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Pfizer Program for the Development of Investigation and Science

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# From the Editor

## Information society: The need to determine the reliability of scientific information

Bustos-Montero Daniel, MD[1,2]

The society we live in has changed drastically in the last decades, mainly as a result of a rapid technological progress that has impacted positively the development of our civilization.

With the coming of technological tools such as Internet, social networks and virtual spaces dedicated to clarify doubts and questions worldwide, citizens started to have access to unlimited information which –depending on its source- has modified people's way of acting and it has become, little by little, part of the clinical tasks of healthcare providers, regardless of the activities that they perform.

Health sciences are not the exception; in fact, it is the field that society has explored the most searching for answers. The reason is very simple: every time topics related to humans' vulnerability are discussed, they will, unavoidably, call the attention of people involved, in order to find out the reason of their illness, if the diagnosis is correct, if the therapeutic options are available, and, in more complicated cases, if they can extend the inevitable.

This new era brings a unique positivism, if one takes into account that a well-informed patient is the best allied to succeed in his/her treatment. However, this unrestrictive access to information urges the health sciences professional to base his/her decision on the best available evidence and to act as a kind of "translator" between the available information and the obvious clinical practice.

Then, how should we focus the search of information? Is the health sciences professional prepared to answer all his/her patients' questions? How to determine if the information available online is reliable? Should we believe in all the information that is written? These questions force us to deal with this topic carefully, and make it necessary for the healthcare professionals to handle the evidence correctly.

Today's world is immerse in an information society, proof of it can be found in the United Nations Educational, Scientific and Cultural Organization (UNESCO)"2010 Science Report"1, published at the beginning of 2011, which intends to appraise science worldwide and the consequent impact it could (or should) have in the development of modern society.

This report is interesting because of the big amount of scientific publications that were reported in 2008 (a total of 986 099), which represents an increase of 34.5% compared with the report from 2002. Data from Latin-American and the Caribbean are noteworthy since the amount of scientific publications increased a 76.5% in the same period, given that they reported 48 791 publications in 2008. (Fig. 1)

This report clarifies that 13% of these publications were biomedical research and 31% were on clinical medicine, which are common topics in the health field. This means that a total of 1179 scientific articles related to those fields are published every day. With this state of affairs, a required

**FIG.1: GLOBAL DISTRIBUTION OF SCIENTIFIC PUBLICATIONS, 2002-2008**

| | TOTAL PUBLICATIONS | | CHANGE (%) | WORLD SHARE OF PUBLICATIONS (%) | |
|---|---|---|---|---|---|
| | 2002 | 2008 | 2002 - 2008 | 2002 | 2008 |
| **World** | 733305 | 986099 | 34.5 | 100.0 | 100.0 |
| Developed countries | 617879 | 742256 | 20.1 | 84.3 | 75.3 |
| Developing countries | 153367 | 315742 | 105.9 | 20.9 | 32.0 |
| Least developed countries | 2069 | 3766 | 82.0 | 0.3 | 04 |
| **Americas** | 274209 | 348180 | 27.0 | 37.4 | 35.3 |
| North America | 250993 | 306676 | 22.2 | 34.2 | 31.1 |
| Latin America and the Caribbean | 27650 | 48769 | 76.5 | 3.8 | 4.9 |

*Taken from 2010 Science Report. UNESCO.

question would be if the healthcare professional would be willing to read that much.

With this in mind, it is obvious the need these professionals have of tools that would help them determine the scientific reliability of these publications, regardless of their source, to be able to guide their patients in a more accurately way. Besides, it is necessary for them to determine if the information is useful or if it could change the guidelines used to treat the pathology researched in the study. To illustrate this, we could mention the article by Antman EM et al[2] which compared the results of controlled randomized clinical trial meta-analysis and the recommendations given by clinical experts, published in the the Journal of American Medical Association (JAMA) and it proved that the experts' recommendations were not necessarily adapted to the most current information. This finding was ratified by Rennie D and Chalmers L in their article "Assesing Authority"[3], published in the same journal in 2009.

To determine the scientific reliability of a publication is a challenge, one which is restricted to a field where clinical practice variability predominates, uncertain or unknown results and a big quantity of problems related to scientific information are presented.

If we take the fact that an evidence based medicine means an conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients4, it is essential to promote the training of health sciences professionals in topics related to scientific information and to develop further their skills, not only to generate knowledge, but to determine what is true in times when everything could be true. ❖

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## REFERENCES

1.UNESCO. 2010 Science Report . Available at www.unesco.org
2.Antman EM et al. Comparison of results of meta-analyses of randomized clinical trials and recommendations of clinical experts: Treatments for myocardial infarctions. JAMA 1992; 268 (2): 240-248.
3.Rennie D, Chalmers L. Assessing Authority. JAMA 2009; 301 (17): 1819-1821.
4.Sackett DL et al. Evidence based medicine: what it is and what it isn't. BMJ 1996; 312:71-2

# Required elements to determine the scientific validity of a published results of a controlled randomized research

Robles-Campos Pilar, MD [1]

Every scientific research ends when the results are obtained and their respective conclusions are reached. This is the basic premise under which, in 1952, Dr. Carl Wiggers called our attention by pointing that "any research effort is not complete until the results are carefully written, thoroughly edited and promptly published in a form that is both clear and useful to others"[1] .

However, the amount of scientific information that is available nowadays is overwhelming. This can be proven by reviewing the information at UNESCO's 2010 Science Report[2] to observe the increase in the number of investigators worldwide (with the exception of some Latin-American countries which, on the contrary, the number tends to decrease), which entails a parallel increase in the number of publications.

With this state of affairs, it is clear that the purpose of every investigation is to contribute to the general knowledge; in that case, do all current publications have unmistakable importance to determine the causality of certain pathology? Not necessarily.

The reality forces the health sciences professional to evaluate, from a neutral perspective, the scientific articles, in order to determine the validity each one has.

There are guidelines to help health sciences professionals when analyzing critically the publications[3,4]. Table 1 shows the ABC for these analysis, which was adapted from the one presented by Guyatt GH et al in 1993.

**Analysis of the Effect Measures of Discrete Data**

Another aspect that has to be analyzed very carefully while reviewing scientific evidence isthe one related to the statistical calculi which become, unavoidably, essential to determine the validity; it is not possible to reach the objective if these variables are not analyzed.

Effect measures of discrete data are one example of how varied can this analysis be and the consequences it could have if interpreted incorrectly.

