Chapter 7
How to Prescribe Information: Health Education Without Health Anxiety and Nocebo Effects

Farzad Goli, Alireza Monajemi, Gholam Hossein Ahmadzadeh, and Azadeh Malekian

> *Human being is more ill, less certain, more changeable, more insecure than any other animal- there's no doubt about that He is the sick animal. Where does it come from? (Nietzsche, genealogy of morals, p. 100)*

Imagine you live in a super intelligent city, in which detectors alert you via audible alarms when you approach potentially harmful stimuli, air or electromagnetic pollutants, allergens, mutagen foods, etc. You can perhaps imagine that every day would be filled with warnings and an undoubtedly large amount of beeps and rings. I think you agree with me that after a while, the alarms could be seriously harmful by themselves, not only because of the constant bombardment of information and sound pollution, but also by making you worried, preoccupied, or irritable. In addition, you may begin to adapt to the situation by adopting avoidant, pessimistic, or suspicious attitudes; or you might find yourself overwhelmed, depressed, and anxious. The overflow of warning signs turns to dangerous stimuli and overwhelming noises. We have a rather limited capacity for information processing, not to mention the possibility that signs may become distorted, misinterpreted, ignored, and/or simply perceived as ordinary noises. This is a transcendental dialectic in which the

F. Goli (✉)
Head of Danesh-e Tandorosti Institute, Isfahan, Iran

Energy Medicine University, Mill Valley, CA, USA
e-mail: Dr.fgoli@yahoo.com

A. Monajemi
Institute for Humanities and Cultural Studies (IHCS), Tehran, Iran

G.H. Ahmadzadeh
Behavioral Science Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

A. Malekian
Psychosomatic Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

F. Goli (ed.), *Biosemiotic Medicine*, Studies in Neuroscience, Consciousness and Spirituality 5, DOI 10.1007/978-3-319-35092-9_7

quality (amount, speed) of signs can induce qualitative changes in our mood, affect, attitudes, and form of life.

Now, the question is what this analogy tends to tell us. Do you find any similarities between this imaginary city and our real-life cities? Have you ever inhaled the air and had the feeling it might cause cancer? Or have you eaten fresh fruit as if it were an antioxidant or anticancer agent? It seems that the warnings are already ringing everywhere for everyone, and that a large number of warning messages comes explicitly or implicitly from the television, newspaper, and even the refrigerator! Our boundaries are surrounded by a vast variety of dangers and the tragedy is that even within these boundaries, there are still a huge number of symbolic dangers – for example, dysfunctional beliefs and traumatic memories – as well as physical ones – for example, metaplastic genes, latent disorders, and aneurysms. How can we stand to live in such conditions?

The answer is very simple: by "neglecting," As Rumi said, "negligence is the column of our world". The idea sounds deceitful and contrary to the prophecy of illumination and modern episteme. Moreover, it seems to stand in opposition to the human's will of knowledge!

According to Nietzsche, we need an informational hygiene system to protect people from information overload and mechanical use of knowledge that mislead us to no-life direction. In the *Gay Science*, he emphasized the evolutionary function of science and the fact that our knowledge must facilitate our adaptation and promote our happiness and vitality. Unlimited semiosis – the flow of signs which has constructed higher levels of organization from the lower orders – can be mentioned as the engine of life and evolution. Yet, it seems that sometimes we need to intentionally inhibit the overwhelming signs in order to help the life-drive. Hence, sometimes we need to reduce perceived significance in order to reduce excessive risk perception and worry. But we can never ignore that we live in the information era and any paternalistic control on information is regarded as censorship and a violation of human rights. Therefore, regarding health, the proper extent to which this is possible for the community education remains a dilemma. In other words, how can we balance our medical interventions in order to achieve higher levels of prevention, lower levels of health anxiety, and nocebo induction seemingly simultaneously?

While we are focused on the literal interpretations of our health education, various thought associations and consequently emotions arise and can change our mood, behavior, and even psychoneuroimunoligic responses into unhealthy ones. In other words, we are trying to figure out how to sufficiently enlighten our community without blinding it by excessive light! In this chapter, we will briefly discuss the complexities of health education and how to formulate the informational interventions on the basis of biosemiotics.

7.1 Risk and Danger

According to German sociologist and prominent thinker in systems theory, Luhmann (1993), "risk" differs from "danger", with danger being attributable to external causes (events) and "risk" referring to our decisions (actions) and a specific form of

dealing with the future that has to be decided in the context of probability. Of course, this distinction is slight because "one person's risk is another person's danger", which points to the key issue of acceptance of risk decisions.

As Ulrich Beck (1992) addressed in his book *Risk Society*, the deadlock of late modernity is that as risks become more complex, because of developing reflexivity, the need for precise calculations increases, leading to growing doubts about the ability of science to control and foresee those risks. Nowadays, our control-seeking attitude has been developed far beyond our ability to control dangers. This imbalance may be due to a raised public demand for health and security as a result of hyperindividualism and hyperextension of harm-avoidant attitudes and behaviors among the public (Throop 2009, pp. 25–40).

The utopia of modern medicine is portrayed as a life without pain and sadness in which people live with optimal social functioning and utopian bodies (Foucault 1994). Believing in medical utopia, paradoxically, convinces us that we are latent/manifest ill beings and our painful life is not the real life. Therefore, releasing life from unpleasant experiences illustrates a grotesque picture of the real life of the human being. In such a worldview, "therapy" is the way toward medical salvation and its consequent terrestrial heaven. Hence, "therapy" could be distinguished as a global morality of the postmodern age. Jürgen Habermas (1987) referred to this normative therapeutic episteme with the term "therapeutocracy", indicating the process which has challenged and intervened in the autonomy of the civil society, with the consequence that it has been turned into a mode of intervention of the human state in addition to the financial outcomes and, more importantly, professional expertise.

Via therapeutocracy, even political and legal problems get reinterpreted in psychopathological and medical terms (psychiatricism and medicalism). At the moment, medicalization, healthism and therapeutocracy are very important terms in sociology and anthropology which implicate how medical norms get transformed into social and oral norms, and how this trend can distort our cognition and emotions, leading us towards maladaptive behaviors.

Any judgment on human nature implicates a sort of qualitative value, for instance, illness is interpreted not only as a hard and unpleasant condition, but also as a "bad" one. In this dualistic world, health is good and illness is bad, happiness is good and unhappiness is bad. Furthermore, the only way to be happy is to independently take the responsibility for yourself and your feelings (Throop 2009, p. 30). Egoism has resulted from, or at least been perpetuated through, the culture of therapy, more specifically of psychotherapy (ibid., p. 29). Because of the darwinistic origins of biomedicine and psychopathology, believing in the "selfishness" of organisms and even genes is the core belief in this model. Obviously, egoism has made extensive and deep impacts on the behavior of social and psychological systems.

We should also mention another factor which increases health anxiety, namely materialistic reductionism. Biomedicine translates the multi-level being of the human to a chemophysical language. This approach has been found very useful in systematizing our knowledge about the body and how to control it; yet it also has psychological implications. Biomedical instruction somehow suggests that "we are

our bodies". Once one accepts such an idea, especially when the body is perceived as if reduced to a chemophysical machine, emergence of obsessive concerns about the body, like those of the ancient Egyptians, would not be surprising. Thus, darwinistic and reductionistic approaches to biomedicine and the individualistic trend of our era could be some of the main predisposing and aggravating factors for the establishment of healthism and its subsequent ever-rising health anxiety.

Now, you can imagine that a hyper-individualized person who deeply believes in healthism, just like the way his ancestors believed in their religion, is afraid of the after life and of course of the judgment of the medicine god. These days we have encountered a sort of mass harsh conscience towards health followed by illness phobias and obsessive avoidance of unhealthy behaviors, just like the epidemics of harsh religious conscience which occurred in Europe during the middle ages as a result of excessive warnings on sin and punishment.

Releasing information resources for general publication is one of the heritages of the massive enlightenment. However, a certain amount of internal and external control over the information flow through the media seems to be seriously needed in order to moderate people's risk perception and health anxiety. We need to formulate a psychologically-hygienic approach to convey health messages and instructions in order to maximize the benefits of positive perceptions (placebo effects) and to minimize the adverse results of negative perceptions (nocebo effect) among the clients (e.g., in cases of giving information about prescribed drugs or producing drug information leaflets). To achieve such an optimal health education and delivery system, we should consider different bio-psycho-social factors which mediate the response of the individuals and societies toward health information. In the next parts, we will explain social and individual aspects of nocebo responses with emphasis on health instructions and warnings.

7.2 The Social Aspects: Medicalization, Healthism, and Life Stylism

Nowadays, talking about our blood cholesterol, blood pressure, prostate-specific antigen, body mass index, etc. has become a part of our everyday lives. These issues have become so integrated, that we forget that they have only recently been medicalized. Medicalization is the process by which medical diagnostics and managements are applied to behaviors, psychological phenomena and somatic experiences not previously within the conceptual or therapeutic scope of medicine (Davis 2010; Long 2011). The concept of medicalization rests on the assumption that while some phenomena belong in the domain of medicine, some do not (Szasz 2007). Therefore, it is very different from natural sciences like physic s or chemistry that cover the entire world and do not demarcate between physical objects and non-physical ones. In other words, demarcation between physical versus non-physical objects through the lens of physics is non-sense. In this sense, everything that we do or happens to

us influences the use of our body. In fact, we could treat everything that people do or that happens to them as belonging in the domain of medicine (Szazs 2007).

Careful examination of the medicalization process shows us that it rests on the basis of healthism. Healthism in extreme versions provides a justification for racism, segregation, and eugenic control, since "healthy" means patriotic and pure, while "unhealthy" equals foreign or polluted. In the weak version of healthism, frequently encountered in Western societies, the state goes beyond education and information on matters of health and uses propaganda and various forms of coercion to establish norms of a "healthy lifestyle" for all (Skrabanek 1994). Therefore, the doctrine of lifestylism, according to which most diseases are caused by unhealthy behavior, provides the required theoretical underpinning of healthism (ibid.). Consequently, human activities are divided into approved and disapproved, healthy and unhealthy, prescribed and proscribed, and responsible and irresponsible categories. Irresponsible behaviors include activities dubbed by moralists as "vices", such as "immoral" sex and the use of drugs – both legal (alcohol, tobacco) and illegal – but it can be extended to not going for regular medical check-ups, eating "unhealthy" food, or not participating in sports.

The term "healthism" was most likely used for the first time by the political economist Robert Crawford whose article, "Healthism and the Medicalization of Everyday Life" was published in 1980 (Crawford 2006). In this article, Crawford described how the new political ideology, which emerged in the US during the 1970s, "[situated] the problem of health and disease at the level of the individual". The term is also known for its use in the book *The Death of Humane Medicine and the Rise of Coercive Healthism* by Petr Skrabanek in 1994. Both authors defined healthism as a powerful ideology because – in secular societies – it fills the vacuum left by religion. The relationship between healthism and religion could be formulated in this way: everything that we do or happens to us affects the use of our body. In principle, we could extend this to belonging in the domain of medicine. Conversely, we could state that nothing that we do or happen to us belongs in the domain of religion. Such, indeed, was the case in ancient times, before people distinguished between faith healing and medical healing (Szazs 2007). Contemporary public health may be regarded as the mirror image of Christian Science.

Everything in our lives – housing, food, education, work, air, and recreation – affects our health. Therefore, everything – not only narrowly defined as health care – belongs in the domain of medicine as health care (Szazs 2007). Drawing a line between health carefulness and health carelessness is informed more by economic and political considerations rather than by medical or scientific judgment. In this sense, we must not only distinguish disease from non-disease, but also distinguish medicalization by compulsion versus by choice (Szazs 2007).

