José Ruben de Alcântara Bonfim

CHRONIC DISEASES, "MEDICALIZATION" AND IATROGENIC

Health physician and PhD in Science.

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 T^{o} address the inter-relationship of these health practice issues, particularly the medical practice, it is appropriate to explain, even briefly, some basic concepts related to these aspects.

CHRONIC DISEASES

It is assumed that chronic diseases refer to those non-communicable (NCDs) – cardiovascular diseases, diabetes, cancer and chronic obstructive pulmonary disease, among others –, which today constitute the largest demand for health services around the world. According to a recent report released by the Pan American Health Organization, with versions in English, Spanish and Portuguese (OPAS, 2015), only half of patients diagnosed and about half of these are treated; these 25% receiving assistance, only about half reach desired goals of medical treatment. I.e., only one in ten people with chronic diseases is treated successfully (Hart, 1992¹ apud OPAS, 2015). As to the appropriate assistance required, one should take into account that

> The integrated management of NCDs is justified for at least three important reasons. Firstly, most people have more than one risk factor and / or NCD (e.g., hypertension and obesity or hypertension and diabetes and / or asthma) [Tinetti;

¹ Hart, JT. **Rule of halves: implications of increasing diagnosis and reducing dropout for future workload and prescribing costs in primary care.** British Journal of General Practice, v. 42, n. 356, p. 116-119, 1992. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1371996/ pdf/brjgenprac00058-0030.pdf.

Fried; Boyd, 2012]. Therefore, it is appropriate to treat these conditions² within an integrated care structure. Another reason why integrated care is justified is that most NCDs impose similar demands on workers and health systems, and similar ways of organizing care and management of these conditions have similar effectiveness, whatever the etiology. Thirdly, most NCDs has primary and secondary risk factors in common. For example, obesity is a major risk factor for diabetes, hypertension, heart disease and some cancers, and heart disease may be a long-term complication of more than one chronic condition, such as diabetes and hypertension (OPAS, 2015, p. 16).

According to Lotufo (2015, p. 51),

However, in Brazil, we will have to include other leading causes of death in men: cirrhosis and liver disease. [...] It is necessary to understand the dimension of this in mortality in Brazil. They represented, in 2012, 62% of deaths from all causes, but excluding external causes (homicide and car accidents, mostly), the proportion reaches 78% of all deaths.

When presenting the 15 leading causes for men and women, between 30 and 69 years, in 2012, the author comments

The excess mortality among men is 38% by liver disease (258%), cardiovascular disease (60%) and chronic obstructive pulmonary disease (34%). Deaths due to cancer and diabetes affect both sexes. Preliminary analysis of the 15 leading causes in both men and women indicates underlying determinants,

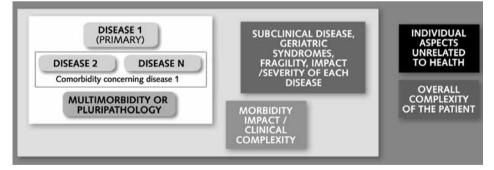
² Condition translates better by state, position or situation, but also disease, illness, affection. For example, the heart condition is a cardiac disease; the skin condition is a skin disease according to Santos (1981, 2007). Navarro (2000) also comments: Condition - Avoid uncritical translation for 'condition', because in medical texts it can have two common meanings: 1. Its most common meaning is not a condition, but disease, process, pain, affection, clinical picture or disorder; [...] 2. State, situation (of a patient or a disease).

such as atherosclerosis and dyslipidemia (coronary heart disease and cerebral infarction), hypertension (intracerebral hemorrhage and cardiomyopathies), obesity (diabetes) and smoking (upper aerodigestive cancer, lung cancer, chronic obstructive pulmonary disease and coronary heart disease). Another very important factor is high prevalence, with high individual consumption of alcoholic beverages: cirrhosis and upper aerodigestive cancers. Add to the impact of the overuse of alcohol other causes of deaths, such as homicides and accidents in general (Ibid, p. 51).

The integrated treatment of chronic degenerative diseases is the greatest challenge of clinical services management, necessarily made interprofessionally, but usually in Brazil prevails the work of the doctor by prescription drug.

PAHO considerations are based on approaches to multimorbidity, as shown in Figure 1 by Martínez Velilla (2013, p. 8).