**TABLE 1: THE ABC FOR A CRITICAL ANALYSIS OF A SCIENTIFIC PUBLICATION**

| | | |
|---|---|---|
| **A. Are the results of the publication valid?** | 1. Was the study about a clearly defined topic? | A study can be defined in terms of the study population, the intervention performed or the outcomes results. |
| | 2. Were the participants allocated to intervention in a randomized manner? | It is important that the random system uses a blind sequence. |
| | 3. Have all included participants been considered properlyy? | Was there a complete follow up for all participants?<br>Were all losses and discontinuations reported as well as the causes?<br>Was the intention to treat analysis done ? |
| | IS IT WORTHY TO CONTINUE WITH THE ANALYSIS OF THIS STUDY? | |
| | 4. Were patients, investigators and clinical personnel kept blinded along the study? | |
| | 5. Were the groups similar at the beginning of the trial? | This is important not only for its statistical significance but also for the magnitude of the differences |
| | 6. Besides the study experimental intervention, , were all groups treated equally? | |
| **B. What results were obtained? Are the valid results important?** | 7. What is the magnitude of the treatment effect? How big was it? | How are the results expressed?<br>What estimators were used?<br>If there was any difference between the groups, was it corrected through a multivariant analysis? |
| | 8. How accurate are the results? | The first option is to look for or calculate the confidence intervals. As a second option, the P value can be used. |
| **C. Are these valid and important results be used clinically?** | 9. Can the results be applied to their environment or local population? | It is important to take into consideration whether the patients being studied are very different from the community in which one practices. The similarity between the environment used for the study and the environment in the community must be analyzed. |
| | 10. Were all the clinically relevant results considered? | If they were not, how does this affect when a decision is being made. |
| | 11. Are the expected benefits worthy if compared with the risks, the prejudices or the costs of applying the results? | Even though it could not be expressed in the article, what does the reader think about it? |

Adapted from Guyatt GH et al. JAMA 1993; 270:2598-2601

There are two types of measures: absolute and relative.

The absolute measures' main characteristic is that they depend on the subject's basal risk, they are unique to each study, and their calculation helps to determine the efficiency of an intervention in a specific field. Some of these measures are Absolute Risk Reduction (ARR), the Number Needed to Treat (NNT) and the Number Needed to Harm (NNH).

Unlike the absolute measures, the relative measures are independent of the basal risk, they allow the comparison amongst different studies and they are very useful to determine the efficiency of an intervention in a more general field. The most commonly used are Risk Difference (RD), Odds Ratio (OR) and Relative Risk (RR).

Table 2 includes a summary of these measures, including their calculation and meaning.

**The Attrition Bias**

The attrition bias makes reference to the systematic differences between study groups regarding the attrition of participants during the investigation. In other words, it means that the information regarding the pool of participants during the study shows differences or omission between the intervention arms, which can affect the results.

An example of this is when the flowchart required by the CONSORT Statement *5* omits the details of the participants that discontinued the intervention. This data is very important for the results and conclusions of the study, since it has to show if there were more withdrawals in one group than the other as well as the reasons for these withdrawals. This situation raise the question on whether one group produces more undesirable effects and if this makes the investigator to explore the phenomena more. If this data is omitted in the analysis, the conclusions could very easily be biased.

To be able to identify this type of bias, the following aspects should be evaluated:

1. How many discontinuations and follow up losses happened during the investigation?

2. Is the attrition the same in both groups?

3. Do these losses affect the results of the study?

If the answers to these two last questions are affirmative, we are in the presence of an attrition bias.

There is not just one solution to avoid or correct this type of bias; on the contrary, it requires an entire strategy to be able to understand the data that is presented. Such strategy could use the following means:

1. To request the investigators more information in order to find out the reason for the missing data so as to determine which ones are related to the intervention. This type of approach, although feasible, it doesn't always work, since investigators scarcely reply to this type of requests.

2. To perform an Intended to Treat Analysis: it is the analysis of a controlled randomized study, which includes all the participants of the research according to the group of intervention they were allocated, regardless

**TABLE 2: EFFECT MEASURES OF ABSOLUTE AND RELATIVE DISCRETE DATA**

| NAME | TYPE OF MEASURE | CALCULATION FORMULA | MEANING |
|---|---|---|---|
| Risk Difference<br>Abbreviation: RD | Relative | RD= a/NT – b/Nc | Difference between the rate (or probability) of an adverse effect in the treatment group and the rate of the control group. |
| Odds Ratio<br>Abbreviation: OR | Relative | OR= ad/bc | How likely would it be for an adverse event to appear if the treatment is used against not using it. |
| Relative Risk<br>Abbreviation: RR | Relative | RR= aNT /bNC | It compares the probability of an adverse event in the treatment group with the probability in the control group. |
| Absolute Risk Reduction<br>Abbreviation: ARR | Absolute | ARR= 1-RR | Decrease in the percentage or prevalence of an adverse event caused by the treatment |
| Number Needed to Treat<br>Abbreviation: NNT | Absolute | NNT= 1-DR= | Number of patients that should receive the treatment to avoid a negative event |
| Number Needed to Harm<br>Abbreviation: NNH | Absolute | NNH= 1/ARR | Number of patients that need to receive the treatment in order to produce an adverse effect. 0 |

A: Number of people exposed to the risk factor that developed the illness. B: number of people exposed to the risk that didnot develop the illness. C: number of people exposed to the risk that developed the illness.
D: number of people exposed to the risk that did not developed the illness.
NT: Total number of people who developed the illness.
NC: Total number of people who did not developed the illness.

of whether they fulfill the criteria of inclusion, the treatment they finally received and the following exclusion or protocol deviation.

To conclude this review, it is worth noting that the connection between the scientific evidence and the clinical practice is based on the understanding of the information published. Science progress wouldn't make sense if its base is not understood by the health sciences professional; otherwise any published finding could be adopted, immediately, in the day to day activities, without even validating its impact.

To generate scientific evidence from a research is the first step in clinical practice, followed by its synthesis and then its clinical recommendation. Finally, the application of these recommendations would be the responsibility of the health sciences professional.

The ideal clinical practice should consider three fundamental aspects: a) the patient's characteristics, b) their preferences and c) the scientific evidence that supports the approach. If any of these three aspects is missing, the goal of restoring a patient's health would not be fulfill. ❖

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REFERENCES

1.Holmes JM et al. Manuscript Preparation and Publication. Circulation 2009, 120:906-913
2.UNESCO. 2010 Science Report. Available at www.unesco.org
3.Guyatt GH et al. User´s Guides to the Medical LIterature: How to use an article about therapy or prevention. JAMA 1993; 270:2598-2601.
4.Guyatt GH et al. User´s Guides to the Medical LIterature: How to use an article about therapy or prevention. JAMA 1994; 271:59-63.
5.Schultz KF, Altman D, Moher David for the CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. BMJ 2010; 340:c332
6.Pineda EB, Alvarado EL, de Canales FH. Research Methodology: Guidelines for the development of health professionals.. Panamerican Health Organization. 1994. ISBN 9275321353 (spanish)
7.Department of Health Analysis and Health Information Systems. Panamerican Health Organization. Interactive course on Biostatistics 1.0. 2006. Available at www.paho.org

# Organ Transplantion in Costa Rica

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Bioethics is defined as the systematic study of human behavior in the fields of life sciences and health care as well as its evaluation in light of ethical and moral values of the society. Bioethics encompasses a moral reflection on the impact that technological advances will have on human dignity and the issues that will inevitably arise from them.[1,2]

Without a doubt, one of the most controversial topics in Bioethics is the implications of organ transplants in human beings. That is, the replacement of an organ or biological tissue taken from a living or deceased donor. This donor can be a relative of the patient or someone who is not related to the patient at all. The donor expresses freely and voluntarily his wish of being so, in an action guided by the ethical principles of pure altruism, gratitude, and without any lucrative incentive. Added to the autonomy principle expressed through an informed consent, organ transplants seek to prevent the patient's death and improve his/her general well-being[3].