As an artificial religion, it has a wide appeal – especially among the middle classes who have recently lost their links with traditional culture and feel increasingly insecure in a rapidly changing world. Healthism is embraced enthusiastically as a path to surrogate salvation. If death is to be the final full stop, perhaps the inevitable can be indefinitely postponed. Since disease may lead to death, propitiatory rituals must prevent disease itself. The righteous will be saved and the wicked shall

die (Skrabanek 1994). The narcissistic cult of youth, health and beauty, preached by health promotionists, increases the feeling of guilt and anxiety in an ageing population who would give anything for a magic mirror which would tell them that they are beautiful and needed. The pursuit of the Holy Grail of health is driven by the mistaken belief that health equals happiness. The New Age acolyte is exhorted to eat less fat, produce healthy bowel movements and buy an exercise bicycle; no more pain or love, no more suffering or despair, no more sacrifice or weeping. While gratuitous violence, terrorism and crime are on the increase, the minders of society talk about tackling the causes of this social unrest. In their beliefs, saving human lives is a noble deed. At best, they will stare at you; at worst, they will try to measure your cholesterol (Skrabanek 1994; pp. 37–41).

Health – like love, beauty, or happiness – escapes all attempts at objectification. Healthy people do not think of health, unless they are hypochondriacs, which strictly speaking is not a sign of health (Skrabanek 1994; pp. 15–53). Similarly, when our organs perform their functions perfectly, we are not aware of them. It is the absence of health that gives rise to concerns about health. The search for health is a symptom of unhealthiness. I call it health anxiety. When this pursuit is no longer an individual concern, but part of everyday life, it undoubtedly becomes a symptom o f a social sickness. Gadamer specifically pointed out this enigmatic nature of health; he correctly showed that health is not something that can simply be made or produced. He questioned the nature of health itself. Can it become an object of scientific investigation in the same way that it is for the individuals when the balance of health is disturbed? For the ultimate aim, after all, must be to regain one's health, thereby forgetting that one is healthy (Gadamer 1996). In Gadamer's view, the mystery of illness bears witness to the great miracle of health that allows us to live in the happiness of forgetting, in a state of well -being, lightness, and ease (Gadamer 1996; p. 87). Therefore, healthiness and forgetfulness belong very closely to each other; in a way that everything that makes us aware of our health makes us sick. Thus, the mystery of health remains concealed. Its concealment belongs to the preservation of good health and this consists in forgetfulness. One of the most important healing powers in our lives resides in the ability to sink into the healing sleep of forgetfulness of every evening (Gadamer 1996; p. 138).

The stated public aim of healthism is the "health of the nation", with an implicit promise of a greater happiness for all. However, there is a huge difference between attempts to "maximize healthiness" and those to "minimize suffering". As Karl Popper (1945) pointed out in *The Open Society and its Enemies*, all attempts to maximize the happiness of the people must lead to totalitarianism. Gadamer elaborated it this way: in the vast technical structure of our civilization, we are all patients. Our personal existence is clearly something which is denied everywhere and yet also always involved in the attempt to regain that balance we need for ourselves, for our lived environment, and for the feeling of being at home in the world. A very crucial point that Gadamer tried to show is that this extension is far beyond the sphere of medical responsibility and includes the integration of individuals into their family, social and professional lives. Hence, medicalization and healthism are not medicine or science, they can be categorized as a semantic-social strategy that

benefits some persons and harms others (Szazs 2007). This does not seem to be an abstract task, but rather something concrete which permanently confronts us. The challenge is the continual one of sustaining our own internal balance within a larger social whole which requires both cooperation and participation. It seems that there are many situations in which we are in a position to not only identify problems which restrict us, but also to discover new possibilities for a more humane arrangement of things as they have been developed in our instrumentalized social organization. This is something we occasionally realize through an encounter with another human being (Gadamer 1996; p. 81).

The role of doctors and other health professionals should be examined and redefined carefully. Furthermore, there is a necessary need to change the role of physicians in this era. Similar to the doctor, the patient should be entrusted with a human life which must now be released from this protective care. Those who have regained health and been given back their life begin to forget the illness, but still remain bound and beholden to the doctor in a specific, if often unspoken manner (Gadamer 1996; p. 43). Jim Windolf (1997), executive editor of *The New York Observer*, wrote that the experts will not be satisfied until every last American is suffering from some kind of disease, disorder, or syndrome (Nye 2003). This pessimistic image of medical doctors in this healthism/medicalization story is very influential. The medical profession faces medicalization in a paradoxical manner. On one hand, particularly its public health branch, medicine provides the required theoretical keystone of healthism – the doctrine of lifestylism according to which most diseases are caused by unhealthy behavior. On the other hand, physicians realized that healthism stimulates the obsession with health that indubitably leads to health anxiety. The physician's role in this present-day notion of medicalization is similarly complex, as he remains an authority figure who prescribes pharmaceuticals to patients.

The role of the patient in this story is also more than a mere victim. The pioneer German neuropathologist pointed out that "the medical treatment of patients began with the infringement of their personal freedom" (Szazs 2007). This quotation rightly emphasizes the relationship between patient treatment and patients' freedom. However, it should be noted that the role of patients has also changed. Once regarded as passive victims of healthism and medicalization, patients can now play active roles as promoters, consumers or even agents of change. Healthism stimulated and aggravated the obsession towards health and, conversely, promoted illness. So how can patients break this vicious cycle? If patients succeed in taking up the same sort of dialogue as they would normally pursue when trying to reach an agreement with someone, this could help to stimulate the ongoing process of easing the relationship between pain and well-being, as well as the experience of regaining equilibrium (Gadamer, p. 137). The main issue that should be addressed here is the understanding of the role of doctors as well as patients in the techno-scientific perspective of medicalization.

The antithesis of medicalization and healthism is the process of paramedicalization, where everyday life comes to the attention of alternative medicine, traditional medicine, or any of the numerous non-medical approaches to health. The concept of paramedicalization was first presented in 1995 by a Finnish sociologist in *The*

Finnish Journal of Social Medicine. Paramedicalization refers to the trend of people placing more and more value on alternative medicine and different beliefs about wealth and health, which are not authorized by modern (Western) medical science. While for modern medicine, healthy state only means the transient absence of diseases, many alternative medicines serve a framework for understanding healthy life without any reference to diseases. Therefore, it seems that in order to manage health anxiety in this era, redefining medicalized problems in terms of alternative medicines is more reasonable. For instance, the medicalization of diet could be replaced by a more healthy type of traditional medicine.

It should be kept in mind that the process of paramedicalization runs concurrently with medicalization. On one hand, some parts of medical institutions treat alternative and complementary medicine as a pseudo-scientific enterprise, on the other hand, alternative and complementary medicine practitioners have been accepted and approved to practice beside modern medical doctors. Therefore, medicalization and paramedicalization can sometimes be contradictory and conflicting, but they also feed each other. They both ensure that questions of health and illness stay in sharp focus in defining everyday life and problems. The dialogue between modern medicine and other traditions should facilitate this process.

In conclusion, medicalization is the process by which medical diagnostics and managements are applied to behaviors, psychological phenomena and somatic experiences, which were not previously within the conceptual or therapeutic scope of medicine. Careful examination of the medicalization process shows us that it rests on the basis of healthism and lifestylism – according to which most diseases are caused by unhealthy behavior, yet, lifestylism provides the required theoretical underpinning of healthism. The medicalization–healthism–lifestylism paradigm contradicts itself by stimulating health anxiety instead of improving health society. It was proposed that paramedicalization could be an option to manage this problem.

7.3 The Individual Aspects: Medical Reality Versus Personal Realities

The perspective towards which medical science is currently headed makes doctors, patients and society unable to become distracted from the subject of disease. Health knowledge – which is distributed widely and concretely in society – has made society hyper-vigilant toward disease-related issues like diagnosis, morbidity, treatment options, medication, drug side effects, and treatment. Etiology and prevention are the two most specific subjects towards which society is hyper- vigilant approaching concretely (Manchikanti et al. 2011; Häuser et al. 2012).

People feel surrounded by pathogens in numerous ever-increasing forms like microbes (viewed as omnipresent microscopic enemies), air pollution, and other sorts of harm expected to be hidden in everything like food, water, textiles, and

electronic devices among others. The medical profession, on the other side, amplifies the same attitude by giving concrete non-individualized stereotypes of advice and explanation (Houston 1938; Hahn 1995, 1997; Dunn 2005; Data-Franco and Berk 2013; Häuser et al. 2012), as well as through labeling, blaming, disputing, ignoring, guilt inducing, drug administering, ordering, recommending, alarming, medicalizing, and fear-provoking (Wells and Kaptchuk 2012).

The concrete and terrifying medical attitude towards human vulnerability makes humans of the modern age feel no more secure than their ancestors who were afraid of large animals, hunger, cold, magic, demons, dragons, swords, and oppressing kings and emperors. Medicine is now faced with a rapidly increasing number of patients who suffer from a new collection of symptoms and rule-breaking courses of illness, which do not fully comply with any definite disease category within the vast classification systems (Hellhammer and Wade 1993; Henningsen, Zimmermann and Sattel 2003). It would no longer be possible for medical science to ignore or dispute so many clients for their atypical complaint s while, at the same time, keeping its professional figure of respect, trust, and authority.

To use labels like "difficult patient" or "medically-unexplained symptoms" – among many others – would no more help the doctor to continue laying back on their old-fashioned all-powerful seat. The future perspective of the medical science has no way other than complying with human autonomy and empowering clients to make their own way towards enhanced health. Such a perspective may not be easily achievable by the medical doctor already brought-up inside the current shell of science. For all events, it may be difficult to adopt a holistic view unless we step out of the current shell. Yet, in this part, we are not going to head towards such a far-awayvague goal. Therefore, without stepping out across the current borders of medical science, later in this chapter we will track medical literature to see if there is already some evidence-based knowledge which advocates taking "realities" into account in respect to human health. For now, we will try to define the way to personal realities and how to respect individual differences in prescribing information in order to minimize the nocebo effect. To trace for nocebo as a mind reality, we can first address the "mind" itself as one of the numerous facts of which the human is made up as a "whole". Hence, we are attempting to form an idea of how far medicine has been viewing the human mind as being possibly relevant when approaching patients. Then, we will try to explore the history of medicine to see where the nocebo concept is present.

7.4 What Is "Nocebo"?

"Nocebo phenomena" referred as placebo's evil twins (Hiskey 2011), have received much less attention in medical documents thus far than their more positively perceived siblings (Enck and Häuser 2012; Tavel 2014). Indeed, it was not until the 1960s when, for the first time, the nocebo effect was documented in medical literature. Yet in terms of human history, it has much older origins. Anthropologically, the

history of nocebo can be traced far back into the past, being referred to as "voodoo death" in some primitive cultures (Cannon 1942, as cited in Esther 2002), then by contributing to "mass hysteria" and "psychogenic mass illness" in the not-so-distant past (Rubel 1964).

In simple terms, nocebo phenomena can be defined as "adverse events caused by negative expectations" (Hahn and Kleinman 1983). They are mainly – but not always correctly – viewed as the opposite to placebo effects, or as their negative equivalents (Hahn and Kleinman 1983). Originally the term nocebo, Latin for "no harm", (Enck and Häuser 2012; Kennedy 1961) was used to describe clinical deterioration aroused by negative expectations towards a pill or medical intervention. It is supposed that in the absence of such negative expectations, the same drug or medical procedure could in fact be either beneficial or at least safe and neutral, but certainly non-harmful.

As you may notice, the agency of the drug or medical intervention was taken for granted in the original definitions of the nocebo effect as well as the innate safety or neutrality of the same drug or intervention (Houston 1938). However, the nocebo story goes beyond such definitions. Evidence implies that when significant pessimistic anticipations are present in one's mind about their medical condition, a clinical deterioration would be more probable even in the absence of any drug or intervention. Such a phenomenon is more precisely called a nocebo response (Kennedy 1961; Hahn and Kleinman 1983). In other words, negative expectations seem to be able to do the job "with bare hands". A typical example is the development of hyperalgesia when, in spite of all evidence to the contrary, the patient continues to perceive their medical condition as progressive and severe (Stam 1984, Stam ans Spanos 1987).