Figura 1. Multimorbidity definitions



Sometimes the primary disease is linked to relevant comorbidities similar to that considered the main disease, settling to a interinfluente relationship, as shown in Figure 2.

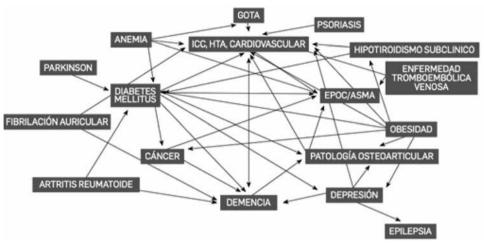


Figure 2. Disease interactions according to recent medical literature (2012)

Notes: EPOC – Chronic obstructive pulmonary disease (COPD); HTA – Arterial hypertension; ICC – Congestive heart failure.

Figure 2 shows that, the older one gets, the more difficult to have a specific condition, since the interaction of diseases which are listed as if they were separate entities in ICD-10 is intense. It is clear, for example, that obesity has relations with subclinical hypothyroidism, osteoarticular disease, depression, congestive heart failure, arterial hypertension, other cardiovascular problems, diabetes mellitus and cancer. These diseases, in turn, also have connections with other diseases, confirming medicine's point of view prior to the current technological stage, that there are no diseases but sick people, and they are not just biological organisms suffering, but social beings who suffer (Bonfim, 2015).

"MEDICALIZATION"

The term "medicalization" is a neologism not yet incorporated in Houaiss Dictionary of the Portuguese Language (Houaiss; Villar, 2001) and has several meanings in the specialized literature, depending on the emphasis of sociological, biological or biopsychosocial approach. For a comprehensive discussion purposes, you can consider the phenomenon according to Orueta Sanchez (2011, p. 151) as "conversion into morbid processes of situations that are and have always been completely normal and that are intended to be solved by the medicine, situations that are not medical but social, professional or of interpersonal relationships".

The authors exemplify (Ibid., p. 52):

- The medical control of certain stages of life (youth, menopause, aging process) is considered necessary;
- Personal/social problems are now understood as medical problems (sadness, grief, post-vacation syndrome, etc.);
- Risk factors are now considered authentic diseases (osteoporosis, hyperlipidemia, etc.);
- Situations or uncommon clinical pictures start to be understood, in an artificial way, as frequent (erectile dysfunction, female sexual dysfunction, etc.);
- Symptoms or mild clinical pictures are seen, in an artificial way, as severe cases (irritable bowel, pre-menstrual syndrome, etc.).

However, one cannot help but reflect on the contribution of Foucault scholars such as Rose³ (2006, p. 9 apud Maturo, 2012, p. 123), which points out that the molecular manipulation is the main feature of our society:

> The "style of thought" of contemporary biomedicine considers life at the molecular level as a group of intelligible vital mechanisms which can be identified, isolated, manipulated, mobilized and recombined in intervention practices which are not constrained by the apparent normativity of a natural vital order.

So, Maturo (2012) states that we live in a society that becomes increasingly *bionics* (expression used by the author), i.e., biology and

³ Rose, N. The Politics of Life. Princeton: Princeton University Press, 2006.

genetics are seen as the main forces that affect human life, with social factors playing a less important role.

He then defines "medicalization" as a process by which some aspects of human life are now considered as medical problems, whereas before they were not considered pathological. The author also believes that Illich (1981), in 1973, made an accurate analysis of the iatrogenesis of many diseases, naming social iatrogenesis the proliferation of diseases caused by the extension of medical categories in everyday life.

Mature (2012) presented a scheme, which can be useful to understand the forces that drive "medicalization". The term "consumerism" refers to consumers who make increasing use of medical terminology in order to analyze their own health because they are influenced by warnings on television and internet searches, and advertisements encourage people to take into account certain needs of health that otherwise they would not consider.