Nowadays biotechnology advances, including surgical techniques and immunosuppression therapies, have shown that the most significant problem concerning organ transplants falls on the shortage of organs that is holding up the implementation of all related programs.

In order to solve this problem and guarantee the respect of ethical principles, several developed nations have created legal regulations to control the disposition of organs coming from living or deceased donors3.

Following the lead of the developed nations, Costa Rica started its own regulatory process in 1973 with the implementation of the Law No. 5560: Organ Transplantation in Human Beings . This initiative captures the concerns of Costa Rican society regarding issues of this matter which was beginning to be discussed gobally. [4.]

In the year 1980, Costa Rica moved on to a different stage with the approval of Law No. 6412 by its Parliament, so-called Law authorizing the Costa Rican Social Security Agency to donate organs in exchange for medicine (Ley para autorizar a la Caja Costarricense de Seguro Social a donar órganos a cambio de medicamentos)., which, as is evident in its name, violates all internationally recognized fundamental ethical principles[4].

History confirms that this matter is of great interest in the medical field for quite a long time already. From a medical point of view, the most important facts encompasses a corneal transplant in 1944, the first kidney transplant in 1969, bone-marrow transplant procedures initiated in 1985, a heart transplant in 1991 and the first liver transplant in 1993. Then, during this same year, a multi-organ transplant was performed: a heart/lung and pancreas/kidney transplant. Finally in 1994, a bone structure transplant was carried out[5].

**Current Regulation:**
**Law No. 7409 Organ and Anatomic Materials Transplants in Human Beings**

In 1994, assuming its responsibility regarding the regulation of organ transplants, Costa Rican Government granted Law No. 7409: a series of regulations directed towards the proper management, distribution and prioritization of donors, organs, tissues and cells involved in a transplant.

Nowadays, this issue raises a lot of questions concerning the scope of these regulations and whether or not the Ministry of Health and the Social Security Administration System (CCSS, per Spanish acronym) are complying with their work while properly distributing and prioritizing available organs under the protection of the well known international ethical principles. These principles are needed to establish the required regulations and to form a regulatory authority for organ transplants[6-10].

This Law includes 28 articles from which we will present a brief summary.

First of all, honoring the Principle of Nonmaleficence, transplantation of organs, tissues and cells will only be performed whenever it substantially improves the health condition e of the patient. The transplantation will only be carried out by physicians with a qualified professional team in a hospital authorized by the local Ministry of Health[6-11].

In a transplant involving a living donor, the donor must be over 18 years old; he/she must in good overall physical and mental health so that his/her rights to the principle of autonomy, beneficence and justice as donor are respected. When the organ of a deceased donor is artificially preserved, a death certificate, subscribed by at least three doctors from the medical center, must be presented. The hospital director and a neurosurgeon or neurologist must be among these three doctors to protect the patient's rights as donor since no personal interest must be superimposed. In addition, the commercialization of anatomic material and human organs is prohibited. Organ banks must keep a detailed record of all organ dispositions and report all correspondent information to the proper commission[11].

In regards to this commission, the current Legislation, valid since October 27th 1994, calls the attention on the importance of its creation. This commission will be in charge of the proper management of organ transplants coming either from living or deceased donors. It will keep detailed record of transplant recipients as well as waiting lists. The commission's main objective will be a better organ distribution according to an adequate prioritization system.

This system is divided into three stages according to the actualization of this Law in 1999. (Table 1)

Article 18's main purpose was the creation of a unique commission which will be in charge of the regulation of all transplant-related procedures. Nevertheless four of the country's most important hospitals did not comply with this policy and created their own regulatory entities. This action did not allow an adequate distribution of available organs which could have been compatible with donors from different hospitals' waiting lists.

However, after 16 years of its publication, this law is under revision since it is obvious that it does not honor most of the patients and

| FIG.1: STAGES ACCORDING TO THE ORGANIC FAILURE, COSTA RICA, 1999 | |
|---|---|
| Stage 1A | Unstable patient requiring inotropic and mechanical support (e.g. Left Ventricular Support Device), life expectancy of less than one month without a transplant. |
| Stage 1B | Unstable patient requiring inotropic and constant mechanical support (e.g. Left Ventricular Support Device ), life expectancy of more than one month without a transplant. |
| Stage 2 | Patients who do not fulfill the previous criteria. |

Source: D.Ch.P. G.V.O May 27 1994.
Strengthening of donation and organ transplant.

donor's rights or covers them just superficially, leaving out keys aspects on this matter.

The regulations on organ donation must aim for three basic general objectives: purpose of organ retrieval, protection of rights for all persons involved in this process and establishment of a clear legal framework for the healthcare professionals to work with[3].

Another key aspect is the quality of the donated organs. Its correct evaluation and maintenance must be guaranteed to increase donation viability, reduce the risk of rejection and avoid disease transmission.

Healthcare professionals should also comply with some basic regulations. They should guarantee the required experience in all professionals carrying out activities related to the search of organs. The required communication mechanisms should also be established to guarantee the correct coordination between medical centers or institutions like the Forensic Medicine System in case of accidental deaths.

A record of all decision making actions regarding organ transplant must be mandatory as well as data confidentiality.

Law 7409 states in its opening articles that organ transplants will only be carried out for therapeutics aims to substantially improve the recipient's life expectancy and quality of life.e. It also prohibits any economic compensation for organ donation and declares minors as potential donors. This law does not prohibit organ donation on handicapped persons or requires a family emotional boundary between the donor and the recipient.

In relation to the deceased donors, this Law declares all persons as organ donors unless otherwise expressed in a presumed consent. However, in case of doubt concerning the decision of the deceased donor, this Law does not entitle his/her relatives to take such a decision in regards to the disposition of the organs. It is widely known that requesting permission for organ retrieval to the deceased donor's family will not increase the number of donors since most of the times the answer will be a simple no. However, doing the opposite, retrieving organs without asking for permission, may only create resentment among the population. The family of the deceased donors is grieving the passing of someone close and therefore it will be unethical to inform them that all organs will be retrieved for donation. This may be considered by certain cultures and religions as an insult or an aggression to the body of the deceased person.

This situation may be avoided by educating the population on the importance of leaving a written decision on whether or not they want to be organ donors. The validity of this strategy lies on the fact that not many people are aware of this Law.

Anyone who meets the required criteria, will be considered as organ donor r passing, unless they have expressed otherwise in a written consent during his/her life. The decision is more complicated when it comes to minors. Article 7 from this Law says that any child over 15 years old will be considered as donor only with the approval of the parents or legal guardian and the agreement of the minor. The intervention of an Ethics Committee is required in most of the cases. In addition, if an adult donor shows greater or similar compatibility with the donor compared to the compatibility of a minor with the same donor, the adult donor will be chosen. The reason behind this decision lies in the complications the procedure may present and the importance of protecting the minor's autonomy.

Article 11 provides that whenever locals or foreigners request or renew their Costa Rican identification card, a consent form must be filled out expressing their desire to become an organ donor or to decline the option. Nevertheless this practice is not taken into action. The same initiative was applied to the Costa Rican driver license and even though the same question is asked to everyone, the driver license is not considered to be a legal document that expresses the final decision of a person.

