Abstract. – Patient recruitment is a critical point of today’s clinical research. Several proposals have been made for improving it, but the effectiveness of these measures is actually uncertain.

The use of Internet (e-recruitment) could represent a great chance to improve patient enrolment, even though the effectiveness of this implementation is not so evident.

E-recruitment could bring some advantages, such as better interaction between clinical research demand and clinical research supply, time and resources optimization, and reduction of data entry errors. It raises some issues too, such as sampling errors, validity of informed consent, and protection of privacy. Research Ethics Committees/Institutional Review Boards should consider these critical points.

The paper deals with Internet recruitment for clinical research. It also attempts to provide Research Ethics Committees/Institutional Review Boards with notes for assessing e-recruitment based clinical protocols.

Key Words: Recruitment, E-recruitment, Clinical research, Research Ethics Committees, Institutional Review Boards.

Introduction

Patient recruitment is a critical point of today’s clinical research. Due to recruitment failure, it is nowadays becoming more and more difficult to start or to conclude clinical trials as well as observational studies.

As it is well known, the consequences of this phenomenon are relevant. In fact, recruitment failure could cause: (1) Unnecessary risks for patients, already enrolled; (2) Useless waste of human resources and money; (3) Difficulty to verify scientific hypotheses that could be potentially valid.

The following data would be able to show the significance of the matter.

Nuttall found that: “early 80% of all clinical studies fail to finish on time, and 20% of those are delayed for six months or more; 85% of clinical trials fail to retain enough patients; the average dropout rate across all clinical trials is around 30%; over two-thirds of sites fail to meet original patient enrolment for a given trial; up to 50% of sites enrol one or no patients in their studies”.

Data of the CenterWatch of Boston show that about 81% of all clinical trials are delayed by 1 to 6 months because of difficulties in recruiting participants, with another 5% postponed 6 months or more.

McDonald et al analyzed 114 trials and they found that just a third (31%) of the trials achieved their original recruitment target and half (53%) were awarded an extension. Moreover, the overall start to enrol was delayed in 47 (41%) trials and early enrolment problems were identified in 77 (63%) trials.

Kitterman et al examined all clinical studies (837) at Oregon Health & Science University (USA) terminated between 2005 and 2009, and they found that 260 of them (31.1%) had low enrolment.

Reasons for not participating in clinical searches are several. On the matter, a report carried out by the Emergency Care Research Institute (ECRI) estimated a percentages of 25% for inconvenience, 20% for concern over experimentation, 19% for potential lack of health benefit, and 14% for physician influence.

So, it is not easy to identify effective strategies for increasing patient recruitment. Several proposals have been made. Caldwell et al identified 66 different types of recruitment strategies for participation in randomized controlled trials (RCTs). They also assessed the effectiveness of these strategies. They found that some of them (such as attendance at an education session, addi-
tion of a health validated questionnaire, a video about the health condition, monetary incentives) seemed to improve recruitment. However, no strategy seemed to be decisive.

**E-Recruitment: Advantages and Effectiveness**

In 2013, 2.7 billion people, almost 40% of the world’s population, were online. In addition, Internet is becoming the most popular source of medical information for patients.

Therefore, Internet theoretically offers unlimited and new chance to connect demand for clinical research (e.g., volunteers, people who wish to participate in research programs, etc.) and clinical research supply (e.g., promoters, sponsors, researchers, etc.). So, the use of Internet for the recruitment process (e-recruitment) could represent a great chance.

E-recruitment services were first used in the mid-1990s to select workers. Since then, they have been implemented into many activities.

The novelty of these services regards the particular type of communication that Internet provides, above all after the beginning of the so called Web 2.0: social networks, blogs, virtual communities, chat rooms, etc. are able to facilitate contact between demand for clinical research and clinical research supply. Internet could be particularly useful to recruit rare disease patients, ethnic minorities and people who are geographically dispersed, as well as Internet is a very important chance for this people.

It should point out that e-recruitment can be functional not only for clinical research supply, but also for clinical research demand: on one hand, promoters, researchers, sponsors, etc. could search potential participants by publishing online advertisements (passive search) or by directly contacting them by online instruments (active search). On the other hand, people who wish to participate in research programs could directly search online advertisements (active search) or just show their availability by electronic advertisements (passive search).

Moreover, Internet can support patient recruitment in a partial or in a full manner. The first case is that of clinical trials: online instruments can only facilitate interaction between promoters and patients, while “effective enrolment” occurs in real settings. The partial manner regards qualitative researches, that could be totally carried out online.

Beyond facilitating interaction between clinical research demand and clinical research supply, e-recruitment could:

1. **Optimize time.** Internet allows to reach a very large number of potential participants in a very short time. Furthermore, it allows researchers to not repeat the same information for each patient, and participants to get information in comfortable surroundings. With regards to studies carried out in real settings (e.g. trials), Internet is able to make meetings with patients more fruitful. In fact, if patients already know information, meetings could be utilized for studying in depth the most problematic aspects of the research.

2. **Reduce costs.** For example, online services allow to reduce advertising costs. With reference to studies carried out totally online, the reduction also concerns transcription services costs. Rhodes et al. estimate a reduction of 20% to 80% of total data collection costs by using electronic instruments.

3. **Reduce transcription errors:** In reference to studies carried out totally online. This aspect could also increase the validity of studies.

4. **Make questionnaires answers more free and authentic.** With reference to totally online studies on anonymous participants. In fact, some studies show that Internet is perceived as a safer place to warrant anonymity.

Despite these advantages, the effectiveness of patient e-recruitment for clinical research is not so evident. Studies on the matter are scarce and controversial. Some of them are the following.