The author also stresses that the use of pharmaceuticals and "medicalization" are not the same. He mentions Abraham (2010, p. 290), which defines "pharmaceuticalization" as "the process by which social, behavioral, or bodily conditions are treated, or deemed to be in need of treatment/ intervention, with pharmaceuticals by doctors, patients or both". The main examples include mood treatment with anxiolytics or antidepressants, treatment of attention deficit hyperactivity disorder (ADHD) with methylphenidate (e.g., Ritalin) and treatment of erectile dysfunction with sildenafil (e.g., Viagra). He adds: "even the treatment of heart-disease risk factors with cholesterol-lowering drugs, such as statins, may be considered an example of pharmaceuticalization" (Maturo, 2012, 125 p.). He notes, accurately, "that all the mentioned diseases could be treated by non-pharmaceutical means, as they were in the past: treatments would be medical, like psychotherapy, or non-medical, such as a change in way of life" (Ibid., p. 125).

Another aspect of great importance in Maturo's scheme (2012), which is supported by Abraham (2010), refers to "deregulation" of government agencies, that in the USA requires, for example, that producers demonstrate the quality, security and eficacidade of their products (but not its therapeutic advance) in order to get a new drug approved by regulatory agencies. He quotes Light (2010, p. 7): "When pharmaceutical companies say a drug is 'effective' or 'more effective', they usually mean more effective than a placebo, not more effective than existing drugs".

The following shows the flowchart of Maturo's article (2012), since it illustrates issues about the concepts of "medicalization", "pharmaceuticalization" and what he calls the bionic society, referred previously.

"Medicalization" machines	
Medical dominance	Biotechnology, "consumerism", care management, pharmaceutical marketing
$\hat{\Gamma}$	
"Pharmaceuticalization"	
Examples: antidepressants, meth- ylphenidate, sildenafil (statins, "stomach protectors" etc.)	Main forces: political economy of pharmaceutical corporations, deregulation of state agencies,"consum- erism", DSM (Diagnostic and Statistical Manual of Mental Disorders)
$\hat{\Gamma}$	
Bionic Society	
$\hat{\Gamma}$	
Problems in bionic society	
Prevention as an individual re- sponsibility, placing aside the social determinants of health	Social problems considered as individual problems, reducing the importance of social policy
$\hat{\Gamma}$	
"Pharmaceuticalization"	

Source: Adapted from Maturo (2012).

IATROGENIC

It is not simple to define iatrogenic and iatrogenic disease. According to Pacheco e Silva (1970), quoting Littré⁴, *iatron* would be the place where ancient doctors kept their instruments and apparatus, performed

⁴ Émile Littré (1801-1881) was the French lexicologist who translated the Hippocratic treaties.

operations, treated wounds, fractures or strains and attended patients. One of Hippocrates' books is entitled *On the workshop of a doctor or iatron;* hence came the expression iatrogenic disease to designate a disease caused by the doctor. Pacheco e Silva (1970, p. I) considers a broader meaning:

Iatrogenic diseases should be only those diseases caused by the doctor when, in conversation with the patient, far from clearing it up, calming him down, comforting him, he inadvertently casts doubt on his mind, arousing fears, phobias, obsessive ideas, distress or neurosis. Instead, for others, this same expression would serve to characterize any disease or morbid state, both in physical and psychic sphere, due to the intervention of the doctor and his assistants, whether it is right or wrong, justified or not, but which results in consequences detrimental to the health of the patient.

Lacaz (1970, p. 4) extends the concept when he says that:

Several factors have interference with the increased incidence of so-called "iatrogenic disease" or "iatropharmacogenetic diseases". Such causes may be remembered as:

1 - Rapid development of the pharmaceutical industry;

2 – Intensive advertising, supported by high economic power industry;

3 – Abusive use of drugs by the people;

4 – Large development of surgery, creating new syndromes;

5 – Lack of preparation of doctos in medical psychology knowledge.

Still Lacaz (Ibid.), as a pioneer in our surroundings and even internationally, points out, undeniably, the influence of pharmaceutical advertising done by the industry, basic cause of iatropharmacogenetic and, by extension, of iatrogenic – decades later it would be known as adverse effects of drugs, currently an important cause of mortality in countries with a record of adverse reactions. In the USA, for example, adverse reactions already constitute the fourth main cause of mortality. Intensive advertising done by the laboratories, especially among young Asclepius, as well as by the press and radio, is another important reason for the casuistry of iatrogenic diseases to be always on the rise. They usually announce triumphs and the "miracles", but not the hazards, the harmful or side effects of drugs. The biggest victim of all this is the public. We should keep a good criterion in reading publications from laboratories (Ibid., p. 4-5).