In relation to the recipient, this legislation does not include any policies regarding the quality of the donated organ. It is true this aspect may be regulated through a series of maintenance and evaluation protocols within each medical center but it is also important to include an article establishing that health authorities must guarantee the quality of the service, materials and technical equipment involve in the donation process (this aspect is superficially addressed in Article 4 of the Law No. 7409).

But this is not the main gap this law has regarding the recipient's rights. The lack of a specific article that regulates and guarantees a fair access to a transplant is one of the main lacks of this legislation, and it is one most currently defended aspects worldwide. Since a distributive justice is one the main ethical principles, a proper and transparent management of the waiting lists should be one of the most important aspect to regulate. Therefore, the Law should specify that a fair organ distribution should be based strictly on medical criteria and nothing else.

Law 7409 is not the only one regulating the controversial topic of organ transplant nationwide. There are other normative texts such as the Code of Ethics of the Costa Rican College of Physicians and Surgeons (Código de Moral Médica del Colegio de Médicos y Cirujanos de Costa Rica), as well as the General Health Law of 1973 (Ley General de Salud) which establishes some guidelines to follow.

The law also establishes the creation of a regulatory commission for organ and human anatomic material transplants under the Ministry of Health. This commission consists of the Ministry of Health or its representative, who will be the Chairman of the commission, the Chief Executive Officer of Costa Rican

Social Security Agency, the Chairman of the Legal Department of the Ministry of Health, the National Attorney or its representative, the Chairman of the Costa Rican College of Physicians and Surgeons or its representative and two physicians from the transplant teams of two authorized hospitals, that should have been appointed according to the regulations established in their respective Codes.

With this state of affairs, on June 14th, 2011, the Mexico Hospital, Children National Hospital, San Juan de Dios Hospital and Dr. Calderon Guardia Hospital, decided to establish a relationship in order to manage the fair distribution of donated organs through the Costa Rican National Transplant Office (ONACOTA per Spanish Acronym).

The main purpose of this office is to educate the health personnel- from the administrative one to the one who deals directly with the families- regarding the importance of informing what is the condition of the patient because, even if the patient is in a critical stage, the health personnel will always do everything possible to improve his/her condition to safe the patient.

According to this office, organs such as kidneys, heart, lungs, pancreas, blood, bone marrow and cornea are amongst the most sought-after tissues of the 25 which are normally used in transplants.

Also, this office reinforces the fact that the extraction of organs, whether from live or death donors, should only be performed with the consent of the family because, even though there are legal documents (such as the driver license) that indicate their consent to donate, they don't have any legal value, according to the current Law, as it was mentioned in previous paragraphs.

**Current Situation of Organ Transplantion in Costa Rica**

In Costa Rica there are four hospitals authorized to perform organ and tissue transplantations: Dr. Calderon Guardia (heart, lung, liver, pancreas, kidney and cornea transplants), Mexico Hospital (liver, kidney, heart, cornea and bone marrow transplants), San Juan de Dios Hospital (kidney, cornea and bone marrow transplant) and Children National Hospital (liver, kidney, bone marrow transplant).

The financial sources come from the budget of the Social Security Administration System (CCSS as per Spanish Acronym), which is assigned to each of the four hospitals previously mentioned.

The hospitals from the CCSS perform an average of one transplant per day; however, this number could increase since the donation from dead donors is increasing nowadays and there are more anti-rejection drugs available in the CCSS.

During 2005, the CCSS performed 393 transplants of different tissues. During this period of time, there were 257 cornea transplants done, most of them performed in Ophthalmologic Clinic . Also, there were 112 kidney transplants between the four national hospitals, and 12 bone marrow transplants.

In the year 2007, the CCSS performed 416 transplants: 11 of liver, 276 of cornea and 129 of kidney. Most of them were done in male patients. During this period, the CCSS also invested $2.9 millions in anti-rejection medications.

From 2003 to 2008, there were 682 kidney transplants performed, according to the

hospital expenses report from the Health Statistics Department of CCSS. 403 of these transplants were performed in male patients. The survival rate in these patients has increased also since it has been reported that during the year of the transplant, there is a 90% rate of survival, and 70% rate during the first five years of the transplant. These patients also require anti-rejection medication, in which the CCSS invested $580 thousand dollars only in the year 2009.

During 2009, the CCSS performed 390 organ transplants (121 of kidney, 12 of liver, 187 of cornea, 32 of bone marrow, 36 of bones and 2 of heart) and invested $4.3 million to buy anti-rejection medication.

The cornea transplants are the most common ones, the CCSS performs an average of 266 of these surgeries per year.

Regarding the bone marrow transplants, from 1995- when this tissue was transplanted for the first time- to 2009, there have been 102 transplants performed. The patients who received the tissue had an average age of 33 years. Of these procedures performed, 45 were autotransplantations and 57 were allotransplantations.

The first procedure in the country using umbilical cord cells was performed in year 2005.

Compared with the successful solid organ transplant model used in Spain, Costa Rica still needs to implement a professional public institution which would detect donors, assign the grafts and coordinate the extraction and transportation mechanism.

Far from managing and providing accurate guidelines about this topic, Costa Rica has been facing great gaps in the regulatory framework through these years.

Nowadays, the bill of law 18246 is being discussed, in which the administration of ONACOTA and the hospitals will work together to maintain the order, respect, and above all, the moral principals when managing, caring and distributing organ, tissue and/or cell transplants. The need to have a communication network among the hospital nationwide, especially the ones specialized in transplantations in the central valley, stands out. The above with the purpose of unifying efforts, and have a system that would allow a timely identification of organs; hence, benefiting a lot of people. ❖

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## REFERENCES

1. Reich WT. Encyclopedia of Bioethics. Macmillam Library Reference. Rev Ed edition 1995. ISBN 978-0028973562
2. Ugalde, J. Aristas de la bioética en Costa Rica. Revista Latinoamericana de Derecho Médico y Medicina Legal. Extraído el 5 de noviembre del 2010. De: http://www.binasss.sa.cr/revistas/rldmml/v6-7n2-1/art5.pdf

3. Leal M. (2006) Ley sobre Autorización para Trasplantar Órganos y Materiales Anatómicos Humanos: ¿es suficiente para regular la actividad de donación de órganos en Costa Rica?. Rev. Costarric. Salud Pública. [online]. (vol.15) p.44-49. Extraído el 5 de noviembre de 2010. De: http://www.scielo.sa.cr/scielo.php?script=sci_arttext&pid=S1409-14292006000100006&lng=es&nrm=iso>. ISSN 1409-1429.

4. Bustos-Montero D. Evolución de la bioética en Costa Rica: una historia reciente. Bioethikos 2007; 1(2):39-44-

5. Caja Costarricense de Seguro Social (Departamento de Estadísticas Hospitalarias). Documentos varios. Extraído el 5 de noviembre de 2010. De: www.ccss.sa.cr

6. Arguedas O. Las células madre y su uso en seres humanos. AMC Acta Médica Costarricense, Biological Abstracts, Chemical Abstracts Service, Latindex. 2010; 52 (4):195-196.