It is easy to imagine that if negative expectations create the adverse effects on their own, they would be able to do it even better if equipped by additional materials – things like the administered pills or the medical instruments applied by the therapists – which may potentially feed the patient's fears and pessimistic predictions.

Somewhat interestingly, nocebo effects have been shown to work through biological mechanisms different from those explained by the medical literature for the placebo phenomena. Therefore, one should resist the temptation to regard nocebo as a simple blocker which undoes placebo's magic spell. Rather, although being an evildoer, unlike the placebo, nocebo acts at least as much powerfully and detectably as placebo does. That is, nocebo exerts its effects independently and objectively, just like what any pill or medical intervention does (Hahn and Kleinman 1983; Benedetti et al. 2006).

The nocebo concept predictably implies that the patient's condition may clinically deteriorate or improve at a slower rate with medical practice in the event that they believe their illness is serious or progressive, or that the prescribed pill or performed intervention is ineffective or hazardous (Milton 1973). This occurs whether the pill/intervention is a real medication/procedure or an inert nocebo pill/a fake non-operating intervention, or even if, despite the patient's belief, no pill/procedure has been applied at all (Data-Franco and Berk 2013).

In a sense, it is to say that our bodies tend to behave or to suffer in the manner which we already anticipate (Häuser et al. 2012). It is particularly alarming when you come to the fact that one's expectation, as a kind of belief, can itself cause illness. We will get to this fact later in this chapter.

At this point, we will briefly demonstrate some of the controversial discussions which the medical literature has raised so far concerning the nocebo concept itself as well as the implications suggested for it in medical practice and clinical settings.

At least partly resulting from the rule-breaking and "out-of-the frame" natures of the nocebo concept and other mental realities, there have been concerns expressed in the medical literature about the emerging attention towards them. A few research studies have emphasized the important limitations which should be considered when trying to translate the nocebo effect into the medical practice (Crombez and Wiech 2011; Bromwich 2012). One of the most familiar examples of controversy is about the application of the nocebo concept in the area of communicating medical news without invading patients' basic human rights (Wells and Kaptchuk 2012; Colloca and Finniss 2012). Also, avoiding the induction of nocebo effects when talking to the patient about the drug facts in terms of side effects, while at the same time respecting their autonomy and keeping ourselves within the borders of truthfulness and trustworthiness (Häuser et al. 2012; Tavel 2014) has given rise to concerns. It should be mentioned that we do not intend to produce a practical guideline for nocebo application in the medical practice here, rather, we are attempting to discuss the concept in order to emphasize the critical need which is felt in the medical practice for taking precautions towards the patients' mental realities and trying to design practical methods to approach the patient's mind in medical practice later on. There are still other major concerns among some medical scientists in respect to the increased attention towards nocebo/placebo discussions. By a surface review of the rather small amount of literature criticizing the published nocebo studies, one can readily infer a large common concern, which has not been greatly explicitly discussed. The concern seems to be a perceived danger which may threaten medicine as a field of science. The threat they perceive is attributed to a growing new trend of ideation which can potentially make fundamental changes to the reasoning rules and thinking styles. It may put medicine – as perceived by those critiques – in danger of becoming insidiously deviated from the mainstream of science; a deviation perceived as potentially destructive, for it may destabilize at least two of the very basic fundaments on which the medical sciences have been ever standing; namely "accountability" on one hand, and the evidence-based nature on the other (Bromwich 2012; Crombez and Wiech 2011; Laarhoven and Evers 2011). Altogether, the rationale behind the critics against nocebo studies highlight some realistic concerns, as inferred below:

When entered into the research and practice area, such abstractive concepts like nocebo can settle down as a core idea around which many other abstractions would develop, most of which not potentially experimental, and hardly ever measurable with certain confidence. This may be the reason why some authors have criticized the studies which try to objectify and highlight the importance of the nocebo effect in clinical settings. Critics claim that such reports tend to describe a hallucinatory world around health events, in which health status is grounded on a non-stable

foundation that is potentially responsive to mental events, just like talking about a magic world where our fears and wishes may find their way into life unpredictably and mysteriously, a world which may never get fitted into any experimental scientific framework (Crombez and Wiech 2011). The final message of such criticism is to remind the medical professionals not to overlook the valuable mainstream facts of their science. It is somehow an alarm to push the attention back to the very original version of the story. At any event, without even the slightest amount of negative expectance, one may get into trouble once they are exposed to a large enough amounts of pathogenic microorganisms, and it would be no more difficult to get afflicted by the real iathrogenesis of a hazardous medical procedure or the objective side effects of a drug. This is definitely not rationale against the nocebo consumptions in essence; rather it is a non-deniable self-evident fact, highlighted as a "take-care" suggestion by those who really care.

From another viewpoint, medical scientists try to warn their colleagues of falling into the opposite extreme of the traditional dichotomous way of thinking about mind and body. The fact focused on by these studies, however, is one in perfect accordance with the concepts of placebo and nocebo. To be clearer, we may reframe the message here to re -state it and to remind us about it before proceeding further to probe the nocebo phenomena. The following is a statement to declare our preliminary agreement: "When trying to weigh different factors which may contribute to human health, one should beware of any temptation towards raising the already neglected place of 'mental reality' from 'nothing at all' into 'everything'. Such an attitude is actually a tendency towards inclining to the opposite extreme, obviously such extreme deviation is far from adopting a holistic approach toward patients, if this is a dream we do all pursue."

7.5 Nocebo: A Response to the Supposed Enemies

Needless to say, medicine has a glorious history. By our time, it has embraced numerous brilliant stories of success. It has been significantly successful in its mission to find a reason for many of humans' physical discomforts. In other words, many enemies or faulty parts have been successfully identified in being responsible for different sorts of human illness. In the past century, micro-organisms were identified, one after another, as the pathogenic factors caused in some of the scariest diseases in human history (Bryson 2003). The big discovery of penicillin took place thereafter, followed by the discovery of other antibiotics and disinfectant agents, generations after generations. Thanks to those honorable achievements, the science of medicine proceeded to prevent and eradicate the fatal disastrous epidemics of infectious diseases.

A great amount of knowledge was also achieved about our immune system, or our body's defense army. Now, the antibiotics could be viewed as weapons that help our body's soldiers win in the battle against micro-organisms – their small yet dangerous enemies. Vaccination was the next magnificent achievement, resembling a miraculous spell which could be casted upon one's body to safeguard it against

some sort of enemies forever. Now, humankind could feel itself getting closer to the so-called spring of eternal life, whose drinking water would result in immortality and everlasting life. The sweet dream of immortality seemed not so far from becoming reality. Humankind was now dreaming to be the only creature on the earth whose generation would not be faced with extinction.

Further in the course of its history, medicine extended its borders further to discover more complex concepts of health and illness beyond the concepts of battle, friend, and enemy. Genetic disorders and inborn errors of metabolism were known, and scientific strategies were developed to improve the preventive and management methods for those disorders. Medical science extended its reach further to grasp an understanding of protective internal resources of health, and about human 's allied parties who guard and improve its health. Along with the rapidly increasing knowledge about diseases and their etiologies, classification systems were developed to categorize the numerous known contagious and noncontagious diseases.

We may get the initial idea here that, by the time medicine had overcome the infectious epidemics, the question of "friend or foe" had somehow emerged as a basic assumption in the public's perception of illness and health. So, we can postulate that the friend vs. foe question was implicitly going on in people's minds at the same time as rapid discoveries about micro-organisms were made, followed by primary scientific attempts to classify them in several ways, for example according to their innate pathogenicity vs. safety for humankind; these were the human first scientific attempts to identify enemies of health.

Again, at this point, it would be worthy to pay more attention to the "friend vs. foe question", and to have examples where the answer to this question turns out to be wrong or different from what medical evidence or human common sense would predict. So, let's review some of the very simple assumptions which may become a source of misunderstanding between both popular and professional health sectors. These facts may also be a basis to explain the important contribution of personal realities in health and illness.

7.5.1 Micro-organisms: Friends as a Rule, Enemies by Exception

By the time the mentioned successes had been achieved by medical science, people – feeling surrounded by so many invisible enemies in the world – gradually got used to viewing microbes as enemies rather than friends. It would make sense at this time, for when you cannot readily differentiate enemies from friends, taking any stranger for an enemy would be a more prudent decision. But nowadays, human beings of the modern age still continue to have a similar attitude.

We frequently forget the fact that, as a rule, micro-organisms have always been and still are our friends and companions; they inhabit our skin, are hosted by our digestive and respiratory tracts and live friendly all over our body. Indeed, we are absolutely dependent to micro-organisms to stay healthy, or better to say, to keep

living for even one more day. While our body is just one of their possible places to reside amongst almost anywhere else, we have no alternative except them to produce vitamins in our gut, to absorb our food, to provide oxygen and energy for us, and even to fight against other small foreign bodies we ordinarily swallow each day.

Hence, the "small living things" who live around us are mostly our friends – not enemies – despite the general presumption which indicates we should either hide from or kill those using antibiotics or disinfectants (Bryson 2003). From a more humble point of view, micro-organisms have been the original inhabitants of our earth who were living on it before we arrived. Indeed, once upon a time, they kindly welcomed us as friends, made rooms for us to live in their kingdom, and helped us survive happily ever after. That was one example, among several others, pointing to basic misperceptions one can have in trying to identify friends and enemies in relation to their health.

7.5.2 Sickness as a Friend's Business Rather than an Enemy's

Even when talking about a pathogen micro-organism, it is still a common mistake to attribute the illness we experience to be caused by that small enemy alone. A major part of an infectious illness does not result from what the micro -organism does to our body, rather from what our body attempts to do to the microorganism (Bryson 2003). Our immune system itself makes some inevitable harm or discomfort to our body while trying to eliminate the pathogens, as it is too hard to keep any battlefield safe from some degrees of collateral damage. So, when we feel sick, the feeling itself – the ill- experience – which is the main reason why we seek help from a doctor does not come from the small enemy itself, rather, sickness experience mostly originates from what our own immune system does to our body for the sake of our beneficence (Bryson 2003). To reiterate, the experience of illness can be more accurately imagined as being caused by a caring friend rather than by the enemy.

It is a distorted dishonest picture to attribute our symptoms to the evil harmful attacks made by small enemies inside our body. Having such a false picture in mind, the sickness state may occasionally turn into an increasingly terrifying experience for us. The false imagination may trigger a vicious cycle of interacting negative anticipations which in turn increase the severity of our suffering. On the other hand, sickness experience, even if being uncomfortably painful, should better induce in us a sense of reassurance and relief if we truly perceive our symptoms and their severity as signs, which indicate that our body is being protected through defensive endeavors of our strong immune system. In the same manner, medical treatment can be imagined as weapons to aid our defensive army. The illness would be perceived as a more tolerable, dignified and surmountable experience when the patient views suffering as a result of supportive endeavors of the body's devoted friends rather than from violent attacks of its enemies.

7.5.3 *Friends Can Sometimes Get Mad and Transform into Dreadful Foes*

The cascade of a disastrous illness can get fired on following behavior by a real friend rather than an enemy – by a native microbe trusted by the host's immune system rather than a foreign body. Every once in a while an unfortunate occurrence takes place in one's body. After having peacefully lived in the same body for many years, a devoted helpful friend microbe accidentally loses its way and gets into a wrong part of body where it is not welcomed from the time of its arrival. Finding itself in a forbidden area and prohibited from going further, it becomes increasingly concerned, realizing that its non-intended entrance is not going to be easily approved by the immune system. Unable to figure out a way out of the crisis, it feels increasingly frustrated and threatened. Then all of a sudden, it somehow becomes mad; in a helpless crazy attempt to save its life or to escape, it tries to grasp anything within its reach. It begins to invade the surrounding body tissue relentlessly and literally eats everything hungrily, helping the disaster develop rapidly. What it does is explicitly mad in a way; if it is not hindered by means of an extensive treatment, it almost certainly ends in the host 's death, which also leaves no chance for the microbe itself to survive afterwards.