Finally, Lacaz (1970) epitomizes the concept of iatrogenic diseases, with emphasis on the perspective of the medical action, the nature of the drug and its characteristics of dispensing. Moreover, he even foreshadows what would be known later as risk-benefit ratio:

Iatrogenic diseases (or "man-made pathologic processes", "therapy induced diseases", "drug induced diseases", "disease caused by drugs") depend on the drug and its nature, the patient, the dose and the duration of treatment, the route of use of the product and the speed of the application. We must insist that *all therapy brings a calculated risk* (emphasis added) (Ibid., p. 6).

In the classic work of Avorn and Soumerai (1983) are proposed education strategies to oppose the induction made by the pharmaceutical industry as to the prescription: they recommended the visit of academic "representatives" to improve the quality of decisions on drug therapy and reduce unnecessary expenses. The same author, Avorn (2003), in criticizing those who think that pharmaceutical advertising has beneficial effects for consumers (in the US is allowed to advertise drugs that require prescriptions, unlike Brazil and most countries), suggests that a greater presence of non-commercial communication, oriented to public health, could produce more useful and cost-effective impact on the health of patients.

Wazana (2000) confirmed the influence of the pharmaceutical industry on prescribers, determining their behavior according to her interest, and Angell's (2004) analyzes extended to the entire spectrum of medical activity the understanding that the pharmaceutical industry produces more harm to patients than previously thought.

The great alarm of the need for reorientation regarding the control of the pharmaceutical industry came with the market withdrawal in September 2004 of rofecoxib (Vioxx®, by Merck Sharp & Dohme, in Brazil), an anti-inflammatory non-steroidal. From that moment, it was clear that something new could emerge in pharmaceutical regulation. That because, according to Drug Watch (2014)

In 2004, Merck withdrew the drug from the market after a study revealed the drug more than doubled the risk of heart attacks and death. By that point, more than 38,000 deaths were related to Vioxx use, and up to 25 million Americans had taken the drug. [...]Vioxx caused so much damage and destruction that some have called it the worst drug disaster in history. The Vioxx scandal wasn't just devastating to the injured patients and their families; it also underscored problems within the FDA. Many suspect that the New Jersey-based Merck and the FDA worked together to keep the drug on the market and quiet the health concerns [online].

The article by López Rodríguez (2015), *Vioxx: Ambition model*, deserves careful examination:

September 30, 2004, Rofecoxib is withdrawn from the market. Better known by its trade name: Vioxx. After being used massively worldwide by over 80 million people, its serious side effects forced it. By its quantity and importance **it is the most severe "poisoning" of the history of humanity and the most important recall of a drug worldwide**. Vioxx case is the paradigm of greed. A harm that afflicts our economic system and particularly, in a severe form, our industrial pharmaceutical system. Our pharmaceutical industry is seriously ill of ambition. Its main objective is no longer improve the health of the population, but the economic benefit. We will see how Merck Sharp & Dohme did not hesitate to manipulate scientific research, falsifying data, hiding and hindering accurate information and manipulating medical professionals. All for the sake of profit [online].

This preamble is preceded by the question: Could there be other cases such as Vioxx or Avandia®⁵?

The article analysis what happened before and after the withdrawal of rofecoxib – and ends with the following reflection:

I want to conclude this on VIOXX with the words of renowned pharmacologist: Joan-Ramon Laporte, director of the Catalan *Institute of Pharmacology Foundation*, who explains to "elmundo. es": 'I do not know of a drug that in such a short time has caused so much pain. Someone asked me if I did not believe that thalidomide had produced more victims, in the early sixties. There were 5,000 cases of birth defects attributed to thalidomide worldwide. Perhaps hormone replacement therapy has led to a number of casualties (fatal and nonfatal) roughly comparable to Vioxx. However, I do not recall that we have never spoken of so many victims of the same drug, in terms of serious and fatal effects. In the case of Vioxx it has become clear that Merck [the manufacturer] knew the cardiovascular risk since 2000, and yet they continued to sell it. In conclusion, a reflection made in the publication of the Catalan Institute of Pharmacology Foundation, and that we will all share: 'After rofecoxib produced hundreds of deaths and serious events in Spain, there appears to be no one responsible. The Ministry announced it opened a claim, but a few days later said it was purely informative. No one asked MSD at least to return the money to the health system, because the supposed advantages of Vioxx were not correct (Moynihan, 2005). No one claims to the competent authority or the Ministry, which had the obligation to

⁵ Rosiglitazone, GlaxoSmithKline. Antidiabetic banned in Europe because of cardiovascular risks; in the US sale is restricted, but in Brazil, its registration was canceled on September 29, 2010.

defend the health of citizens. Other pharmaceutical policy, to defend the citizens of the distortions disseminated with commercial purposes, is needed" (Butlletí Groc, 2005).