7. Arguedas O. Tipos de diseño en estudios de investigación biomédica. AMC Acta Médica Costarricense, Biological Abstracts, Chemical Abstracts Service, Latindex. 2010; 52 (1): 16-19. .

8. Arguedas O. Elementos básicos de bioética en investigación. AMC Acta Médica Costarricense, Biological Abstracts, Chemical Abstracts Service, Latindex. 2010; 52 (2):75-79

9. Ley N° 7409: Autorización para Trasplantar Órganos y Materiales Anatómicos Humanos, publicada en La Gaceta 177 del 19 de septiembre de 1995. Recuperado el 5 de noviembre del 2010 (11:18 pm) ¿SITIO WEB?

10. Caja Costarricense de Seguro Social y Centro de Desarrollo e Información en Salud y Seguridad Social. (2007). Normativa relacionada con la bioética en salud. (pp.83-88). Costa Rica: Editorial Nacional de Salud y Seguridad Social.

11. Procuraduría General de la República. Sistema Costarricense de Información Jurídica. Extraído el 5 de noviembre del 2010. De: de : http://www.pgr.go.cr/scij/busqueda/normativa/pronunciamiento/pro_repartidor.asp?param1=PRD&param6=1&nDictamen=8295&strTipM=T.

12. Ley de trasplante de órganos y materiales anatómicos humanos. Autorización para trasplantar órganos y materiales anatómicos humanos. (2008). [html]. Fecha de última modificación: No indicada. Extraído de: http://www.scielo.sa.cr/scielo.php?pid=S140900152009000100008&script=sci_arttext

13. Angie López Arias -Periódico Al Día. (febrero 13, 2011). Trasplantes de órganos no avanzan [html]. Extraído el 31 de mayo de 2011. De: http://www.aldia.cr/ad_ee/2011/febrero/13/nacionales2679790.html

14. D.Ch.P. G.V.Q., (27 de mayo de 1994). No.7409 La Asamblea Legislativa de la República de Costa Rica Decreta: Autorización para Trasplantar Órganos y Materiales Anatómicos Humanos. [PDF]. Extraído el 17 de junio de 2011. De: http://www.cendeisss.sa.cr/etica/ley7409.pdf.

15. D.Ch.P. G.V.Q., (27 de mayo de 1994). Fortalecimiento de la Donación Altruista y Trasplante de Órganos. [PDF]. Extraído el 20, 6 del 2011. De: http://eurosocialsalud.eu/files/docs/00101.pdf

16. Ultima Hora - La Nacion, (Martes, 14 Junio 2011). CCSS abre Oficina Costarricense de Trasplantes de Órganos [html]. Extraído el 20, 6, 2011. De:http://www.noticias.cr/news/ccss-abre-oficina-costarricense-de-trasplantes-de-organos

17. Rodríguez S., Irene La Nación, ALDEA GLOBAL (viernes 1 de julio del 2011) Iniciativa para mejorar donación y trasplantes. CCSS abre Oficina Costarricense de Trasplantes de Órganos.[html]. Extraído el 18, 6 del 2011. De: http://www.nacion.com/2011-06-14/AldeaGlobal/ccss-abre-oficina-costarricense-de-trasplantes-de-Organos.aspx

18. Vega, Elena J. La Prensa Libre. (Lunes 27 de junio de 2011). CCSS no sabe cuántas personas esperan por una donación de órgano. [html]. Extraído el 30, 6 de 2011. De: http://www.prensalibre.cr/pl/nacional/45826-ccss-no-sabe-cuantas-personas-esperan-por-una-donacion-de-organo-.html

19. Fundación Mundial de Trasplantes para Niños Costa Rica. ¿Qué es la donación de órganos. Jul 1 2011. Disponible en www.fundetran.org

20. La Jornada. Crece el tráfico de países pobres a ricos. (2011). Fecha de última modificación: No indicada. Extraído el 02 de julio de 2011. De: http://www.jornada.unam.mx/2007/04/03/index.php?section=cienciias&article=a03n1cie

21. Deen Thalif. Salud: ONU en guardia contra tráfico de órganos. (2011). Fecha de última modificación: No indicada. Extraído el 02 de julio del 2011. De: http://ipsnoticias.net/nota.asp?idnews=93611

22. Associated Press. (2009) Black market organ trade still thrives in Egypt Lack of transplant law is key problem, but country is starting to take action. [html]. Recuperado el 30 de junio 2011 de http://www.msnbc.msn.com/id/29740869/ns/health-health_care/t/black-market-organ-trade-still-thrives-egypt/

# Historical reflections about antibiotic-therapy. Second part: The Syphilis

Lovato-Gutiérrez Pedro, MD, MPH [1]

The concept of an illness being a divine punishment in many cultures has almost always been linked to a religious nature[1]. It was inevitable for men to transform that religious and/or magical thinking into a logical one, obviously without setting aside the first one. The logical aspects linked to the knowledge of the time were added little by little to the empirical medicine. This broadened the therapeutic options of the time and it was a great progress of medicine as such. The understanding of the therapeutic actions was added to the primitive concept of the effects brought by medication[1,2].

People influenced by these ideas set the beginnings of the rational explanation that distinguishes west medicine. These cultures determined that some infectious diseases, specially the epidemic ones, had a supernatural origin; while the etiological thinking group of the time, attributed them to natural causes that could be treated with earthly remedies[3].

Syphilis represents all of the above in human history. The humans struggle to defeat the illness that pushed the intellectual resources to the limit. There are at least three theories about the origins of syphilis: its apparent origin in the New World, known as the Columbus hypothesis; the mutation of a trepanematosis which already existed in Europe, known as the pre-Columbus hypothesis, and the theory about its transportation from Europe to America. The main questions revolve around the disease that already existed and pre-Columbus Europe (before 1492): was it really syphilis?[4,5]

There is little evidence of Periosteal reaction in Europe before the XII century a.c.. The existing evidence correspond to isolated cases for which alternative diagnosis are more probable. To try to attribute syphilis disorders in isolated individuals could identify marginal values of a different disease[6,7].

Christopher Columbus came from mainland Europe, where there is no evidence of any treponematosis case before 1942. According to what is known, the treponematosis originated in Africa as a pinta[8,9,10]. Afterwards, it moved through Asia to North America, where it appeared as a bejel-shaped mutation. The bejel also moved through Asia to North America; however, it was in this last region where another mutation appeared which produced syphilis[11,12].

The term syphilis is first used as a consequence of a big epidemic that devastated Europe at the end of XV century, but it was known as Morbus italicus, hispanus, germanicus o gallicus depending on who gave it the name. Morbus gallicus is the term largely used in latin texts, this is mainly because it was related to the invasion and conquest of Naples by the French king Charles VIII[13,14,15].

It is believed that during the siege, French prostitutes had sexual intercourse with Spanish soldiers, contracting syphilis in this way. Later they transmitted it to French soldiers, who withdrew quickly due to a mysterious epidemic; hence, the name morbo gallico[16,17,18].