The story above is a typical portrait of a known infectious disease of the modern age called "necrotizing fasciitis". It is either seriously fatal (as death occurs within a few hours to a few days if treatment is unavailable or proves ineffective) o r terribly disfiguring (if the victim is lucky enough to survive, thanks to an extensive rigorous medical and surgical treatment).

The causative micro-organism is a bacterium that lives innocently in its own neighborhood in the human gut for years, but very rarely, it happens that it wanders about in an absent-minded state, where it then gets into the blood stream. As a result, it is brought to another part of the body, like the fibro-muscular tissues, where it becomes mad, violently invading the tissues, triggering a battle in which it keeps fighting mercilessly. Altogether, it creates a very scary disease (Bryson 2003).

This was an example of an exceptional event happening in spite of what we already expect to happen according to the medical knowledge we have acquired about the innate characteristics of a friend-labeled micro-organism. This example shows us the fact that health events are not solitary events to be defined by absolute innate traits of friendship or enmity, rather they are made of complex interactions between the potential friends, potential enemies, and their environment and the interaction itself is affected by a sort of mutually-formed perception generating reciprocal attitudes of enmity or friendship.

7.5.4 When Insiders Are Interpreted as Strangers: Auto-immune Disorders

As previously mentioned, at the very first step of its critical defensive role, the immune system tries to screen out all foreign cells (potential enemies) through filtering codes and causing them to be inhibited, killed, by-coated, deported or eliminated, altogether it inhibits them from further progression inside the body. From time to time, the body's army mistakenly identifies insider organisms — mostly a tissue of the body itself — for enemies or aliens.

As a result, the immune system, which is naturally designed to ensure the safety of the body's organs through fighting their enemies, imposes a war against the self-tissues. The war is called as an auto-immune disorder, that is, a disorder which occurs when the immune system fights against one's own body. Sometimes, this results in only mild to moderate auto-immune reactions and disorders, but more typically, an auto-immune disorder is an insidious, enduring, and destructive disease process. Put in the center of a shooting target, the body tissue stands helplessly with raised hands aimed at by the armed forces of its own land.

As unfair as it seems, this would inevitably be a self-defeating battle for the invader in the long run as well, for it has ended in the body's diffused destruction which would eventually also be destructive to the immune system itself. It looks like an army who devastates its own homeland by becoming preoccupied by suppressing a perceived threat from people living inside. It keeps its right eye closed to the destruction caused by itself, until the time eventually comes where it realizes that the war has left extremely little resources within the entire land – far less than what the army itself would need to survive. This is a typical example of what happens when a cascade of harmful events gets turned on crazily as a result of a falsely-perceived threat, rather than a true one. In another word, the catastrophe comes from a misperception, better to say "a perceived reality", which triggers the serial events leading to the disaster regardless of the fact that the perceived reality is not compliant with the objective reality which is often simply referred as "reality" itself – here also called the medical reality.

Emphasized in the above examples is the fact that the content of any perception is sort of a reality. The perceived reality is a real version of reality, as real as being able to go beyond other realities in making actual effects. If something is perceived as an enemy by our immune system while we perceive it as a friend in our mind, two sets of opposing mental realities are really there, one in our mind as a whole person, and the other in the virtual mind of our body. Once your body perceives an enemy – whether you and your respected medical science believe it or not – you may get into trouble by the reactions it makes.

The other arresting notion is that, very often the answer to the critical and strategic "friend or foe?" as a "perceived reality" which determines what happens next. In other words, "reality as perceived by sort of mind" defines the body's reactions. In this way, "mental reality" can be referred to as what is perceived by the whole person's mind or "mental mind", while immunity reality can be labeled on what is

perceived by the virtual mind of the person's immune system or by "body's mind", and "medical reality" can be referred to what is perceived by the doctor's professional uptake and/or medical scientific evidence or by the "medical mind".

The upshot of the above discussions is to say that in order to achieve a reliable understanding of illness experience and/or to exert predictable modifications on any health outcome, we first need to figure out an overview of the interactions between different existing realities which eventually fulfill the actual answer to "friend vs. foe", "harmful vs. non- harmful", and "beneficial vs. non-efficient and/or maleficent" doubts. Hence, the final picture would be demonstrated by an overall shared answer or by the dominant reality which would provide a brighter and more predictable picture in case the answer is highly agreeable by all parties.

7.6 Paternalistic Medicine: Why Has the "Human Mind" Been Ignored in the Area of Human Health?

As an observable fact in the course of enormous scientific achievements, medical science has never been completely ignorant towards the human mind, thoughts, beliefs, conceptions, and perceptions. As discussed before, assumptions of a "perceived friend" vs. a "perceived enemy" can be found implicitly included in the documents of the young-aged conventional medicine. However, it seems surprising that the human mind, in spite of its great potentialities, has not been significantly credited by medical science as an active agent able to impact health via its perceived realities; whereas the "immune system's virtual mind" has been implicitly approved by this science in that it can exert impacts on health through perceived realities, even if those realities are in contrast with an objectively-manifested evidence-based reality.

This discriminative attitude towards the whole person's mind as compared with the virtual mind of one of their body systems may be partly due to the dichotomous approach toward mind and body in medicine. Such an approach is very common. However, when the doctor tends to examine topics in the overlapping zones of the two kingdoms, they find that the intersecting borders are extremely challenging to define.

7.7 The Nocebo Effect and the Omnipotent Doctor Picture

As mentioned before, identifying pathogen micro-organisms as major enemies of human health puts the medicine profession in a unique position. Predictably, it was increasingly viewed by the public as a scientific profession of warfare against enemies of human health. In the same way, medical doctors were viewed as commanders whose intelligent tactics in the battlefield had led humankind into the glorious

victories against dreadful enemies of health. Viewing illness as a battlefield inside the body made people increasingly vigilant about their health hereafter.

One further important outcome of those significant progresses was likely the attribution of super-human potentials to medical doctors by general ideas. As an authority figure whose knowledge and expertise was likely to be sooner rather than later needed by everybody as a matter of life or death, it is not strange after this point in history to imagine the doctor perched on a throne of unchecked power, in front of which even the most merciless kings might someday bow their heads. How would you – when in desperate need of life saving help or pain relief – look upon a knowledgeable helpful figure that possesses those skills which you lack? The view would imaginably reflect a sense of respect as well as an implicit helpless obedience mixed with a hopeful reliance. This was how doctors adopted a paternalistic attitude toward their position to take care of their patients.

The paternalistic view is one which allows the doctor to take the place of a kind father feeling granted both the wisdom and the right to decide on behalf of patients as if they were his children. Such a position, aside from all the valuable power and authority from which medical experts had benefited, made them vulnerable as they were pushed to introduce themselves as omnipotent characters to feel competent in their profession.

At the same time, for people seeking help from such authority figures, no room was left to inquire about the logic behind or alternatives to the doctor's decisions. For a long time since then, doctors have covered their true human face with an omnipotence mask. However, in the following decades, the omnipotence image gradually grew to a more challenging problem, both for doctors and patients. Because while moving further, the variety of health problems referred to the medical care systems was rapidly increasing; faster than that of the new codes and terms being added to disease categories in the medical classification systems and much faster than the developed treatment protocols. Consequently, doctors were facing numerous health concerns, for the management of which they could find no magic spell in their chest; a situation which could be interpreted as a flaw in the image of omnipotence already included in the "good doctor" picture – in their own minds as well as the public's.

Approaching the present day, it seems that both medical doctors and their clients still have the image of the doctor as a kind of "omnipotent figure". For doctors, this tendency may be linked to their initial motives of their job (i.e., to save human lives and to reduce their pain). Studies have shown that when the prognosis of a disease is not promising, doctors feel reluctant to let the patient and the family see the condition as it really is unless having already been trained in specific communication skills to break bad news (Buckman 1992; Wells and Kaptchuk 2012; Schuricht and Nestoriuc 2013). In similar studies, doctors have declared they tend to keep themselves disengaged from their patients when some "less than good" medical news is supposed to be delivered and that they assume the reason to be their deep wish, as the medical doctor, to be able to manage any human suffering (Buckman 1992; Fallowfield and Jenkins 2004).

Even in the modern age, it seems that the doctors still try to fit themselves to an image they perceive as being portrayed of them in the public's mind; a portrait which reflects traits of wisdom, profound miraculous knowledge, good intentions of help, and a superior curing power; in short, an image of omnipotence. You may notice that doctors have not willingly given up their "omnipotence figure" even when faced with patients who present a very complicated illness pattern which can neither be easily assigned to any disease entity or explained by scientific medical knowledge, nor is going to get managed effectively through the evidence-based medicine. Such situations would be frustrating to doctors whose professional self-esteem is deeply rooted in the "omnipotent doctor" archetype. Bearing in mind such a professional self- image, the doctor would perceive their public creditability as being threatened whenever they find themselves uncertain or non-efficacious in diagnosis and management of a medical condition.

While any medical doctor – sooner or later during his/her career – would inevitably be faced with their own limitations (or with limitations of the medical science itself), their self-esteem would not necessarily be threatened in such situations unless they have been strongly pushed to turn their mind's distorted wishful image of the omnipotent doctor into reality. Indeed, acquiring insight toward one's personal and professional limited efficiencies would release the medical doctor from their historical discomfort towards admitting the dark sides of their own knowledge or their scientific field. It would also allow them to assume a non-conditional and non-judgmental attitude toward the patients, even towards patients whose suffering patterns do not match any known diagnostic categories or do not respond to any sort of evidence- approved treatment.

The point is that medicine is increasingly faced with patients whose physical symptoms are hardly ever compatible with the criteria of any specific known disorder or syndrome (Henningsen et al. 2003). There are also a growing number of instances where a patient's subjective complaints can be sensibly attributed to one disorder or a list of differential diagnoses; but when the patient's condition are investigated thoroughly by extensive clinical and laboratory exams, the objective findings fail to confirm any of the diagnoses or simply rules them out (Barsky et al. 2002; Colligen and Murphy 1979; Mills 2006).

Looking throughout history, one may realize that two things have so far substantially helped doctors not to get frustrated when they are pushed to their limits of professional potency: so-called technical language and scientific literature. They have helped the vulnerable medical doctor to restore at least some superficial appearance of their omnipotence figure in the public view. After all, the doctor would still remain as the man of science who knows the technical name for any mysterious illness and they are also the one who can bring wise recommendations out of his chest to be obediently followed by the patient. As a result, the public maintains the view of the doctor as the large alliance of human health who knows health enemies and diseases well enough to call them by their names and is able to classify patients according to their illness type.

As a communication aid, terms like "difficult patient" as well as descriptions such as "medically unexplained symptoms" and many others have been added to medical terminology to categorize a large group of various patients under a single

name. On one hand, those labels make it possible for medical doctors and psychiatrists to communicate their shared experiences of helplessness to each other. On the other hand, it works as an excuse for the medical doctor to minimize the fact of their ignorance and despair toward these conditions in a manner of grandiosity or innocence. When frustrated, human beings tend to put a label on things, persons, or situations in order to convey a meaning of severity, strangeness, or bizarreness; such a label acts as a remedial tool to relieve their feelings of despair. In the same way for medical doctors, medical terms implying severity or complexity induce a feeling of regained mastery, as if they have somehow grasped the diagnosis or they still own the knowledge as the doctor and/or as if they were not responsible for the patient's continued suffering.