Nothing about the subject is known in Brazil.

The bottom line is that many drug regulatory authorities give priority to the process of approval and not to patient safety (Lexchin, 2015). The author exemplified that the FDA wanted to add an alert in the rofecoxib label about the cardiovascular risks after the VIGOR study (Vioxx GI Outcomes Research), but there were objections from the pharmaceutical industry; the outcome of negotiations exceeded one year and finally led to a change: instead of being inserted in the section "alert", it ended in the less prominent section, "precautions", which they said to be of unknown clinical significance. Lexchin (2015) concluded that the first step to decrease the number of people who die as a result of drugs is to understand that questions should be focused and involve the best resources in post-registration surveillance system, giving the safety level of drugs the same importance as to their approval and increasing the transparency of information from both pharmaceutical companies and the pharmaceutical regulatory authorities.

This is in line with the conclusions of Onakpoya, Heneghan and Aronson (2015), who found 95 drugs withdrawn from the market between 1950 and 2013 to cause death. All were taken in at least one country, but at least 16 remained on sale in some countries. Withdrawals were more common in European countries; few were registered in Africa (5.3%). The closer the release date the sooner deaths have been reported. However, in 47% of cases, more than two years elapsed between the first notification of death and the withdrawal of the drug, and this gap has not improved in the last 60 years.

In Brazil, nothing is known about this serious public health problem, not only because the reports of severe adverse reactions are extremely inadequate, but also because reports of death attributable to drugs are rare.

FINAL CONSIDERATIONS

Any educational intervention with prescribers in the Brazilian Public Health System, or elsewhere, requires careful attention to identify the phenomenon of over-diagnosis and subsequent over-treatment, especially pharmacological underlying the interrelationship of chronic diseases, "medicalization" and iatrogenic.

Moreover, it is essential that prescribers, dispensers and everyone that deals indirectly with drugs understand the concept of quaternary prevention.

Excessive diagnosis and treatment

Welch, Schwartz and Woloshin (2011, p. xiv), in a simple, but accurate way, say that overdiagnosis is not only an excessive diagnosis, but also "occurs when people are diagnosed with diseases that never cause symptoms or death." They explain:

Early diagnosis is the goal. People seek care when they are well. Doctors try to identify disease earlier. More people have early than late disease detection, so there is more diagnosis – including those who have no symptoms. Some of these people are destined to develop symptoms. Others not – they are diagnosed by excess (Ibid., p. xv).

They continue:

So the problem of excessive diagnosis originates directly from the expansion of the set of persons diagnosed: from individuals with disease (those with symptoms) to individuals with abnormalities (those without symptoms). The problem is aggravated further according to the definition of what constitutes an abnormality that is, increasingly, broad (Ibid., p. xv). And conclude:

Since doctors do not know who is diagnosed excessively and who is not, patients with excessive diagnosis tend to be treated. However, a patient diagnosed by excess does not benefit from treatment [...] he can only have damages. It is a simple fact that almost all treatments have the power to cause some damage (Ibid., p. xv).

It is a kind of early diagnosis without the possibility of real development of the disease. If it evolve, it is often bypassed by non-pharmacological interventions (nutrition, adequate physical activity, change in lifestyle, preventive attitudes towards the occupation risks, etc.). Finally, a series of steps which, when taken, prevent pharmacological intervention. If necessary, it certainly will be done with more safety for the patient, in case it really is, for manifesting a disease identified by strict criteria.