## Syphilis and its Relation to Current Medicine

The word "syphilis" comes from a pastor named Syphilus, a character in a poem called Syphilis sive morbus gallicus. This poem was written in the XVI century (1530) by Girolamo Fracastoro de Verona (1483-1553), an Italian doctor who was a colleague of Copernicus, and who followed the humanists' costume of the time of altering the name; hence, the name "Syphilus". In the poem, Syphilus, a pastor hero, is punished with a diseased by the god Apolo. Syphilus was punished for blaspheming against the god Sun, when he built prohibited altars in the mountain. Syphilus, who was regretful, pleaded to the goddess Diana for a cure and, goes with her to an afterlife trip. Diana gave Syphilus the guaiac (holy wood). What is great about Fracastoro's story is not only that he described the guaiac tree as a therapy for syphilis, but also that he illustrates, for the first time, a germ-based theory, which revolutionized the traditional pathology [19,20,21].

The syphilis has received different names during history; for example, the venereal and pudendagra. This last one was quoted by Gaspar de Torella, a historian and mathematician who took the task of describing the disease in 1924[22]. Other names are: gallic disease, French disease, Naples disease. It was called the bubas disease by Spaniards, pua by the Indians, frenk pocken by Germans and English, and the great vérole by the French.

The name "syphilis" was coined definitively in the XIX century. It comes from the greek terms siph "pig" and philus "love". Frascastoro was the first one to refuse using the term Morbus gallicus, and replaced it by lues or plage, the old name with which the disease was described [24,26,27].

The name "syphilis" was quoted by Hippocrates in his play "Epidemics" and by Sucruta in his play "Ayurveda" in old India. It also appeared in Edwin Smith's Egyptian papyrus, and in "De Re Medica" by Celso, a latin writer who lived in Roma, which also gives important information about the disease[28].

In the XII century, Alain de Lisle talked about lesions as consequence of pleasures of the flesh. In 1502, Juan Almenar, a Spanish doctor, explained the way it was transmitted and excluded the clergy men who got infected by "a corruption in the air" [29,30,31].

## The Holy Wood

In 1517, Nicolas Paul published "Treatment for the morbos gallicus with guaiac tree", where he says that since syphilis had an American origin, it could be treated with guaiac, which also had an American origin. The guaiac, considered a remedy for the venereal, came from West Indies and the spiritual religious of those times believed that God has placed the remedy right next to the disease[31].

## The Mercury

A famous saying said: "One night in Venus's arms leads to a life in Mercury". The mercury was a frequent ingredient, although not very effective, of several treatments against the syphilis.

With the mercury treatment, the patient presented undesirable symptoms such as stomatitis, vomiting, nephritis, diarrhea, amnesia among others. Based on this, it was justifiable that for a long period of time, a lot of patients and doctors preferred the "holy wood" instead of the risks caused by mercury. This caused that doctors would take into consideration the risks of mercury and the need to have a more accurate use of it.

Teofrasto Paracelso, also known as Paracelso (Paracelso means "superior than Celso" in Latin), who was believed to have achieved the transmutation of lead into gold through some alchemist procedures and who also coined the name of the zinc by calling it "zincum", contributed a lot to the practice of using mercury. He was aware that the problems produced by the high doses of mercury were worse than the illness itself[32,33,34].

Paracelso prescribed the mercury treatment in small doses to reduce its toxicity, which was later known as "toxic doses" in pharmacology. It's not surprising then the medical concept that "only a virtuous man can be a good doctor".

According to Paracelso, instead of using mixtures of vegetables, they should use poisons, which could achieve a recovery once the toxic properties were removed; therefore, the mercury, an arcane per excellence, should be deprived of its "roughness" and turn it into medicine by the correct chemical procedures. He also considered the use of arsenic to treat syphilis, going ahead P. Ehrlich for about three centuries.

Paracelso based all these on his deep knowledge of the traditional medicine and opened new ways to interpret diseases and pharmacology. He based his theories in his own experience and criticized the surrounded ignorance. His thinking, typical of the Renaissance, was full of contradictions. Being a man raised in the Christianity as well as the Neo-Platonism, he was very optimistic about the possibilities of science[35, 36].

As a result of the first international conference for the prevention of syphilis and other venereal diseases, held in Brussels in 1899, Alfred Fournier created a medical specialty of syphilography which used epidemiological techniques as well as statistics to stress the fact that the disease not only affected people with a doubtful reputation, but all social strata; that women got infected before men, and that it was overwhelming the number of women with a low-income background who got infected since they were forced into prostitution. Based on Fournier's work, periodic publications specialized in syphilis were created, which prepared the way for clinical investigation.

On Marsh 3rd, 1905, the zoologist Fritz Schudinn discovered, through a microscope, the spirochete in a blood sample of a patient with syphilis. One week later, he observed, together with Hoffmann, the appearance of the same spirochete on samples taken from different part of the body of a patient with roseola lesions [37,38].

In 1906, August Wassermann invented a coloration diagnostic evaluation that allowed identifying the disease, even though there were some false positives.

### The 606

In 1907, Paul Ehrlich had created at least 606 different substances or "magic bullets" designed to counteract a variety of diseases.

Most of them turn out to be ineffective, but the "606 preparation" showed to be effective against the spirochete. It was the hydrochloride dioxidiaminarsenobenceno, in other words, an arsenic-based salt. The 606 had a great boost at the beginning. In the Wiesbaden Internal Medicine Congress, held on April 19th, 1910, Ehrlich delivered his first lecture about his investigation, which had reached its highest peak at that point. He told to the congress that in October 1909, 24 syphilis patients had been treated with the "606 preparation", which he called salvarsan. Its chemical name is arsfenamina.

Although they tried to hold the product back until it had been tested in hundreds of patients, Ehrlich could not stop the growing demand this new drug had. The salvarsan also had some enemies: the Russian orthodox church, for example, believed venereal diseases should not be treated because they were God's punishment for immorality. On the other hand, the German police did not support the marketing of salvarsan because they wanted to avoid prostitution. It took Ehrlich four years to replace the 606 for the 914 or neosalvarsan, a much more soluble and easy to use product that did not lose its efficacy[39,40].

In 1911, Noguchi cultured the treponema and 1913 the central nervous system was isolated.

The discovery of salvarsan was not only a great significant medical progress, but it also promoted a social change that ended up affecting the way people perceived the disease and society. It's even incredible to read reports that describe the use of combinations of arsenic with bismuth or mercury.

**The Penicillin**

In December 1943, Mahoney, together with Arnold and Harris, published a report in The American Journal of Public Health and The Nations Health, in which the use of penicillin to treat four primary syphilis patients with good initial results was reported for the first time. Very soon there was an effective, simple and safe medication to treat and eliminate de T. pallidum. It was proved then, that a concentration of 0.03 U per milliliter was effective. Six years later, in 1949, the first T. pallidum immobilization test was performed by Nelson and Mayer.