Similarly, for many systems of medical education, giving the situation a medical name has become one of the most valued aspects of the medical knowledge regardless of whether it implicates any beneficial outcome to the patient or not. Indeed, stigmatizing seems to be utilized to compensate for the times the omnipotence picture is not going to hold true. Medical doctors who care about the final mission of their job should ideally be extremely cautious when u sing terms like "difficult patient" because many professionals and patients perceive it as intended to mean something like "the non-important annoying patient". This kind of discriminative interpretation is closely linked to such labels which makes it much more difficult – not easier – for the patient to regain their health. This is one of the alarming points of which medical doctors need to be beware; causing the patient harm via stigmatizing them with medical terms.

Other than medical labeling, what most medical doctors do in such situations is to refer those patients to psychologists and/or psychiatrists, a decision which is neither readily welcomed by the patient nor perceived as an attempt intended to help; it is rather assumed as a sort of rejection or punishment as their symptoms have not been confirmed by the doctor as medically valid or as important. Moreover, even when such a patient visits a psychiatrist, it is very likely they will put the doctor in the same puzzling situation (i.e., a situation in which the patient's complaints don't indicate a clear-cut disorder and/or cannot get managed by medical interventions).

Indeed, occasions in the medical practice where the physically ill are not managed as predicted or get referred to psychologists and/or psychiatrists are unique opportunities in which medical science has to accept the "mind" as a relevant factor associated to human health. This can allow medical science to go beyond its conventional borders and acknowledge the vital presence of mind, mentality and intellectuality in the kingdom of human health. Thus far, however, medicine has not done many favors for such medical conditions except granting them a name in medical terminology. New trends, qualities, and presentations of medical conditions are now reaching such a fever pitch that we have no escape from again looking into our knowledge of human health, especially the gaps or areas where we have recurrently failed to achieve our goals. This would force us to probe medicine deeper in the typical zones where mind–body issues apparently merge into one another – where medicine is getting closer to giving up on denying the mind's contribution to human health.

There is an ancient (Islamic) quote which says "people are enemies toward what they do not understand" (Imam Ali, Nahjolbelagha). In the above historical overview of medicine, you see examples to such a wise quotation. Doctors tend to deny pain or suffering that they do not thoroughly understand. Also, they assume a rather defensive attitude towards any approach to those aspects of the whole person, to which medical science has been highly ignorant so far. And on that sobering note, it is time to tap the medical literature to see whether and how the mind's contribution to health can be acknowledged in the context of evidence-based medicine.

In summary, for medicine, the mind and realities perceived by it are among the dark sides of the human whole towards which it has been so far both ignorant and non-tolerant; while harm and benefit are the two most basic concepts in human health which are objectified through the effects of different friend or enemy factors. Those effects, as explained before, have been found not to be absolutely innate and predefined, but rather partially and reciprocally defined by (altered by/mediated through) a sort of "friendship" vs. "enmity" as perceived by a vigilant health-aware perceiver.

7.8 Contribution of Various Realities in Health, Emergence of the Nocebo Concept in Medical Literature

We are going to review the relevant medical literature in respect to the association of "harm," "health," and "mind" organizing existing knowledge – however limited – about the neglected sides of the human whole including the mind, thought and emotions. We will review the literature to figure out what else one can do/avoid to maximize beneficence and/or minimize harm in medical practice beyond what one was already trained for in the conventional diagnosis and treatment system. First, we will focus on how to avoid causing harm with a closer look at the nocebo documents, facts, and discussions. Then, we will try – if at all possible – to develop a rough preliminary evidence-derived map to exploit the human mind as one of the health alliances when approaching a patient in medical practice. Through a rather extensive review in the medical literature, we may head towards answering the following questions: (1) How can negative expectation turn into a reality? (2) Are some people more prone than others to being effected by nocebo effects? (3) How could a "nocebo-effect" become possibly induced, predicted, prevented, or stopped? In other words, we are going to examine different factors associated with the nocebo effect to obtain some strategies aimed at preventing it in the medical practice.

7.8.1 How Can a Negative Expectation Turn into Reality?

Expectance theory is so far the most inclusive theory among several theories which try to explain nocebo and placebo responses (Häuser et al. 2012). It postulates that the mechanisms, which mediate a placebo response, are activated through positive

expectation linked to reward expectation traits and/or states while those of a nocebo response are induced by negative ones related to anticipatory anxiety traits and/or states.

In respect to psycho-physiological mediation, reward expectation has been linked to reward dependence traits or states, modulation of the brain reward system in the limbic area and increased dopamine and endorphin release. On the other hand, anticipatory anxiety has been associated to harm avoidance traits or states, increased brain stem and nociceptive activities, Cholecystokinin (CCK) neurohormone secretion, hyper-activation of the hypothalamus-pituitary axis, and increased blood levels of ACTH and cortisol hormones (stress hormones) (Häuser et al. 2012; Spiegel 1997; Kennedy 1961; Hahn 1997). These biological events are all in reciprocal interaction with each other and with situational precipitating and perpetuating factors as well as psychological situational factors like past experiences, emotional status, motivation, belief, therapeutic milieu, doctor-patient relationship, and received information (Brañas-Garza et al. 2010). Several documents show that placebo effects are associated with a person's tendency toward optimism and social desirability, while the nocebo effects are linked with their tendency toward pessimism (Brañas-Garza et al. 2010; Friedman and Booth-kewley 1987; Jakšić et al. 2013; Cooper and Tape 2001). The therapeutic environment can modulate both therapeutic and adverse effects of an active drug as well as the placebo/nocebo-response in antidepressant drug therapy (Henningsen et al. 2003; Bingel 2013). Those who had received placebo drugs but believed they had taken antidepressants – as they had been already told they would receive either an antidepressant or an inert drug – reported the vast majority of side effects in clinical trials. Indeed, the experienced adverse effects had been caused by the negative emotions or the psychosocial stress of anticipating receiving psychotropic drugs (Barskey et al. 2002).

In the same way, in clinical placebo-controlled trials, it has been shown that a quarter of depressive patients who did not adhere to treatment or discontinued it due to experiencing specific drug side effects were those who had received placebo. This highlights the fact that anticipatory anxiety combined with a pessimistic inclination exerts such a great impact on an individual's physiological sensations that they experience the same symptoms as if they had received the psychotropic drug itself (Cooper and tape 2001; Jakšić et al. 2012).

Depressive emotional states (or traits) are shown as the upstream mediator in nocebo effects. It has been shown that in persons who are already prone to negative expectations (e.g., in depressive patients who naturally expect that things won 't change for the better), nocebo impacts are much stronger than placebo can compensate for. Therefore, it would not be surprising that coercive therapy or patients' lack of belief in treatment, as well as a history of poor response to previous treatments, have strong adverse effects on the eventual success of antidepressant therapy (Hahn 1997; Hauser et al. 2012; Colloca 2012). Based on evidence, both anticipatory anxiety and reward expectance are modulated, activated, or precipitated by learning experiences which include information (given by clinicians) and the history of previous successful/unsuccessful therapy (Hauser et al. 2012; Hahn 1997).

7.8.2 *Are Some People More Prone than Others to Be Affected by Nocebo Effects?*

Individual differences in nocebo and placebo responses are a self-evident fact justifiable by that previously mentioned about mediating mechanisms as well as by several other bio-psycho-social predisposing and situational explanations; yet, valid studies have rejected the old notion that a sort of purely inherent specific vulnerability towards the nocebo response might exist. Inter-individual variation studies which identify predictors of nocebo responses are currently a major point of research attention. Early studies describing placebo-prone personality traits have been criticized by other researchers later on for methodological biases as well as flaws in their conceptual framework. In the past decades, researchers have tried to re-examine the findings of the earlier studies with more robust research frameworks.

At this point, we tend to briefly introduce the results of the third set of studies. The overall agreement over which studies have been generally congruent is that definite correlated situational factors should be specified if any individual variable is to be regarded as associated with a placebo or nocebo response (Crombez and Wiech 2011; Jakšić et al. 2013). In this way, by linking them to their specific correlated situational variable(s), old studies have been revived and the findings of even older studies re-validated. Thus, by defining the preliminary situational conditions, some predictive factors of the nocebo and placebo responses explored in those studies are now revisited and defined again (Jakšić et al. 2013).

Kennedy (1961) had emphasized that a nocebo response is a subject-centered reaction. He specifically referred to the nocebo reaction as "a quality inherent in the patient rather than in the remedy". Taking note of the nocebo definition, this is a clearly valid statement that the negative expectation – as the cornerstone of any nocebo response – is a reality in the patient's mind, not in the received pill or intervention. Yet, evidence rejects the idea that once an individual manifests a nocebo/placebo response to one treatment, they will present such a response to other treatments as well; this disconfirmation implies that in the same person, nocebo/placebo response varies according to situational and other interacting conditions. Similarly, evidence did not support the existence of a so-called "placebo-prone personality" (McGlashan et al. 1969).

Also, through a well-credited study, Lasagna, Mosteller, von Felsinger and Beecher (1954) revealed that before administering a drug or a medical procedure, one can by no means reliably pre-differentiate individuals who would manifest a placebo response from those who would not according to measurements of their individual characteristics. Moreover, hypnotic susceptibility has been disconfirmed as a predictor of a nocebo/placebo response in any individual (McGlashan et al. 1969; Stam 1984; Stam and Spanos 1987). On the other hand, there are several studies which indicate that there are major individual differences in positive vs. negative expectations towards an ongoing or upcoming event in some defined situations (Hahn 1997). As already highlighted, some specific personal characteristics have been again approved for their association to nocebo responses if mediated by spe-

cific defined situations. Specific situational variables have been also defined as mediators of specific nocebo associated traits (Stam and Spanos,1987; Drici et al. 1995; Mills 2006; Jakšić et al. 2013).

7.9 Revisited Association of Personality Traits and Nocebo Response

7.9.1 Pessimism Versus Optimism

Several studies introduced pessimism as a predictor trait for a nocebo response toward a pill. This is in line with the expectation theory (Barskey et al. 2002; Data-Franco and Berk 2013). Pessimistic individuals have been described as having more nocebo-prone personalities only if there is some sort of deceptive negative expectancy concerning the drug, but not when they are truly informed to expect positive effects along with unpleasant symptoms.

In the same way, optimistic individuals tend to benefit from placebo pills more than the pessimistic ones, provided that they are truly informed about the possibility of some positive effects, but not when they are somehow deceived by information which contains some sort of embedded negative expectation (Stam and Spanos 1987; Drici et al. 1995).

7.9.2 Neuroticism Versus Agreeableness

These are other traits found as predictors of nocebo and placebo responses respectively. Neuroticism is defined as the tendency to experience negative affect. Agreeableness, on the other hand, is a trait of accepting differences and adapting to variable degrees of the unwanted or the uncertainty in various situations.

7.9.3 Agreeableness Versus Hostility

Agreeableness is the predictive trait for a higher placebo response which is facilitated through a healthy therapeutic relationship. Conversely, angry hostility, as a facet trait of neuroticism, is highly correlated with not benefiting from a placebo analgesic treatment, even when positively introduced in general ordinary hospital settings (Mills 2006).

7.9.4 Resiliency Versus Non-resiliency

By definition, resilient individuals are those who are better able to recover from negative emotional experiences and flexibly adapt to the challenges of stressful situations. Resiliency and non-resiliency are known as predictive traits for higher placebo and nocebo responses respectively (Mills 2006; Jakšić et al. 2013).

7.9.5 Suggestibility Versus Non-suggestibility

The suggestibility trait was the most popular personality characteristic introduced by the old studies, followed by and closely related to the hypnotizability (Eysenck and Furneaux 1945; Cooper and Tape 2001). Altogether, researchers do not yet believe that there is a general factor of suggestibility yet (Mills 2006; Sedgwick 2013). However, the concept of suggestibility was an initiation for more active researches to find individual variables related to nocebo and placebo. Research studies had also proposed two different factors of suggestibility namely primary or idio-motor suggestibility and secondary suggestibility or gullibility or indirection (Eysenck and Furneaux 1945). The latter had been known as associated to a higher placebo effect; yet, there are no empirical demonstrations to support the reliability of the secondary suggestibility as well as the whole concept as a predictive factor for placebo/nocebo response (Jakšić et al. 2013; Mills 2006).

