2450 Translation Quality Metric Task Force. Translation quality metric – surface vehicle standard. Available from: http://standards.sae.org/j2450_200508, 2005.
3. Crimson Life Sciences. Medical device labeling survey by Crimson Life Sciences exposes serious translation risks, Reuters, 19 March 2009.
4. European Business Forum. Mead Johnson Nutritionals product recalls (Brief Article) HighBeam Research. (2010 March 4). Available from: www.highbeam.com/doc/1G1-134816639.html, 2004.
5. Honert M. Klinik setzte 47 Patienten falsches Gelenk ein. Der Tagesspiegel, Available from: www.tagesspiegel.de, 11 August 2007.
6. Garcia-Castillo D, Fetters MD. Quality in medical translations: a review. J Health Care Poor Underserved 2007;18:74–84.
7. National Standard Guide for Community Interpreting Services. Available from: www.multi-languages.com/materials/National_Standard_Guide_for_Community_Interpreting_Services.pdf. Toronto, Canada: Healthcare Interpretation Network (HIN); 2011.
8. DuBay WH. The principles of readability. Available from: www.eric.ed.gov/ERICDocs/data/ericdocs2sql/content_storage_01/0000019b/80/1b/bf/46.pdf, 2004.
9. Huth EJ. How to write and publish papers in the medical sciences. Baltimore, London, Munich: Williams & Wilkins; 1990.
10. Lannon JM. Technical communication. New York, Madrid, Amsterdam: Longman; 2000.
11. Wegner MV, Girasek DC. How readable are child safety seat installation instructions? Pediatrics 2003; 111:588–91.
12. Hoppe IC. Readability of patient information regarding breast cancer prevention from the web site of the national cancer institute. J Cancer Educ 2010;25:490–2.
13. Knapp P, Raynor DK, Silcock J, Parkinson B. Performance-based readability testing of participant information for a Phase 3 IVF trial. Trials 2009;10:79.
14. Barrio-Cantalejo IM, Simon-Lorda P, March Cerda JC, Prieto Rodriguez MA. [Grammatical readability of the package leaflets of the medicinal products most widely consumed and generating the highest expense in Spain during 2005]. Rev Esp Salud Publica 2008;82:559–66.
15. Zeiger M. Essentials of writing biomedical research papers. Mcgraw-Hill Higher Education; 1999.
16. Didaoui M. Translation quality: a pragmatic and multidirectional approach. In: Schmitt PAJH (ed.). Translationsqualität. Leipziger Studien zur

angewandten Linguistik und Translatologie ed. Frankfurt: Peter Lang; 2006.
17. FDA. Record of Telephone Conversation, Hiberix. Available from: www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm182111.htm, 2009.
18. O'Neill M. Who makes a better medical translator: the medically knowledgeable linguist or the linguistically knowledgeable medical professional? A physician's perspective. Am Translators Assoc Scholarly Monogr Ser 1998;X:69–80.
19. Waldo ML. Demythologizing language difference in the academy: establishing discipline-based writing programs. Mahwah, NJ: Lawrence Erlbaum Associates; 2004.
20. Bourelle A. Lessons from Quintilian: writing and rhetoric across the curriculum for the modern university. Available from: www.worcester.edu/Currents/Archives/Volume_1_Number_2/CurrentsV1N2BourelleP28.pdf. *Curr Teaching Learn* 2009;1.
21. Hall M. Book review on "Demythologizing language difference in the academy: establishing discipline-based writing programs". Composition Stud 2005; 33:137–40.
22. Quintilian. Institutio oratoria (translated by Murphy JJ). Carbondale, IL: Southern Illinois University Press; 1987.
23. Thielmann W. Deutsche und englische Wissenschaftssprache im Vergleich. 3rd ed. Heidelberg: Synchron Wissenschaftsverlage der Autoren; 2009.
24. Stanford Encyclopedia of Philosophy. Available from: http://plato.stanford.edu/entries/globalization/, 2011.

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Google translation

It can be quite handy to pop a simple French or German text into Google translation if you just want to get the general gist of what it means in English. Google is not great at tenses, e.g. I found that text written in the past tense in German was translated into the past perfect in English. And Google cannot be accused of lacking fantasy. Here is an example.