**TSUS**

To conclude, there are 14 TSUS articles (Tuskegee Study of Untreated Syphiulis); two of which have been published twice. Nine of them were published in different journals. Three articles that described the existence and continuity of TSUS were published in the American Medicine Association (AMA) journals. In 1946, two of those three articles were published when AMA created "Principles of Ethics Concerning Experimentation." ❖

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## REFERENCES


1. Abraham EP, Chain E. An enzyme from bacteria able to destroy penicillin. Nature 1940; 146:837.
2. Abraham EP, Chain E, Fletcher CM, Gardner AD, Heatley NG,Jennings MA, Florey HW. Further observations on penicillin. 1941. Lancet 2: 188-189.
3. Ackerknecht EH. Medicina y Antropología Social. Ed. Akal,1985.
4. Ackerknecht EH. Therapie von der Primitiven Hiszum 20.Jahrhukdert. Enke. Stuttgart, 1970
5. Belmonte A. Terapéutica antibiótica. Universidad de Santiago de Compostela. Santiago de Compostela, 1981.
6. Bulloch W. The History of Bacteriology. Oxford University Press. Oxford, 1936.
7. Bustinza F. La penicilina y los antibióticos antimicrobianos. ED. Plus Ultra. Madrid, 1945.
8. Campillo. La enfermedad en la Prehistoria. Introducción a la Paleopatología. Salvat. Barcelona, 1983.
9. Carpentier J, Lebrun F. Breve historia de Europa. AlianzaEditorial. Madrid, 1994.
10. Cohen ML. Epidemiology of drug resistance: implications fora post-antimicrobial era. Science 1992; 257: 1050-1054.
11. Coleman K, Athalye M, Clancey A, Davison M, Payne DJ,Perry CR, Chopra I. Bacterial resistance mechanisms astherapeutic targets. J Antimicrob Chemother 1994; 33: 1091-1116.
12. Courvallin P. Evasion of Antibiotics. 1971 Quebec. Ed. Butterworths, London, pg. 649.
13. Cowen DL, Segelman A B. Antibiotics in Historical Perspective. Merck & Co., Inc. (EEUU). 1981
14. Chain E, Florey HW, Garnerd AD, Heatley NG, Jennings MA, Orr Ewing J, Sanders AG.
15. Penicillin as a chemotherapeutic agent. Lancet 1940; 2: 226-228.
16. C Garrison FH. History of Medicine (4.º ed.). Filadelphia y London, 1929.
17. Gracia Guillén D, Albarracín A, Arquiola E, Erill S, Montiel L,Peset JL, Somolinos J, Laín Entralgo P. Historia del Medicamento. Ed. Doyma. Barcelona, 1985.
18. Grandes biografías de Planeta De Agostini (Barcelona). Fleming. 1995.
19. Granjel LJS. Historia General de la Medicina Española. Ed. Universidad de Salamanca. Salamanca, 1978-1982.
20. Guerra F. La medicina precolombina. Ediciones de Cultura Hispánica. Madrid, 1990.
21. Singh AE, Romanowski B. Syphilis: Review with emphasis on clinical, epidemiologic, and some biologic features. Clin Microbiol Rev 1999;12:187-209.
22. Tognotti E. The rise and fall of syphilis in Renaissance Europe. J Med Humanit 2009;30:99-113.
23. Kontokostas K, Kousoulis A. Syphilis in history and arts. Athens: John B. Parisianos; 2008.
24. Eatough G. Fracastoro's Syphilis. Introduction, Text, Translation and Notes. Liverpool: Francis Cairns; 1984.
25. Shakespeare W, Henry V. Act 5. Massachusetts: Digireads; 2005.
26. Cheyne G. The English Malady (1733) edited by Roy Porter. London: Routledge; 1991.
27. Fournier A. Syphilis et marriage. Paris: G. Masson; 1880.
28. Morens DM, Folkers GK, Fauci AS. Emerging infections: A perpetual challenge. Lancet Infect Dis 2008;8:710-9.
29. Schoch-Spana M, Bouri N, Rambhia KJ, Norwood A. Stigma, health disparities, and the 2009 H1N1 influenza pandemic: How to protect Latino farmworkers in future health emergencies. Biosecur Bioterror 2010;8:243-54.
30. Subba Reddy DV. Antiquity of syphilis (venereal diseases) in India. Indian J Vener Dis 1936;2:103-42.
31. Pearce JM. A note on the origins of syphilis. J Neurol Neurosurg Psychiatry 1998;64:542,547.
32. Inchkeith. In: Lewis S, editor. A Topographical Dictionary of Scotland. Edinburg: Peter Hill; 1846. p. 555-84.
33. Shelton MH. Syphilis: Is it a mischievous myth or a malignant monster? California: Health Research, Mokelumne Hill; 1962.
34. Barquet N, Domingo P. Smallpox: The triumph over the most terrible of the ministers of death. Ann Intern Med 1997;127:635-42.
35. Sabbatani S. Physicians and philosophers tackling Cupid's disease: Combating syphilis in the 18th century. Infez Med 2008;16:108-15.
36. Dunglison R. Dunglison's Medical Dictionary - A Dictionary of Medical Science. Philadelphia, USA: Collins; 1874.
37. Haas LF. Girolamo Fracastoro 1484-1553. J Neurol Neurosurg Psychiatry 1991;54:855.
38. Perrot G. History of art in Phrygia, Lydia, Caria and Lycia. London: Marton Press; 2007. p. 62.
39. Thyresson N. Girolamo Fracastoro and Syphilis. Int J Dermatol 1995;34:735-9.
40. Stamatakos I. Dictionary of the ancient Greek language. Athens, Greece: Phoenix; 1972.
41. R. M. White, Unraveling the Tuskegee Study of Untreated Syphilis, Arch. Intern Med. 2000; 160: 585-598.

# Comments on the CONSORT Statement to Report Controlled Randomized Trials[1-6]

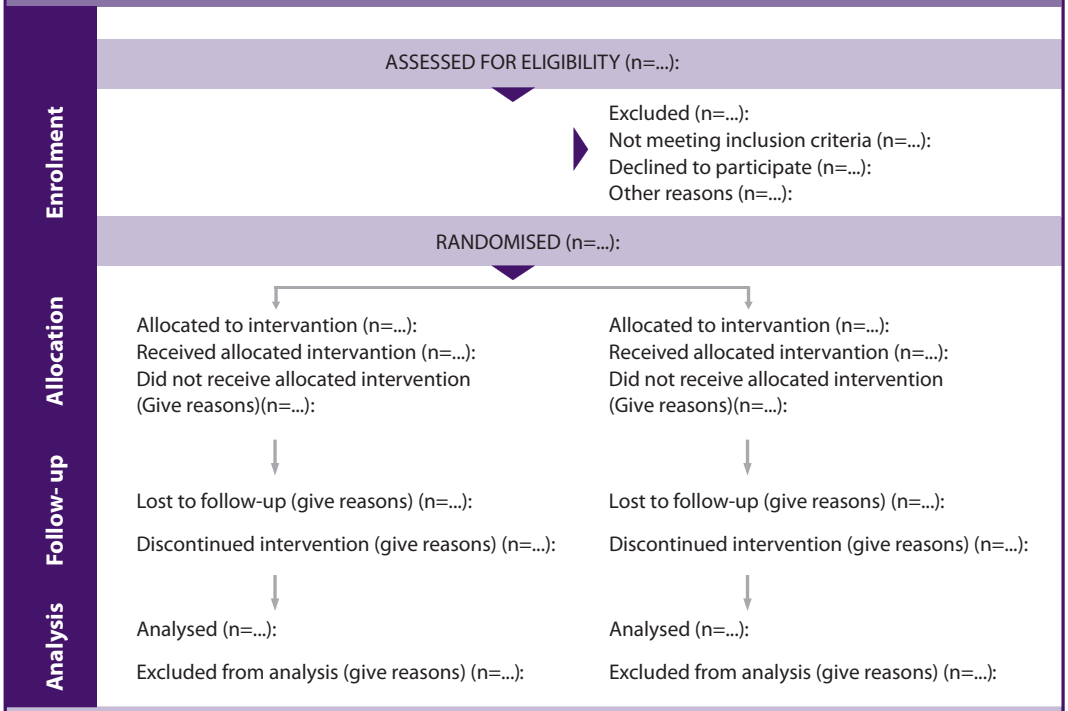
Bustos-Montero Daniel, MD[1,2]

In the 1990s, the scientific information experienced an exponential growth, and as an inevitable consequence, a decrease in the quality of scientific publications, which were being accepted in different scientific journals worldwide, was observed.