Quaternary prevention

Before considering the known definitions of prevention, which is based on the sequence of the supposed natural course of the disease (according to the model of Leavell and Clark expanded), i.e., primordial, primary, secondary, tertiary and quaternary prevention, Segura (2014, p. 181) warns:

> Interventionism is particularly acute in the area of prevention, especially clinic, but also in public health. This has led to a considerable distortion of the concept of prevention [Starfield; Hyde; Gervas, 2008] and the need to approach it from the perspective of prudence, since preventive measures are not exempt of side effects and also because although «they can bring great benefits for the community, they offer little to each individual participant», as Geoffrey Rose explained when describing the so-called "prevention paradox" [Rose, 1981]. Caution and prudence that refer to the more traditional ethical

and professional considerations, among which stands out the well-known *Primum non noccere* [Herranz, 2002], inspiration for one of the four basic principles of bioethics, the avoidance of harm, which is not limited to do no harm but also requires learning what is harmful and considering that to try it can expose people, object of our inquiry, to the risk of suffering it [The Belmont Report, 1979].

So it does not incur in the possible intervention problems in the field of prevention, quaternary prevention, formulated to reduce iatrogenic problems, should follow its peculiar object, as suggested by Martínez González et al. (2014, p. 396. e2):

according to Marc Jamoulle, Belgian doctor creator of the concept, is «to identify patients or groups under the risk of overmedicalization to protect them from invasive medical procedures and offer instead procedures or care ethically acceptable» [Nève; Bernstein; Terra, 2013]. Developing quaternary prevention is a specific and urgent need for the developed societies, in which coexist tremendous paradoxes: an excellent but progressively unsustainable public medicine, with unjustified medicalization; a population increasingly dependent on the health system, despite having better health indicators than ever; patients with unlimited health claims promoted by our own medicine, which arrogantly [Sackett, 2002] has generated in the public the idea that everything is preventable and curable; and a medicine that offers preventive programs and evidences of all kinds not always supported by scientific evidence nor valued by health professionals themselves.

The education of the prescribing physician, besides being continued in the matters relating to the risks of a prescription, has to be conservative in the sense indicated by Bonfim (2015, p. 27): The conservative prescription was known by other names equally valid as healthy skepticism (on drugs prescription), or cautious prescription, more prudent, rational. This is nothing more than an improvement that doctors and clinical pharmacologists, for decades – without any other intention but the search for rationality in therapeutic act – have recommended, everywhere, to generations of prescribers.

In addition, the ultimate purpose of the therapeutic act is to guarantee the decision making by those who are being taken care of, because (Ibid., p. 61)

> It seems that in our country doctors do not yet fully understand that the administration of health services is an integral part of the complete process of prescription, and often the prescriber does not consider other side, which is the need for a patient to be instructed by the doctor and the health team to acquire the capacity to decide.

Prescribers that are aware, or sometimes by intuition, often follow the suggestions of Gale (2009, p. 1980) to avoid committing the seven deadly sins of drugs prescription, very usual in the treatment of chronic diseases:

1. Use of pharmaceutical products to treat a non-pharmaceutical problem;

2. Assume that new drugs are better;

3. Repeat prescriptions that do not have rational purpose

4. Use a drug to counteract the adverse events produced by another;

5. Overestimate the benefits of the intervention;

6. Seek the dream of longevity beyond the domains of common sense;

7. Reduce the quality of the life you are trying to improve.

None of us is innocent of these sins, and the safety of drugs should be less of an issue if it was true.

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References

Abraham, J. The Sociological Concomitants of the Pharmaceutical Industry and Medications. In: BIRD, C. et al. (Eds.). **Handbook of Medical Sociology**. Nash-ville: Vanderbilt University Press, 2010. p. 290-308.

Angell, M. Investigaciones. La verdad sobre las compañías farmacéuticas. Boletín Fármacos, v. 7, n. 5, p. 49-56, nov. 2004. Available at: http://www.saludy-farmacos.org/wp-content/files//nov04.pdf. Access on: 10 jun. 2015.

Avorn, J. **Advertising and prescription drugs: promotion, education, and the public's health.** Health Affairs, Millwood, supl. web exclusives: W3-104-8, janjun. 2003. Available at: http://content.healthaffairs.org/content/early/2003/02/26/ hlthaff.w3.104.long. Access on: 10 jun. 2015.

Avorn, J, Soumerai, SB. **Improving drug-therapy decisions through educational outreach. A randomized controlled trial of academically based "detailing"**. The New England Journal of Medicine, v. 308, n. 24, p. 1457-1463, jun. 1983.