However, studies on suggestibility and hypnotizability have proposed that in stress situations, highly suggestible people tend to suspend their critical judgment and mental editing function. The mental editing function helps the person to decline the expected when it is disconfirmed through the evidence (Laarhoven et al. 2011). In extreme situations, many individuals experience a natural trance state in which they are highly suggestible (Harrington 1998; Drici et al. 1995). In other words, the error detecting mechanism in our brain is sensitive to a lack of confirmation of that which we had expected. This cognitive system may fail to do its performance in extreme stress situations; hence, the person tends to become more suggestible (Spiegel 1997; Mills 2006). This implies that inducing extreme measures of stress to human beings may make the individual suggestible enough to become enchanted into accepting any received information while their judgment system is turned off.

7.9.6 Extroversion Versus Introversion

In a few studies, a higher nocebo response has been found to be associated with introversion traits, while extroversion traits have been shown as associated with a higher placebo response. Again, this is in accordance with previous associations of variables like harm avoidance, neuroticism, reward dependence, and pessimism

(Mills 2006). The concepts of extroversion/introversion can be also linked to a new discussion on the internal and external locus of control.

7.9.7 Internal Versus External Locus of Control

People seem to attribute life events as happening either through their own will and behavior (internal locus of control) or to be brought about by external factors out of their control (external locus of control). The style of attribution may substantially differ for negative or positive events respectively. It is also linked to other situational factors. There might also be some individual variations in the attribution style in relation to personality traits along with situational factors. Conceptually, external locus of control can be imagined as linked to the extroversion concept; introversion traits on the other hand, seem to be conceptually close to internal locus of control, consequently, to a higher nocebo responsiveness (Hahn 1997).

When a person regards a disease to be at least partly caused by an unhealthy life style, their attribution style is one with internal locus of control. But when the person believes their illness has absolutely resulted from genetic predispositions or from air pollution, whether the belief itself is true or not, they attribute the event to an external locus of control (i.e., they perceive the locus of control as situated somewhere out of reach of self-regulation). Possible inter-relationships between internal versus external locus of control and a higher nocebo/placebo responsiveness, respectively, should be investigated more comprehensively in future.

7.9.8 Nocebo/Placebo Response and Temperamental Traits

While a reward dependence temperament has been found to contribute to placebo responsiveness, anxious emotional traits and an associated "harm avoidance" temperament have been associated to nocebo responsiveness (Hahn 1997; Colloca and Grisson 2014).

7.9.9 Nocebo/Placebo and Cultural Issues

"Ethno-medicine" as an element of culture can serve as a healing function; yet, it may be sometimes associated with higher nocebo responses in its members by giving them noxious, rigid, and rough information on the symptoms, etiology, and treatment of diseases (Hahn 1997).

7.9.10 Nocebo/Placebo and Attachment Theory

There are interesting studies which have tapped into the attachment theory in relation to placebo/nocebo responses. Studies have revealed a connection between an insecure attachment base with a low responsiveness to placebo effects (Enck and Klosterhalfen 2007, Mclean et al. 2007).

7.9.11 Nocebo/Placebo and Type A Versus Type B Personality

There are also a few studies which have proposed the "type A" personality as being prone to a nocebo response and the "type B" personality to placebo responses (Colloca 2012; Data-Franco and Berk 2013; Pietrie 1948). In another study, a lower score of time discount factor manifested as "impatience" or indirectly "time punctuality" has been found to be associated with vulnerability to "anticipation anxiety" and, therefore, a "nocebo pain response". It showed that impatient patients who value only very near events tend to take into account only negative effects of a medical procedure (costs), and a higher pain anticipation; while those patients who tend to value the far future beneficial outcomes when judging the present costs tend to have less negative pain anticipation (Brañas-Garza et al. 2012).

Concepts of impatience and low time discount seem closely related to traits of the so-called type A personality, so it seems there is an agreement between this study and the aforementioned study results. Self-scrutiny is another concept which has been linked to both the type A personality and negative anticipation leading to a higher nocebo responsiveness. From a temperamental standpoint, one can find an association between the so-called personality type A and a combination of harm avoidance and novelty seeking temperaments (Colloca and Grillon 2014). The inferable picture would be one of energizing persons who push themselves towards achieving the novel while at the same time tending to avoid any harm and hazard; you may see that such tendencies are very challenging. On the other hand, one can associate the type B personality to a temperament of lower novelty seeking and lower harm avoidance, as well as higher agreeableness, flexibility, and resiliency all in accordance with a lower nocebo responsiveness as well as a higher placebo responsiveness.

7.9.12 Other Associations to Nocebo Responsiveness

Other traits or states which have been revealed to be associated to a higher nocebo response include: higher levels of generalized distress, anxiety, depression, a heightened index of suspicion, a tendency towards somatization, symptom exaggeration, and a hyper-awareness towards bodily sensations (Friedman and Kewley 1987).

Evidently, in medical practice, patients who consider themselves as "especially sensitive to drugs" should be considered as particularly prone to manifest nocebo responses (Barskey et al. 2002).

7.10 How Situational, Temperamental and Other Psychobiological Factors Interact When One Faces an Unwanted Event

7.10.1 Active Harm-Avoiding Individuals

Such a person can be described as one of low flexibility who attributes control to an internal locus. Such a person may tend to overestimate the uncertainty (due to negative expectance); therefore, they may become over-engaged in trying out additional prophylactic and diagnosis attempts to prevent a negative event – for example, a disease.

From time to time, the active harm avoiding person can become hostile towards related-others when facing the unwanted. It can be a kind of defensive mechanism. In other words, having a tendency towards self-blaming when faced with the unwanted, the person sometimes projects the tendency to blame themself toward others; for example, the person feels guilty for not being able to prevent the negative event. This feeling grows more and more painful and reaches a point which is unconsciously non-tolerable by their mind, so they project the self-blaming toward others causing others to feel hostile towards them, which is much less difficult than feeling hostile towards oneself. Overt hostility would get presented only if such a person has a low predisposition for becoming dependent on social rewards; otherwise, they perhaps either continue blaming themselves rather than projecting it outward or try to hide their anger and hostile feelings towards important others to avoid losing possible social rewards from them.

There is still another problem, which high harm-avoiding controlling people may face in the health area; that is, by actively detecting threat alarms and trying to control them, they may find themselves in a non-tolerable over-focused state where they become concerned about their own controlling capabilities and push themselves towards controlling the risk factors even more. If such a person has a high novelty seeking temperament at the same time, they may occasionally experience some intrusive thoughts of self-harm or recurrent impulses to behave as opposed to what they desire. This can also originate from pessimistic traits which lead them to expect negative outcomes (the anxiety aroused from anticipating the loss of control over risks and hazards). When the urge for having health hazards under control reaches an extreme, such individuals are susceptible to experience paradoxically-intentioned impulses and drives or obsessive paradoxical ruminations which severely increase their anxiety.

For example, when the individual decides to control their weight, they begin to control their calorie intake; the greater the preoccupation with controlling the calorie intake, the greater the concern of being incapable to do so. Anticipating giving up control, the opposite images become anxiously aroused in their mind, pushing them towards eating delicious and forbidden materials. The impulses and the opposing rumination may eventually make their mental challenge and the consequent anxiety feelings more than tolerable so that they may act according to the impulses; they may give up the resistance towards a mental obligation and attempt to eat big amounts of delicious high calorie foods even when not hungry. Such undesired behaviors turn into a vicious cycle in which overeating increases self-blaming thoughts and the negative affect and leads to increased anticipatory anxiety and obsessive ruminations of "beware alarms" again. The resulted anxiety and self-blame in turn amplifies the paradoxical impulses and the cycle continues. Later we will discuss the public health educational implications of such a vicious cycle.

7.10.2 Passive Harm-Avoiding Individuals

When a person with a high harm avoidance trait perceives the locus of control to be external, they tend to somehow passively avoid the danger, but not actively undertake the prophylactic behaviors or utilize the protective measures. Such persons feels helpless toward harm and give up trying to change the adverse situations for the better very early in the process. They tend to blame others or external factors, complain about the unfortunate events, feel hopeless, and think that there is no helpful option of behavior to improve the situation. Nevertheless, if such a person has a strong temperamental trait of reward dependence, in addition to their harm avoidance traits, they may be rather compliant, just as if attached to a supportive medical care system that may be regarded as a source of social rewards.

7.10.3 Passivity in Low Harm-Avoiding Individuals

As an extreme opposite to the high harm-avoiding individuals, a low harm-avoiding individual perceives an external locus of control, and due to a lower harm avoidance, may be neglectful and careless towards health, unless they have acquired deep insight and commitment through personal growth. Such a person tends to take it easy and behave carefree. They are not driven by their health care or its inherent traits; thus, they may not feel pushed towards complying with the preventive or treatment advices or drugs unless they are already justified and insightful toward them. They would also perhaps not readily adhere to the medical systems when becoming sick. Yet, if such an individual is predisposed to a high reward dependency, it is inferable that once adherent to a medical care giver (e.g., a medical doctor), they would perhaps comply with the recommendations to feel socially rewarded by creating a good relationship to their doctor.

7.10.4 Active Controlling in Low Harm-Avoiding Individuals

A more active non-harm-avoiding individual who attributes control to an internal locus can be a person who may realistically and reasonably analyze the cost-effectiveness issue and tailor their health-related behaviors to the standards derived from such an analysis. Indeed, healthy behaviors for such a person are majorly dependent on other inherent or acquired characteristics like the power of reward dependence traits, insight, health knowledge, and availability of a qualitative open health system.

It is time to shift our attention from the biological and psychological variables towards the social factors linked to nocebo/placebo concepts. Reviewing the literature here, we tend to figure out how all of the previously mentioned factors may be connected and re-explored to become applicable in the society and health systems. As concepts of risk, danger and cost-effectiveness are embodied in all social issues, we are going to elaborate on these concepts in relation to negative and positive expectations toward health.

7.11 Risk, Danger and Cost-Effectiveness and the Public Health Behaviors

Health protection is essentially linked to the concepts of risk and danger. As already mentioned, dangers are threats originating in the environment. Thus, they are situational factors against which we protect ourselves by regulating our distance to them. Risk, on the other hand, is another related concept rooted in our behaviors and choices. For example, sun exposure is a known risk factor for skin cancer and eye lens cataracts; here, sun exposure is the risk and cancer or cataracts are the dangers. Yet it would not be possible for us to avoid sun exposure completely. So we choose to wear sunglasses and use sunscreen, which do not provide total avoidance – these are protective factors and our choices. We tend to gather information about risk factors to apply proper protection to control the risks and, thereby, avoid the dangers.

As our knowledge about risk gradually increases, we sense more threats and expect more negative events. This will in turn increase our tendency to control the risks. As nobody can undertake all of the known prophylactic measures, the extent of prophylactic behaviors that we would apply turns to a matter of cost-effectiveness. We should assess costs and effects and figure out how and what to what extent we can control risks and to avoid dangers.

It is the exact point where the individual factors get taken into account. Like any other choice in our lives, individual 's choices and decisions for health are made by weighing costs versus effects. Needless to say, the decision about how to s et the cost versus efficacy measures is partly made according to the personality traits and characteristics. It also depends on the severity of the danger, the feasibility of risk

control, and the significance of the person whose health is being considered for the one who overtakes the costs.