Worried about this situation, in 1993, a work groupof 30 experts -including medical journal editors, investigators, epidemiologists and methodologists- gathered in Otawa, Canada, defined 32 items every scientific publication should include. These items were named the Standardized Reporting of Trials (SORT).

During the same period of time, but independently, another group called Asilomar Working Group on Recommendations for Reporting of Clinical Trials in the Biomedical Literature, were working towards the same objective.

**FIG.1: FLOWCHART OF THE PROGRESS THROUGH THE STAGES OF A RANDOMIZED PARALLEL –GROUP TRIAL**




*Adapted from Shultz KF et al. BMJ 2010; 340:c332.

Following the recommendation of Dr. Drummond Rennie, editor of the Journal of the American Medical Association, both groups gathered in Chicago in 1996.

These two groupsdecided to join efforts with the purpose of improving the quality of the reports that resulted from the randomized parallel-groups clinical trials, believing that these type of trials "when appropriately designed, conducted and reported represent the gold standard in evaluating healthcare interventions".[1]

As a result of the work of this group, the Consolidated Standards of Reporting Trial Statement (which adopted later on its abbreviated name CONSORT) was created. Its first version was in 1996, and its most recent version was in 2010. This statement consists of 7 sections, which are divided at the same time in 25 variables. These variables were put together in a check list in the following way:

1. Title and abstract (Variables 1A- 1B)
2. Introduction (Variables 2A- 2B)
3. Methodology (Variables 3A-7B)
4. Randomization (Variables 8A-12B)
5. Results (Variables 13A-19)
6. Discussion (Variables 20-21)
7. Other information (Variables 23-25)

One of the greatest contributions from CONSORT Statement is the flowchart of the process a randomized parallel-group trial must follow through the fulfillment of 4 stages very well established: Enrolment, Allocation, Follow-up and Analysis. (Fig. 1)

Nowadays, the CONSORT Statement has been adopted by a vast majority of scientific journals and it is mandatory in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (writing and editing for biomedical publication) from the International Committee of Medical Journal Editors (ICMJE).

Without a doubt, the CONSORT Statement has improved the quality of the reports of randomized parallel-group trials; however, still, a lot of results are inadequate. ❖

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REFERENCES

1.Schultz KF, Altman D, Moher David for the CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. BMJ 2010; 340:c332
2.Pocock SJ, Hughes MD, Lee RJ. Statistical problems in the reporting of clinical trials. A survey of three medical journals. N Engl J Med. 1987;317:426-32. [PMID: 0003614286]
3.Altman DG, Doré CJ. Randomisation and baseline comparisons in clinical trials. Lancet. 1990;335:149-53. [PMID: 0001967441]
4.The Standards of Reporting Trials Group. A proposal for structured reporting of randomized controlled trials. The Standards of Reporting Trials Group. JAMA. 1994;272:1926-31. [PMID: 0007990245]
5.Working Group on Recommendations for Reporting of Clinical Trials in the Biomedical Literature. Call for comments on a proposal to improve reporting of clinical trials in the biomedical literature. Working Group on Recommendations for Reporting of Clinical Trials in the Biomedical Literature. Ann Intern Med. 1994;121:894-5. [PMID: 0007978706]
6.Begg C, Cho M, Eastwood S, et al. Improving the quality of reporting of randomized controlled trials. The CONSORT statement. JAMA. 1996;276:637-9. [PMID: 0008773637]

# Reading Suggestions

WORLD HEALTH ORG.
NONCOMMUNICABLE DISEASES
Country Profile 2011.

ISBN 9789241502283.
Available at http://www.who.int/nmh/publications/ncd_profiles_report.pdf

INTERNATIONAL PERSPECTIVES: COMMUNICATING THE NONCOMMUNICABLE.
Journal of Health Communication 2011; 16 Suppl 2.

Available at http://www.tandfonline.com/toc/uhcm20/16/sup2

# Recommended Events

2011 AMERICAN HEART ASSOCIATION CONFERENCE
ORLANDO CONVENTION CENTER

Nov. 12-16 2011
Orlando, FL, USA
www.heart.org

2011 ADVANCING ETHICAL RESEARCH CONFERENCE

Dec. 1-4 2011
National Harbor, MD, USA
www.primr.org

HOW TO BECOME A CARDIOVASCULAR RESEARCHER

Dec. 2-3 2011
Washington DC, USA
www.cardiosource.org

# Author's Guidelines

Manuscripts presented for publication on this journal must adjust to
the ethical considerations and technical criteria established on the "Uniform Requirements
for Manuscripts submitted to Biomedical Journals",
developed by the International Committee of Medical Journal Editors.

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Next, essential elements that must be included in the articles:

**Title Page:**

• **T**itle: Must include all the necessary information for its electronic retrieval. There should not be any abbreviations.

• Authors: Name and last names of author or authors and institutional affiliation(s).
Name of department(s) or institution(s) where the work was carried out.
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• Correspondence: Name and mailing address, telephone and fax numbers of the author to whom any correspondence should be addressed.
Sources of support: list of contributors, in the form of grants, equipment, drugs, or others.

• Short title: maximum 40 characters (including letters and spaces), on the footer of this section.

• Number of: pages, figures and tables (if any).

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Consists of a declaration of all potential conflicts of interest that the authors could have. To make this declaration, the form located at the following address may be used: http://www.icmje.org/coi_disclosure.pdf.

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• Abstract: This section must provide the context for the study and must include the study's purpose, basic procedure(s), findings, conclusions and sources of support. No abbreviations, references or footnotes may be used.

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• Methods: Clearly describe the design of the study, methods of selection of participants (if any), apparatus, laboratory analysis, procedures and statistical analysis used.

• Results: Results should be presented in a logical sequence in the text. It may contain tables and illustrations. The data represented in tables or illustrations may not be repeated in the text; tables and illustrations should be numbered consecutively with Arabic numerals, each one presented individually by means of a centered title, and any explanation note at the bottom. Figures and images must be of a professional quality. X ray films, pathologies or scans must be accompanied by their respective units or marks.

• Discussion: Emphasize the new and important aspects contributed by the study and the conclusions that follow from the available evidence. Do not repeat the same information in different sections.

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