Bonfim, JRA. Análise da prescrição de fármacos não constantes da Relação Municipal de Medicamentos Essenciais do município de São Paulo, 2008-2013. 2015. Tese (Doutorado em Saúde Pública) – Faculdade de Saúde Pública, da Universidade de São Paulo, São Paulo, 2015. 763p.

Butlletí Groc. La decepción de los coxibs. Butlletí Groc, v. 18, n. 1, p. 3, jan-fev. 2005. Available at: https://ddd.uab.cat/pub/butgroc/butgrocSPA/butgroc_a2005m1-2v18n1iSPA.pdf. Access on: 10 jun. 2015.

Drug Watch. **Vioxx Recall Information**. Maio 2014. Available at: http://www. drugwatch.com/vioxx/recall/. Access on: 10 jun. 2015.

Gale, EA. **Collateral damage: the conundrum of drug safety.** Diabetologia, v. 52, n. 10, p. 1975-1982, out. 2009. Available at: http://www.ncbi.nlm.nih.gov/pub

med/?term=collateral+damage+the+conundrum+of+drug+safety. Access on: 10 jun. 2015.

Herranz, G. **The origins of "Primum non noccere"**. BMJ letter. Set. 2002. Available at: http://www.bmj.com/rapid-response/2011/10/29/origin-primum-non-nocere. Access on: 10 jun. 2015.

Houaiss, A, Villar, MS. **Dicionário Houaiss da Língua Portuguesa**. Rio de Janeiro: Objetiva, 2001.

Illich, I. **A Expropriação da Saúde: Nêmesis da Medicina.** Tradução de José Kosinski de Cavalcanti. 4. ed. Rio de Janeiro: Nova Fronteira, 1981.

Lacaz, CS. Doenças iatrogênicas. Conceito. Classificação. Importância do seu estudo. In: Lacaz, CS, Corbett, CE, Teixeira, PA. **Doenças Iatrogênicas**. 2. ed. rev. e amp. São Paulo: Sarvier, 1970. p. 3-14.

Lexchin, J. **Why are there deadly drugs?** BMC Medicine, v. 13, fev. 2015. doi: 10.1186/s12916-015-0270-2. Available at: http://www.biomedcentral.com/content/pdf/s12916-015-0270-2.pdf. Access on: 10 jun. 2015

Light, DW. Bearing the Risks of Prescription Drugs. In: LIGHT, D. W. (Ed.). **The Risks of Prescriptions Drugs**. New York: Columbia University Press, 2010. p. 40-69.

Lopéz Rodríguez, L. **VIOXX: paradigma de la codicia.** NoGracias, 27 april 2015. Available at: http://www.nogracias.eu/2015/04/27/vioxx-paradigma-de-la-codicia/. Access on: 10 jun. 2015.

Lotufo, PA. **Um desafio para 2025: reduzir a mortalidade precoce por doenças crônicas em todo o mundo.** Diagnóstico & Tratamento, v. 20, n. 2, p. 51-52, 2015. Available at: http://www.apm.org.br/publicacoes/rdt_online/RDT_v20n2. pdf. Access on: 10 jun. 2015.

Martínez González, C et al. **Prevención cuaternaria. La contención como imperativo ético.** Anales de Pediatría, Barcelona, v. 81, n. 6, p. 396.e1-396.e8, 2014. Available at: http://www.analesdepediatria.org/es/prevencion-cuaternaria-lacontencion-como/articulo/S1695403314002835/. Access on: 10 jun. 2015.

Martínez Velilla, N. **El desafío terapéutico de la multimorbilidad.** Boletín de Información Farmacoterapéutica de Navarra, v. 21, n. 3, p. 1-12, maio-jul. 2013. Available at: http://www.navarra.es/NR/rdonlyres/8E20EDDC-EB73-40DA-B8F4-4CE3F96235D4/264988/Bit_v21n3.pdf. Access on: 8 jun. 2015.

Maturo, A. **Medicalization: Current Concept and Future Directions in a Bionic Society.** Mens Sana Monograph, v. 10, p. 122-133, 2012. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3353591/?report=reader. Access on: 10 jun. 2015.

Navarro, F. **Diccionario crítico de dudas: inglés-español de medicina.** Madrid: McGraw Hill/Interamericana, 2000. p. 105.