An instance would be as follows: A father takes his 6-year-old child to a pediatric clinic twice a year for the recommended 6-month-interval visits to the family physician to monitor the child's health status. Four years ago, the same physician had diagnosed the father as suffering from high blood pressure and recommended him to visit the clinic in 3-month intervals to monitor his blood pressure; yet, by now, he has missed all but two of the appointments for himself, while his child's regular visits have never been missed. This father seems to be readily willing to pay the needed costs for the sake of his child's health (the cost here is taking the child to the health clinic regularly and devotedly) while he tends to ignore his own health and not pay the cost of adhering to a 3-month-interval follow-up program.

When you donate your kidney to a loved one, you altruistically choose some risks which may present the danger of renal failure. However, you choose to do it for saving the life of a loved one. Even as a matter of generosity, the act of donation still depends on the situational factors; for example, if the one in need of your kidney were a 90-year-old far away relative, you might not be as generous.

7.12 Social Iatrogenesis: The Nocebo Response Induced by Social Health Systems

Could any harm be caused through the "beware of harm" messages which the media distributes amongst the public? Let us discuss the answer through an example:

Leila is a single 22-year-old female university student who lives in a big city with her parents. Leila has always sort of anxiety; she describes herself as an ever-worried girl. Temperamentally (suppose that you know), Leila has traits of high harm-avoidance combined with high novelty-seeking traits. She also feels a constant urge to put all minor and major life issues under her control as soon as possible. Regarding attribution style, Leila tends to attribute events to an internal loc us of control. She believed that she should be in control of her life; she feels responsible and tends to blame herself for all minor and major problems which arise in her own life every now and then. However, when things get out of her control, she tends to blame others as well if they have somehow contributed to the problem (albeit very slightly) through their minor mistakes and faults.

On the other hand, Leila is proud of the areas of her life which are under her control (e.g., body fitness) and dislikes people who don't care about their own body weight, fitness, and health. Yet, since a few years ago, she has been privately blaming herself for areas of personal weakness or failure (e.g., for not being able to establish a durable friendship, as well as for having lost her natural feelings of happiness a few years ago for no clear reason). Leila actively avoids exposure to health hazards as much as she can. As her mother is a breast cancer survivor, Leila found her own mind increasingly preoccupied with how to avoid the general risk factors

of cancer, especially those risk factors which are almost always out of her control such as air pollution and stress. Air pollution and stress are the two risk factors, which her mother blames frequently for her breast cancer development.

Leila tries to stay at home whenever the weather reports the air pollution to be above the healthy standards. She also tries to manage her stress by participating in meditation training groups, practicing muscle relaxation techniques, and regular exercising. Yet Leila still suffers from constant distress, far beyond what is needed for keeping things under control. Leila tends to avoid stress, yet she bears substantial extra stress whenever a stressful event happens to her. When a stressful situation is over, Leila experiences even more stress than that of the situation itself; thinking over and over about why she has been faced with it and how she could have prevented it.

Leila has gathered a vast amount of information about cancer, healthy life style, stress management, air pollution hazards, and other such issues through numerous health education websites, workshops, seminars, books, magazines, T.V, and radio programs, and the hospital clinic staff who treated her mother's cancer. Recently, Leila has begun taking part in self-help groups for family members of breast cancer survivors where she receives a lot of new information in each session alongside support and empathy. She regularly visits her family physician and has shortened the interval between the visits; sometimes, she even asks for an extra visit to inquire about something she has found in her breast exam or to discuss some other bodily concerns. The family doctor is a middle-aged man who has a calm and accepting attitude and reassures Leila in each session.

In general, health hazards which one tries to avoid or to control can be classified into two groups: the first group of risk factors is tangible, avoidable or controllable; the other group of risk factors is sort of vague, general, less avoidable, an d less controllable. Not drinking non-pasteurized milk to prevent brucellosis is an example of the first group of hazards. Stress is the most typical hazard of the second group.

In Leila's case, although her mother was once advised by her doctor to avoid stress, no further information had been delivered on how much stress can be harmful or how to avoid it. Any stressful life event thereafter, including even minor daily hassles, preoccupies Leila's and perhaps her mother's minds. Moreover, from time to time, an argument happens in which Leila blames her mother for a stressful reaction towards a recent event, while her mother blames her husband as a major source of stress causing her breast cancer. Leila once talked to her family physician about the distress she experiences just while trying to avoid other types of stress, and the doctor tried to reassure her by saying that stress is unavoidable. However, Leila feels even more anxious thereafter, as she assumes she is be completely helpless towards stress as an important risk factor which, according to the doctor's comment, is always present and constantly causing harm.

Leila is an extreme example of harm-avoidant individual who tries actively to control almost all controllable health hazards she knows as far as possible; however, she is becoming more and more hyperaware of the uncontrollable ones. As a result of her pessimistic attitude toward health, Leila tends to overestimate the non-

controllable risk factors and keeps trying to find a way to exert control over them. When she was an adolescent, Leila witnessed her mother's breast cancer diagnosis despite her devoted attention and care towards all hygienic advice, maintaining a healthy diet, doing regular sports, and performing other measures of prevention. At that time, Leila herself was assessed for possible genetic receptor similarities between her mother and her to determine if some preventive interventions would be needed. Leila was relieved when she was informed that the assessments had categorically ruled out such a similarity.

As for genetic vulnerability, there is no other controlling or preventative strategy, Leila tries to forget about it; yet, she feels some constant fear of the danger somewhere in the back of her mind and she compensates by increasing her prophylactic behaviors. The positive side of her awareness is that Leila is rather engaged in prophylactic and health perpetuating activities. Yet, the negative side is that Leila cannot relax even when the known controllable risk factors are already properly controlled. This is somewhat due to the result of her pessimistic and non-flexible attitude towards health, which is partly due to her general negative affect and biologic pessimistic predispositions combined with her childhood experiences as a psychological predisposing factor.

Gradually, this non-relaxing hyper arousal state becomes more complicated by disturbing signs and symptoms related to an increased autonomic response such as insomnia and palpitations. These symptoms in turn dramatically increase Leila's anxiety and concerns about stress avoidance. As an upshot, due to everything mentioned thus far, the story ends with Leila suffering from severe panic attacks and being referred to a psychiatrist for treatment of her panic disorder. This is a typical example in which negative expectation and anticipatory anxiety develops into a disturbing anxiety disorder, which in turn may be regarded by the patient as a source of risk. No matter how hard we try, we will never be able to control, prevent, or eradicate all health hazards. All we can do is to keep a reasonable distance from dangers and utilize the preventive measures.

7.13 But How Far a Distance Should We Keep from Danger? Where Can We Feel Safe?

These questions are difficult to answer because the attitude towards health is widely variable among individuals and societies. So far, there has been no rule for quantifying the reasonable amount of concerns one should have regarding a health condition. This is not a question about choosing cost versus effect, but a question of where to stand in between the two. When looking at the spectrum of cost-effectiveness, healthy behavior, preventive activities, health status, and checkup measures, among many others, behaviors are considered as costs and staying healthy is the effectiveness. At all costs, we have to accept various amounts of uncertainty in life including, to some extent, out-of-control events such as various sorts of

accidents or natural disasters. We also need to be able to face various extents of the unpredicted negative events in our daily life while we continue feeling secure and confident otherwise.

The proper amount of costs to be paid for health depends on the threshold beyond which our life quality becomes impaired; in other words, seeking health is reasonable as far as it serves to maintain or improve our quality of life, and we should reconsider costs and effectiveness as soon as we find ourselves harming the quality of our life in pursuit o f better health. Flexibility as a facet of both concepts of agreeability and resiliency is a trait or a situational attitude which allows us to be comfortable with various degrees of uncertainty in various situations, or allows us to keep our basic feeling of security when facing the unpredicted. When facing the unwanted, a highly flexible person can accept, to some extent, the uncontrollable event; they are also able to and tend to face the unpredictable events even with the knowledge that may possibly fail at controlling it.

Again, we shall never know with certainty how much flexibility is enough or proper. The optimum threshold or cut -off point of flexibility would be no more specified than the point or degree beyond which our life quality would be improved or maintained while we are assuming healthy behaviors and avoiding risky ones. For example, by managing stress in pursuit of a higher health, Leila is standing in the zone of healthy health-related behaviors as far as she sticks to a healthy diet, exercises regularly, adheres to the standards of preventive measures, has desirable social contacts, continues doing leisure activities, and so on. However, she has entered the unhealthy zone as soon as she finds herself thinking over and over about the amount of stress she has experienced recently, becomes preoccupied with questions regarding the consequences of too much stress, feels unhappy and worries, tends to lose her social contacts, avoids interpersonal stressful situations, and feels dissatisfied with herself or discontent with her health behaviors.

To reiterate, among the mentioned variables associated to negative expectancy, no individual trait or emotional state can be the etiology on its own; but the interaction between such factors with different situational specificities can determine different health outcomes. Again, as an example, Leila might have developed less negative anticipation if she had not been faced with her mother's disease during her early adolescence or if she could have expressed her concerns to the doctor. In the latter case, the doctor could have educated her about the concepts of positive stress, as well as negative and optimal stress. Such insight might release her from the responsibility to abolish stress from her and her mother 's lives. There is a great deal to be discussed about the doctor–patient relationship and how to convey health-related advice. At this point, we may simply focus on a very narrow segment of the very broad issue of communicating health and medical information to people. To avoid causing harm by inducing negative expectations as health care professionals, we are going to highlight one important rule of communication, possibly among several others. The rule we intend to discuss is almost always applicable in any society or medical/health setting regardless of what the message is, who the messenger is, and with whom the message is to be shared.

7.14 How Can We Intensify Nocebo Responses?

It is time to sum up the various biopsychosocial factors which cause us to be prone to the nocebo effect. In a reverse way, we will show here how we can increase our chances of becoming sick and actualize negative health expectations. Figure 7.1 represents a schematic model of nocebo production which is based on the previous documents and reasons we discussed before.

As shown in the diagram, the main determining factors are hyperindividualism as a global trend, harm avoidant temperament, passive attitude and/or pessimism as predisposing factors, and stressful events and traumas as triggers and/or aggravating factors. The hyperindividualism draws almost all of our attention to our body and its functions as the crucial prerequisite of being a worthy individual. Acceptance of defects, losses, disorders, and death in such an egoistic worldview is very complex and challenging. Medicalization, healthism and lifestylelism and their taboos, instructions and rituals ensure the sanctity of individual life. The overwhelming health warnings induce anticipatory anxiety and subsequently avoidant trends in modern societies. To avoid potential dangers, we should keep a healthy distance by thinking and screening, along with any other reassurance seeking measures. The tragic fact is that when you mention more parameters by higher sensitivity, the uncertainty will paradoxically rise. This vicious cycle induces health anxiety and consequentially avoidant behaviors.

Avoidance of dangers is a very effective and preliminary adaptive behavior but it needs some degrees of acceptance of unpleasant events in order to organize our coping. Otherwise, avoidant behavior could become an uncontrollable maladaptive behavior which restricts access to our resources and makes our self-image more exposed and labile although it is directed towards maximum security. Therefore, excessive avoidance paradoxically makes us vulnerable and anxious. It facilitates negative expectations and, consequently, nocebo responses.

An empathic and illuminating doctor–patient communication and referring the individual to a psychotherapist in serious cases can change the client's interpretation and moderate health anxiety and its consequences. Negligent and disease- oriented approaches to these clients make them prone to nocebo effects and gradually may cause organic disorders. After a glance at nocebo semiosis and its psychophysical pathways, it is time to discuss how we can change the processing of signs towards salutogenesis and higher health.