Original German: Ende Juni, Anfang Juli bin ich dann eine Woche nach Kroatien zu meinem Bruder gefahren. Er hat dort einen Wohnwagen in einem Nudistencamp stehen.

Google translation: Late June, early July, I'm a week after Croatia to my brother is run. The bear has a caravan in a nudist camp standing.

My translation: End of June, beginning of July I then went to Croatia to my brother for a week. He has a caravan standing in a nudist camp there.

I have translated *bin gefahren* as *went* but the literal translation would be *drove*. There is no hint of 'run' nor any sign of bears in the original German text.

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Concepts from the linguistic crossroads

What's in a word…?

Ever thought about what a word is? In rather technical terms, a word may be defined as 'a sequence of letters with an orthographic space on either side'.[1] Taking a more philosophical stance, a word is 'the smallest unit of language that can be used by itself'[2] and that has literal (semantic) or practical (pragmatic) meaning.

We tend to think of a word as the very element in a language that carries meaning. Yet, meaning can be carried by units smaller than a word – morphemes. A morpheme cannot be further broken down into other elements of meaning and very often cannot be used on its own. For example, the morpheme 're', such as in 'rebuild' or 'recapitulate', means 'again', and cannot stand alone. The morpheme 'hyper' in 'hypersensitivity' means 'excessive' and is also used in composite words although it has, since the early 1940s,[3] also been used as a stand-alone colloquial shortening of 'hyperactive'.

cross·road *noun* 'kro\s-ˌrōd *also* -'rōd\
a: the place of intersection of two or more roads
b: (1) a small community located at such a crossroads *(2)* a central meeting place
c: a crucial point especially where a decision must be made[4]

Morphemes can have a grammatical function, e.g. the suffix 'ity' in 'hypersensitivity', where it forms an abstract noun from an adjective. Also, morphemes may be used to form a plural (text**s**) or a tense (report**ed**) or to turn an adjective into an adverb (hyperactive**ly**).

Why would this be of relevance for translation? Because very often there is no one-to-one relationship between word and meaning in different languages. In isolating languages, such as Vietnamese, there is a one-to-one correspondence of morphemes to words, i.e. any one word contains only one morpheme. By contrast, the two-morpheme English word 'disbelieve' is represented by two German words, i.e. *nicht glauben*, and the German *Handrücken* is 'dorsum of the hand' in English. Overall, therefore, an element of meaning represented by a single word in one language may be represented by a number of words in another.

In the language of medicine, many terms are made up of Greek or Latin roots, but they may also originate from common speech. The same register in different languages may make different use of these Greek, Latin, and common-speech roots. For example, the English 'metacarpals', made up entirely of Greek morphemes, is *Mittelhandknochen* in German, consisting of common-language morphemes only. The Greek-derived term *ephelides* finds its English equivalent in the Scandinavian-derived two-morpheme word 'freckles', which in German becomes the three-morpheme *Sommersprossen*, a word which also highlights an additional aspect of meaning, namely that freckles, or 'summer sprouts', appear on the skin when exposed to the summer sun.

In translation, words may pose a problem when they refer to culture-specific concepts, such as the English 'copyright' and the German *Urheberrecht*, which, although very often used interchangeably, have rather different meanings. The English morpheme 'copy' derives from the Latin *copiare*, meaning 'to write in plenty' or 'to write an original text many times'[3] and placing the emphasis on who holds the right to reproduce or commercialize a piece of intellectual property. The German morpheme *Urheber* derives from the Old High German *urhab*[5] and focuses on who 'brought into being' or 'created' a piece of intellectual property. The difference in meaning between the two composites, therefore, should not come as a surprise.

More often than not, of course, meaning is carried by structures larger than a single word.

