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TITLE: Web-based Randomized Controlled Trials in Orthodontics

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Abstract

Randomized controlled trials (RCTs) are considered the gold standard to evaluate the efficacy of orthodontic treatments being the most credited source of scientific evidence in orthodontics. Frequently, RCTs are planned as multicentre trials, with the intent of increasing the statistical power and to raise the precision of outcome estimates. However, the management of large scale RCTs requires a thorough organization more than conventional RCTs. Indeed, the need of high accuracy and standardization in data collection, and the need of research aids, secretariats, staff and patient training, and organizational meetings make these studies time-consuming, high-priced. and, on the whole relatively complex to carry out correctly.

A web-site was developed to support a large scale orthodontic RCT which aimed to evaluate the efficacy of a functional appliance. The web-site was located as a domain at <http://www.ortodonzia.unina.it> on an independent server.

Web-sites can increase the quality of data collection, simplify the randomization process, assure a faster data collection, and improve trial monitoring. Web-based RCTs have the potential of leading to a globalization in orthodontic research and speeding up the run for evidence in orthodontics.

Introduction

Evidenced based dentistry (EBD) ¹ has a growing impact in orthodontics. As a matter of fact, in the last decade, many researchers have chosen to perform clinical trials in order to test the efficacy and the reliability of orthodontic procedures ²⁻⁴. Among the several research tools available, randomized controlled trials (RCTs) are still considered the best source of scientific evidence⁵⁻⁶ for evaluating the effects of dental and medical treatments.

Frequently, RCTs are planned as multicentre trials, with the intent of increasing the statistical power and to raise the precision of outcome estimates ⁷. Nevertheless, the management of multicentre large scale randomized trials requires a thorough organization more than conventional RCTs. Indeed, the need of research aids, secretariats, staff and patient training, and organizational meetings makes these studies time-consuming and, on the whole, high-priced. In addition, a Coordination Centre is certainly advocated⁸ to correctly manage different research units.

Nowadays, Internet and the World Wide Web are widely accessible being appealing tools for conducting RCTs because of their technologic capabilities, ease and relatively low cost.

The interactivity in the Web scene has been suggested to increase the compliance in users while conducting surveys.⁹ In recent times, the need of affordable and high-quality research has addressed clinicians to perform web-based clinical trials. Web facilities have been used for research protocol spreading, randomization, data collection and trial monitoring. ¹⁰⁻¹³

Several studies have reported that web-based trials provide numerous benefits, by enhancing research staff training, improving trial monitoring and administration ¹⁴, reducing noticeably the inconvenience of large scale trials ^{2,13,14,15-18}.

However, although successful in many medical fields, the web revolution seems still only to brush dental research, and even less orthodontics. ¹⁹

Recently we developed a web-site to support a large scale orthodontic RCT which aimed to evaluate the efficacy of a functional appliance. Our intent was to develop a system suitable to facilitate data collection, increase data quality, enhance trial management and to provide

an efficient tool that could link, and directly manage, several research units spread all-over Italy.

Web site

A web-site was built and located as a domain at <http://www.ortodonzia.unina.it> (link to RCT Sander) on an independent server within the same university. Hypertext mark-up language (HTML), Java scripts and a computer equipped with an Intel Pentium M Processor 760, 2.0 GhHz were used to build the web pages. Namo Web Editor 5.0 (SJ Namo Inc, San Jose, CA.), Adobe Photoshop 6.0 (Adobe Systems Inc.), Microsoft Power Point (Microsoft Corporation), Jasc Paint Shop Pro 7.0 (Corel Corporation) were used to make the graphical user interface (GUI). The website was optimized for Microsoft Internet Explorer 5.0 and above at a resolution of 1024 x 768 pixel. Since the trial involved Italian orthodontic departments, web pages were written in Italian.

The website was structured into three areas (*i.e.* general information, patient management and user's guide; Fig.1).

In the general information area, general information about the research project was provided, *i.e.* the entire research protocol was available on-line and all the clinical procedures necessary for the trial were fully described in an on-line check-list.

In this section, "all the things to do" (*i.e.* recruitment phases, data collection, dental impressions, photographs etc) were fully described step by step. In addition, Microsoft PowerPoint slides concerning the laboratory procedures used to build the functional appliance and clinical charts were available. The general information area was access free.

The patient management area was structured for data entry and consulting. Once patients were judged eligible for the study, their data were entered in an on-line form developed for data capturing. In this area, dental and body measures were collected and digital records uploaded. In order to avoid missing data, drop-down menus and check boxes were extensively used. Finally, a custom made Java script was developed to check the mandatory and the incorrect fields. The script was structured to stop the submission process as form

field were incomplete, blank or filled with inappropriate (*i.e.* qualitative data versus numerical data entry and vice versa) or incorrect (*i.e.* date formats, metric and weight measurements) data. An example flash movie of the real-time data verification is available at <http://www.ortodonzia.unina.it/chart.html>.

The randomization process was automatic and available on-line. After first data entering, enrolled patient were randomly allocated to two different groups by means of a block randomization. A custom-made on-line software was implemented in order to use gender and research centre as stratifying factors. Identifiable personal data of patients were not available on-line and subjects were identified by a five digits ID. The access to this section was restricted to authenticated users and protected by encryption, remote firewalls, and passwords.