Frawley et al. compared the rates of recruitment and retention to a multi-centred RCT of a pelvic floor muscle training intervention for women with pelvic organ prolapse. Targeted Facebook™ advertisements resulted the most efficient method of direct recruitment.

Fernández et al. compared the efficiency and cost of recruiting Hispanic men who have sex with men (MSM) from Internet chat rooms versus community venues. Internet recruitment resulted more efficient and somewhat less costly than community recruitment.

In a similar manner, Raymond et al. compared three recruitment methods among Hispanic MSM with respect to demographic and risk behaviours, one sample was obtained using time location sampling at venues in San Francisco, one using a venue based like approach on Internet
and one using direct-marketing advertisements to recruit participants. The physical venue approach was most successful in completing interviews with approached men than both Internet approaches.

**Evaluating E-Recruitment Based Clinical Researches**

The use of Internet to assist the recruitment process raises some issues, that should be taken into account by Research Ethics Committees (RECs)/Institutional Review Boards (IRBs). In other words, when RECs/IRBs assess e-recruitment based protocols, they would have to consider very carefully the following aspects (also considering that there is no specific guideline) (Table I):

1. **Sample representativeness.** An area of concern with any sampling is the ability to be representative. Sample representativeness affects validity and generalizability of study results. Researchers need to be aware of limitations in terms of representativeness of the Internet population. In fact, Internet population is not homogeneous in terms of: a. gender: men use Internet more than women (41% men and 37% women); b. age: young people use Internet more than old people (35% of Internet population is under 25 years old); c. geographic region: Asia has the world’s largest Internet population, Europe, North America, Latin America, Africa, Middle East, Oceania follow. Moreover, Internet use is correlated with education and income. Therefore, e-recruitment raises the issue of sample representativeness. Anyway, the demographic profile of Internet population is fluid and it is predicted to become increasingly representative of the general population.

Finally, as a consequence, RECs/IRBs, particularly statisticians, would have to evaluate very carefully sample representativeness.

2. **Validity of the informed consent.** Informed consent is a “process” of communication between researcher and participant which starts before the subject is enrolled into the research and prevails during the ongoing study in an appropriate way. Information should be provided to the participant in an adequate and comprehensive manner. There should always be enough space for answers to questions that might arise throughout the course of the study. The consenting process has to assure the participant understands. The real understanding could be tested by oral or written tests too.

E-recruitment based studies carried out in real settings do not raise specific issues concerning informed consent. In these cases, Internet is just a mean of advertising and the consenting process occurs in real settings. Therefore, RECs/IRBs would have only to verify on line information. This control by RECs/IRBs is very important as it can protect from possible frauds. For example, the Office of Inspector General of the American Department of Health and Human Services reviewed 22 clinical trial Web sites and 110 clinical trial listings. It found that most of the clinical trials excluded key information; no one had any information about risks to human subjects; 77 failed to identify the sponsor for the clinical trial; 69 did not indicate the phase of the clinical trial, and 56 lacked a general description of the protocol. Fully carried out online studies are quite dif-

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**Table I.** What RECs/IRBs would have to consider very carefully in the case of e-recruitment based protocols.

<table>
<thead>
<tr>
<th>Concerns</th>
<th>E-recruitment based researches totally carried out online</th>
<th>E-recruitment researches carried out in real settings</th>
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<tbody>
<tr>
<td>Sample</td>
<td>– Evaluate sample representativeness since Internet population is not homogeneous</td>
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<tr>
<td>Informed consent</td>
<td>– Verify information reported on line</td>
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<td></td>
<td>– Require to arrange procedures for verifying information understanding (for instance, targeted answers or telephone interviews)</td>
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<td></td>
<td>– Require to arrange procedures for checking Internet users’ identity (for instance, by sending identity documents)</td>
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<tr>
<td>Personal data</td>
<td>– Check the existence of adequate measures to protect personal data (also by web experts)</td>
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<tr>
<td></td>
<td>– Gather information on how proponents reach participants (for instance legal use of cookies, text files, etc)</td>
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ferent: in this case, it is difficult to check “real” understanding because no personal encounter takes place.
To add to the complications, there is no possibility to check indubitably one’s identity. This impossibility exposes to risks of improper uses (for instance, persons having antiscientific behaviours that participate in studies just to invalidate them).
A further issue connected to participants’ identity concerns emotional impact: in fact, information concerning some studies may frighten vulnerable people.
Considering these difficulties, RECs/IRBs would have to: a. check very carefully online information; b. require to arrange procedures for verifying information understanding (for instance, targeted answers or telephone interviews); c. require to arrange measures for checking identity (for instance, by providing identity documents).

3. Protection of personal data. E-recruitment could affect the protection of personal data in two ways. The first one concerns the security of web sites, databases, servers, accounts and so on, that could be accessed by malicious people. The second one concerns the means by which proponents reach potential participants. In fact, some of these means could be ethically questionable. For instance, there is a heated debate on the use of cookies, text files able to track Internet users’ preferences, that are frequently used by the e-recruitment services.
Therefore, RECs/IRBs would have to: (1) check the existence of adequate measures to protect personal data (also by experts); (2) gather information on how proponents reach participants (in this context, RECs/IRBs could also favour the institutionalization of certified societies to support proponents).

Conclusions
Patient enrolment is a critical point of today’s clinical research. Several proposals have been made for improving it, but the effectiveness of these measures is not so evident.
The use of Internet could be a great chance to improve patient recruitment, even though its effectiveness is uncertain as well as its real utilization. E-recruitment could bring some advantages as well as ethical concerns, that RECs/IRBs should take into account.
Anyway, some of the issues raised by e-recruitment will require further in-depth examinations from an ethical, deontological and legal point of view.

Conflict of Interest
The Authors declare that there are no conflicts of interest.

References
2) AVAILABLE ONLINE AT: http://www.centerwatch.com/.