7.15 The Way Out of Iatrogenic Nocebo Effects

In this framework, biosemiotics could be a common language which helps us follow the flow of signs through the physical, mental, and interpersonal worlds. Signs create our health conditions and forms of life in the form of electric and electronic signals, protons, molecules, and cells; concepts, emotions, beliefs, and dreams;

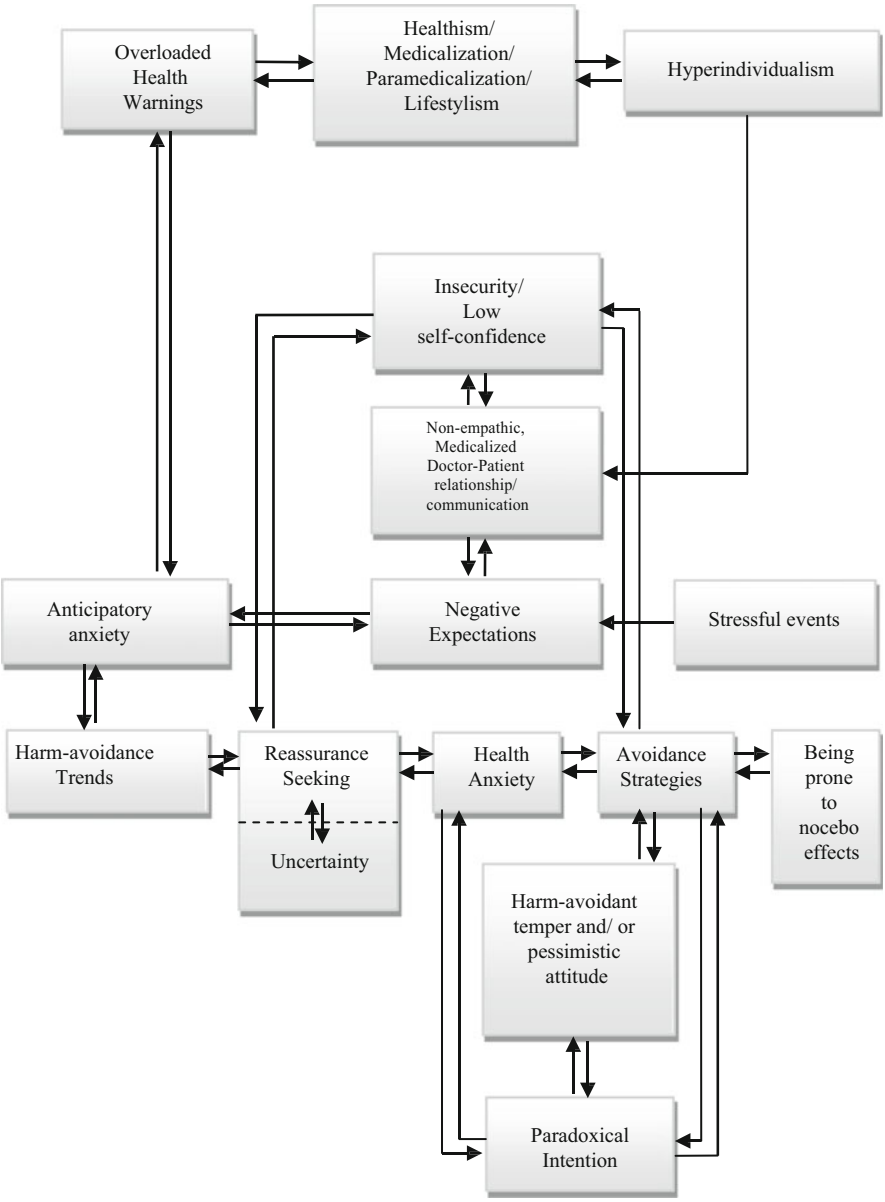

Fig. 7.1 The biopsychosocial pathways of inducing and reinforcing nocebo responses; a reverse modeling

relations, contracts, and laws. To reorganize the meaning and effect through this multilevel system, we need a more complex and integrative model for health education. Health behavior change and psychoimmune modulation as the main objectives of health education are related to cognitive-emotional reprocessing; thus, it requires a systemic model to formulate autonomic, effective, and safe informational interventions.

In the following, some of the considerations in a biopsychosocial health education to maximize the placebo responses and minimize the nocebo responses are briefly discussed, and the systemic worldview, resource-based approach, qualitative life, and health continuum are highlighted.

There is no way to neglect our experimental science and no need to abandon the objective, pathological, and disease- oriented approach to health, but it is not sufficient. Also, the interpretation of the health phenomena in this context leads us to a paranoiac worldview and brings about more insecurity and anxiety. We are seeking an integrative way to reinterpret health and illness in order to optimize health education and minimize the nocebo effect of our informational interventions. Our vast and valuable knowledge and experiences in the systemic approach to life and health – especially in the recent decades – provides an integral platform to profit by complementarity of the quantitative-qualitative knowledge, the pathologic-salutogenetic practice and the reductionistic-holistic epistemology.

7.15.1 Systemic Worldview

At first glance, it seems that these shortcomings are inevitable costs of individuality and development; however, it can be considered as a transitional condition from the traditional to the postmodern episteme. Our findings in physics and systemic biology show us that we are not alienated individuals "in" relation to the others, but we are holons; living systems which are emergently constructed from the lower levels of organization, and, at the same time, a part of higher health in the hierarchy of life (see, e.g., Wilber 2007; Luhmann 1995; Simon 1969).

Our self-actualization is related to our understanding of our biopsychosocial matrices. Beyond the local survival struggles, we can find a universal harmony, which cooperates genes (Ridley 2008; Attwater and Holliger 2012), increases significance of signs (Sørensen et al. 2012) and promotes evolution and nurtures a symbolic planet (Margulis 2008). Our hyperindividualism, alienation, selfishness, and consequently, our health anxiety could be moderated via this systemic worldview. We as holons would be more secure than lonely selves surrounded by countless dangers and threatened by numerous faults and risks.

7.15.2 Resource-Based Approach

Naming the illness experiences in the form of categorical concepts has gradually represented the disease as bad character that threatens our life, especially when we put a disease's name in the subject of a sentence. We implicate that disease is an intelligent animated entity and it is not very far from the shamanistic physiopathology.

The so-called facts like "diabetes can cause tingling and numbness" is formally very similar to this shamanistic explanation "black wind causes seizures". Our warning messages that serve to avoid dangers and dangerous behavior are more focused on the disease and its consequences. The pathological approach is appropriate for medical education and practice, especially in acute conditions; but for living with a chronic illness and community education, salutogenetic and resource-based approaches seem more effective and less harmful (see, e.g., Antonovsky 1987; Ray and Keenet 1993; Golembiewski 2010). Focusing on how to find and actualize our resources, how to change our lifestyle, and how to promote our self-efficacy would be more helpful than increasing fear of the dangers of pathogens and diseases, and the risks of maladaptive behaviors.

7.15.3 Qualitative Life

Objectivity and quantitative research are of the main values of modernity and, of course, biomedicine. The main reason for emphasizing these concepts is to avoid an illusionary world and metaphysical dogmas and to find repeatable and falsifiable facts; however, qualitative aspects of life and being values are also unfortunately neglected.

The epistemological objectification in biomedicine has gradually turned to the ontological objectification and the human being has been transformed into a naked object.

Objectification of human beings is a real threat for a qualitative life. It makes us profoundly vulnerable and prone to insecurity, meaninglessness, and alienation.

According to philosopher Martha Nussbaum (1985), a person is objectified if they are treated:

- As a tool for another's purposes (instrumentality).
- As if lacking in agency or self- determination (denial of autonomy, inertness).
- As if owned by another (ownership).
- As if interchangeable (fungibility).
- As if there is no need for concern for their feelings and experiences (denial of subjectivity).

Unfortunately, as you can infer from the cases, some degrees of all of the modalities of objectification are recognizable through biomedical research and/or practices. To de-objectify human beings, we should highlight qualitative aspects of lives and

draw our attention from "doing" values (quantity of life, social function, and anthropometric indexes) to "being" values, such as wholeness, truth, playfulness, and self-sufficiency. To establish a qualitative life, we need to live our being values and develop our presence (Maslow 1968, p. 83; 1975, 44–50).

7.15.4 Saying Yes to Life

Acceptance of unpleasant events (dangers) and commitment to our performances (risks) is a good initiation for being present and tolerant. Acceptance and commitment therapy (ACT), as an integrative-existential therapy, emphasizes the acceptance of present-moment experiences including thoughts and feelings (Schneider 2008, p. 219). There is plenty of evidence which determines the efficiency of this approach, especially in anxiety disorders such as panic (Lopez and Salas 2009) and obsessive-compulsive disorders (Rosa-Alcazar et al. 2008).

It seems that development of self-awareness is developed only to which extent we can accept the events; otherwise, it could be turned into self-consciousness and, consequently, obsession and anxiety. Highlighting being values and empowerment of acceptance could moderate our health warnings and prevent the nocebo effect. A humanized human could be more secure and adaptive than an objectified one.

Drawing a sharp line between health and illness makes us fearful and worried about slipping into the illness world and turning into a sick person. This binary system is not only inappropriate in establishing adaptive coping strategies, but also is basically not true. A health continuum model could be more realistic and helpful – a scale which interprets our health conditions by degrees of wellness-illness. By this model, we would be more flexible and we could form a unique strategy for health and illness, health promotion – and our main objective – higher health. Even a person at the final stages can think about changing his attitude towards higher levels of consciousness and bliss. Therefore, the will to achieve higher health and consciousness evolution, as entelechy of mankind, could be the context in which we interpret all of the health and illness phenomena in it in a more active and effective manner.

7.16 Some Practical Notes

The following is a summary of the practical implications discussed in the chapter:

1. Advice for health may sometimes impair the receiver's health if it produces enough negative expectencies.
2. There are so many things in the world which may potentially harm our health. There are massive amounts of information available regarding health hazards. As innocent and beneficial such information may seem, they can burst into

harmfulness for health once they are conveyed to a health-anxious society via non-appropriate public messages or news.
3. Medical science – the profession of health – should consider delivering its scientific material with proper hygienic methods; otherwise, it may act as a source of contagious infection when spread among people.
4. The outcome of a negative health message varies significantly, at least partly depending on where it goes. If it lands on the fertile ground of pessimistic, inflexible and overanxious harm avoidance, it will almost certainly cause harm. If it find s its way to the optimistic, resilient, and agreeable ground of reward expectance, however, it may never grow into significant harm.
5. An innocent factor, which has been perceived as an enemy for health, may express some real enmity even if regarded as friend by the medical orthodoxy.
6. The key to a healthy life is not doing too much to improve health, neither is it avoiding too many things in order to prevent illness. The key is to live modestly, to keep committed toward improving our life quality at any time – whatever our health status is – and to positively look forward to a better health in the future.
7. There is no point in hiding from stress, it is always around us. Some stress is essential for completing daily tasks; all we should do is positively manage the extra amount.
8. As health professionals, we should better educate people on what to do in order to enhance their health, rather than what not to do to avoid illness.
9. As health professionals, we should educate ourselves in how to reframe medical facts into positive facts.
10. As health professionals, we should stand on the safe side of all forms of education by trying to enhance optimism and avoid creating negative expectance.
11. As health professionals, we should get trained on delivering bad news in a good yet truthful way. This skill should be regarded as one of the most important parts of educational curricula for all medical sciences students.
12. Human health control has been programmed inside humans themselves. It is neither in the doctors' hands, nor in the advanced medical schools, hospitals, books, or evidence-based knowledge. All medical professionals can do is to become familiarized with this locus of control in order to direct it towards the right outcome; this would be possible only through adequate communication. Hence, becoming skillful in the communication field is the primary footstep for anybody who is going to be a medical doctor or a health expert.

It is remarkable here that we need to figure out an evidence-based protocol to apply the concepts of mental reality (including positive or negative expectance) for enhancing human health. That is our hope and idea that we intend to convey. There was a broad area and a great deal of science to address related to the topic of this chapter – too much to thoroughly accomplish. Yet, we hope to have opened the discussion in order to stimulate the professionals' minds once again to this topic. A great deal of further communications and reflections is needed before being able to present an organized and comprehensive illustration of this topic in a not-so-far future.

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