Individual usernames and passwords were built using a custom-made software and were provided to research unit coordinators. The access to the data of patients recruited in each dental clinic was restricted to the investigators belonging to the same research unit. The access from other research units was forbidden.

Data were transmitted to the national coordinator unit (University of Naples Federico II) and stored on a remote database. Records were then uploaded on the web-site in the same section. By browsing this area, authenticated users were also able to view patient data and the current status of research.

Finally, an user's guide was developed in order to address clinicians to the correct use of the web site, as well as of all the research and clinical procedures.

Discussion

The quality of orthodontic clinical studies has been recently subject of discussion. Indeed, it has been suggested that, in order to obtain definitive answers concerning orthodontic, and in particular, functional therapies ²⁰, the quality of orthodontic studies has to be enhanced.

The collection of data, as well as the research management, still represents crucial phases of clinical trials. In particular, the accuracy and the standardization of data collection are of fundamental importance while conducting surveys.

Recently electronic data capturing (EDC) systems have been introduced in dental research to enhance the quality of clinical studies. EDC has given the possibility of reducing the time needed for data collection and improved the quality of collected data. Recent reports confirm that the shifting from paper based data collection (CRF) to EDC has facilitated collection of data²¹, centralizing their analysis, and reducing trial time, and costs^{16,22}.

Among the different tools available for EDC (*i.e.* local electronic databases, client-server technology, web sites), the web-based systems are certainly promising because of the great familiarity of people with web-surfing.²³

Web-sites provide numerous benefits to investigators. First of all, a more accurate data collection is certainly possible. Indeed, the use of drop-down menus, check boxes and java applets in web pages reduces data entry errors, as typos, and avoids missing data. Next, since users are addressed to make their choice among listed parameters given in drop-down menus and click check boxes, the standardization in data collection can be easily accomplished. Also, the randomization process can be easily assured on-line in real-time, by developing custom-made softwares that randomly choose the subject allocation, after first data entering.

Web sites certainly provide a faster data collection, and reduce the average time needed for carrying on a RCT. With paper based data collection, data were primary collected on paper charts, then, after a visual checking, they were stored on local databases and sent to coordination centre. With web-sites, only an investigator has to do is to log-in, insert the data of a patient, wait a second to let them be verified, and upload digital records.

Moreover, these systems improve trial monitoring, by directly managing several research units in real time. Scientific protocols, check lists, informed consents for patients can be easily stored on-line and downloaded within seconds. This, in turn, enhances trial

administration, and let researchers and clinicians spend less time in administration and bureaucracy and focus more on patient health.

With respect to research reporting, web facilities can be used to provide real time and updated research information and facilitate the reporting of costs. Easily, it is possible to download and print updated reports from the remote database.

Finally, a central on-line web database offers the opportunity to quickly expand studies to private dental offices and clinics. Also, feedbacks could be easily received by research units by developing on-line forums in order to enhance the quality of the trial.

Web site requires only a computer equipped with internet connection.

It is important to stress that database over the internet should be managed using security policies. To maintain security of network and data resources, continuous monitoring of network activity is also mandatory. Generally, website security is warranted by encryption and firewall, which can guarantee both safe transactions and safe transfer of information. Cryptographic protocols similar to those used for on-line transactions might be applied also to WEB-based RCTs. **In general, several versions of [protocols](#) such as **transport Layer Security (TLS)** Protocol and **Secure Sockets Layer (SSL)**, can be used in order to provide [security](#) and [secure](#) data integrity for communications over [TCP/IP](#) networks such as the [Internet](#).** The use of these protocols along with a firewall prevents unauthorized accesses to computers located in a local or remote network. These systems regulate data transfers between computer networks by means of several trust levels, defined by network administrator.

Nevertheless, few limitations can be discussed concerning the use of web based facilities for research. It could be argued that still not all clinicians have internet connection in their dental offices. Tackle this problem is not difficult. Indeed, the globalization in mobile communication has provided cheap and efficient mobile internet connections for costumers.

More important, as web tools must provide an accurate data collection, comply with the guidelines available for correct data management, being also easy to use for guests, their cost is expected not to be affordable. In this sense, Dental Societies and Universities should

work in order to develop flexible systems that could be easily customized to different research topics. However, several efforts are still necessary in the World wide web community to uniform the security policies in managing data over the internet. Indeed, while the criteria for data protection are quite similar in European countries, different policies should be applied between different continents.

Finally, a lack of attitude and a difficulty in shifting from paper-based methods to electronically source documents in dental clinical trials is still present.¹⁷ Unfortunately, a solution for this problem does not depend on technical features, but only on the motivation of researchers, who should make efforts to understand and accept the advantages of a new, easy to use, and fascinating methodology.

Conclusions

The implementation of web based RCTs has the potential to increase the quality of data collection in orthodontics and enhance all the phases of a clinical study. Remote data collection and validation by means of web-tools is a useful promise. Internet based solutions are also helpful to coordinate research centres separated by great distances, and have the potential of enhancing research management by improving personnel training, trial monitoring and patient care. Web-based research has the potential of leading to a globalization in orthodontic and dental research and speed up the run for evidence in orthodontics. Although the Web facilities have been extensively advocated in medical research to facilitate the research procedures, the motivation of the investigators is still essential for shifting from paper based data collection to web-based solutions, more than the wide offer of technical supports available for conducting *e-clinical* research.

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Figure Legends

1. Structure of the Web-site