References

1. Baker M. In other words. A coursebook on translation. London, New York: Routledge; 2010.
2. Bolinger D, Sears D. Aspects of language. New York: Harcourt Brace Jovanovich; 1968.
3. Harper D. Online Etymology Dictionary. Available from: www.etymonline.com/
4. Webster's International Dictionary. Available from: www.merriam-webster.com/
5. Digitales Wörterbuch der Deutschen Sprache. Available from: www.dwds.de

LINGUEE has come of age

www.linguee.com

The web service Linguee – the search engine combing the internet for translated texts and making them available as a bilingual data pool that can be searched for words and phrases – has truly come of age. After a 1-year beta testing phase, the full version of Linguee, the then German–English bilingual translation tool, went live in May 2010. Since then, Linguee has expanded its service to include English–Spanish, English–French, and English–Portuguese as additional language pairs and has come to rank among the top 100 websites in Germany.

A specialized computer program – a web crawler – automatically searches the internet for webpages containing bi- or multilingual content. The texts are evaluated by a machine-learning algorithm, and translated sentences and words are extracted. The system is capable of autonomously learning to filter out the best translations based on quality criteria continuously refined on the basis of user feedback. Of the more than a trillion sentences that Linguee computers have already compared, only the top 0.01%, i.e. 100 million of the translated sentences, have been retained.

Linguee presents words in context

One major advantage over traditional dictionaries is that Linguee presents any word or phrase in the context of an entire sentence.

Many of the texts Linguee is based on derive from European institutions or EUR-Lex, the database of EU legislative texts. For example, some of the text pairs displayed when looking for German ways of translating the phrase 'application for marketing authorisation' are displayed in Figure 1.

Linguee provides direct access to the source texts

A really nice feature of Linguee is that it does not only display translated sentence pairs, but also takes you straight to the documents the translation derives from. For example, clicking the 'eur-lex.europe.eu' hyperlink in Figure 1 opens to the original publications in both languages – in our case the relevant EU Regulation.

Linguee: a vast collection of human translations

Of note, Linguee is not an automatic translator like Google Translate or Microsoft's Bing Translator. These tools, although helping you understand the gist of foreign language text, may not always use the correct term or phrase in a given context because they do not understand the subtleties of language. By contrast, what Linguee displays is human-translated entries, showing you how other people have solved a particular translation problem. Although, as with any linguistic resource or dictionary, caution is required when making your choice, Linguee is a highly valuable addition to any multilingual toolkit.

For more information, go to www.linguee.com/

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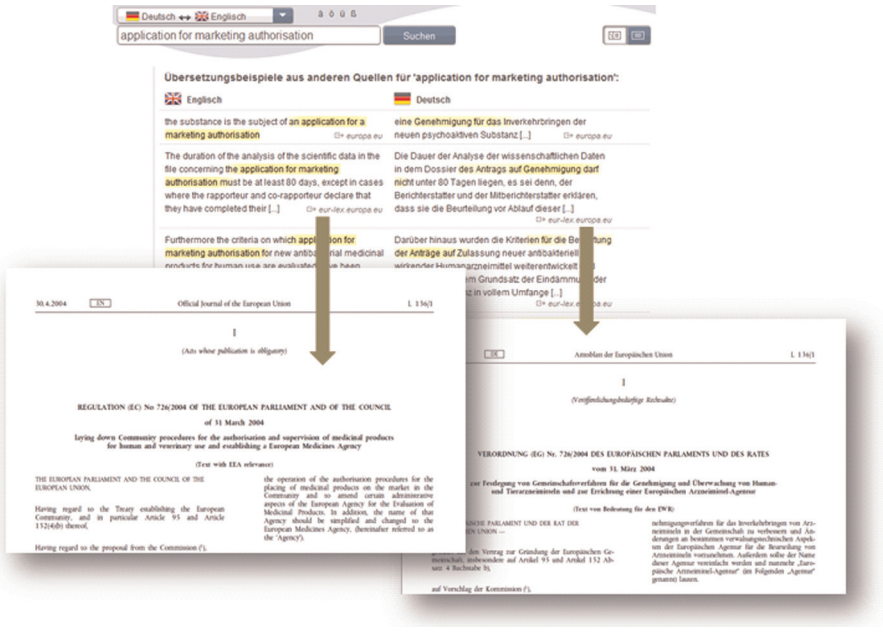

Figure 1: Linguee search result.

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