Nève, J, Bernstein, J, Terra, MA. **Prevención cuaternaria, uma tarea explícita del médico generalista. Una entrevista com Marc Jamoulle.** Archivos de Medicina Familiar y General, v. 10, p.23-26, 2013. Available at: http://archivos.famfyg.org/revista/index.php/amfyg/article/viewFile/130/116. Access on: 10 jun. 2015.

Onakpoya, IJ, Heneghan, CJ, Aronson, JK. **Delays in the post-marketing withdrawal of drugs to which deaths have been attributed: a systematic investigation and analysis.** BMC Medicine, v. 13, p. 26, 2015. Available at: http://www. biomedcentral.com/content/pdf/s12916-014-0262-7.pdf. Access on: 10 jun. 2015.

OPAS. **Cuidados inovadores para condições crônicas: organização e prestação de atenção de alta qualidade às doenças crônicas não transmissíveis nas Américas.** Washington, D. C.: Opas, 2015. Available at: http://www.paho.org/hq/ index.php?option=com_docman&task=doc_view&gid=29753+&Itemid=999999 &lang=es. Access on: 10 jun. 2015.

Orueta Sánchez, R et al. **Medicalización de la vida (I).** Revista Clínica Médica Familiar, v. 4, n. 2, p. 150-161, 2011. Available at: http://scielo.isciii.es/pdf/albacete/v4n2/especial6.pdf. Access on: 9 jun. 2015.

Pacheco e Silva, AC. Prefácio. In: Lacaz, CS, Corbett, CE, Teixeira, PA. **Doenças** Iatrogênicas. 2. ed. rev. e amp. São Paulo: Sarvier, 1970. p. I.

Santos, AS dos. **Guia prático de tradução inglesa: comparação semântica e estilística entre os cognatos de sentido diferente em inglês e português.** 2. ed. rev. E amp. São Paulo: Cultrix, EDUSP, 1981. p. 93.

Santos, AS dos. **Guia prático de tradução inglesa: como evitar as armadilhas das falsas semelhanças.** ed. rev. amp. e atualiz. Rio de Janeiro: Campus/Elsevier, 2007.

The Belmont Report. **The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research**. Ethical Principles and Guidelines for the Protection of Human Subjects of Research. The Belmont Report. Washington, D. C.: US Department of Health and Human Services, 1979. Available at: http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html. Access on: 10 jun. 2015.

Tinetti, ME, Fried, TR, Boyd, CM. **Designing health care for the most common chronic condition–multimorbidity.** The Journal of the American Medical Association, v. 307, n. 23, p. 2493-2494, 2012. Available at: http://www.commed.vcu. edu/IntroPH/Chronic%20Diseases/JAMAMultimorb.pdf. Access on: 10 jun. 2015.

Rose, G. **Strategy of prevention: lessons from cardiovascular disease.** BMJ, v. 282, p. 1847-1851, 1981. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1506445/pdf/bmjcred00661-0031.pdf. Access on: 10 jun. 2015.

Segura, A. **Prevención, iatrogenia y salud pública.** Gaceta Sanitaria, v. 28, n. 3, p. 181-182, 2014. Available at: http://gacetasanitaria.org/es/prevencion-iatroge-nia-salud-publica/articulo/S0213911114000429/. Access on: 10 jun. 2015.

Sackett, DL. **The arrogance of preventive medicine.** Canadian Medical Association Journal, v. 167, p. 363-64, 2002. Available at: http://www.cmaj.ca/content/167/4/363.full.pdf+html. Access on: 10 jun. 2015.

Starfield, B, Hyde, J, Gervas, J. Health. **The concept of prevention: a good idea gone astray?** Journal of Epidemiology & Community Health, v. 62, p. 580-583, 2008. Available at: http://jech.bmj.com/content/62/7/580.full.pdf+html. Access on: 10 jun. 2015.

Wazana, A. **Physicians and the pharmaceutical industry: is a gift ever just a gift?** The Journal of the American Medical Association, v. 283, n. 3, p. 373-380, jan. 2000. Available at: http://jama.jamanetwork.com/article.aspx?articleid=192314. Access on: 10 jun. 2015.

Welch, HG, Schwartz, LM, Woloshin, S. **Overdiagnosed. Making people sick in the pursuit of health.** Boston: Beacon Press, 2011.