



Review Article

**A Critical Indication of Contemporary Ethical Dimensions of Placebo in Medicine**

Chimezie Nnadozie<sup>1</sup>, Franca Nneka Alaribe<sup>2</sup>, Victor Nnadozie<sup>3</sup>

<sup>1</sup>Department of Philosophy, John Vianney Seminary, Pretoria, South Africa

<sup>2</sup>Department of Biomedical Sciences, Tshwane University of Technology, Pretoria, South Africa

<sup>3</sup>Teaching and Learning, College of Humanities, University of KwaZulu-Natal, Durban, South Africa

**Correspondence Author:**

Gabriel Chimezie Nnadozie (PhD)

Email:chimeziennadozie@gmail.com

**Received for publication:** May 30, 2017; **Accepted:** September 5, 2017.

**Abstract**

The rational for placebo in medicine is a dynamic one and its mutating ethical dimension is being fostered in three basic viewpoints which are: that placebo is obsolescent due to increase in diagnostic and medication possibilities; that placebo is fraud and deception of patients; and that placebo uses as medical research tool can be avoidable. In a nutshell, with advancements in medicine, placebo has grown morally vague to the extent that the imperative point of departure for a placebo ethics ought to be to find the moral foundation of placebo. Hence, alongside expounding a moral foundation of placebo in medicine, this paper brings critical insight to bear on the approach and the grounds warranting ethical valuation of placebo use in medicine today.

**Keywords:** Placebo, Placebo Ethics, PCT Ethics, ACET Ethics, Biomedical Ethics, Placebo Justification

**INTRODUCTION**

Placebo in medicine is quite old but its ethical concerns are not. The ethical concerns of placebo in medicine mutate alongside trajectories in medical advancements and practices. Thus, rationalising use of placebo from a medical ethics perspective would certainly mean that we examine understandings of contemporary justifications for scope and veracity of placebo use in medicine. This means that for us to understand the current justifications of placebo use in medicine, there is the need to first understand the main concepts that underline current uses of placebo where its ethical concerns emerge. In this paper, we try to examine the mutating trends and ethical justifications for placebo use in medicine and the underpinning current concepts. The sections that follow progresses the discussion on two broad headings: concepts of placebo in medicine; and avenues and current rational for ethical valuation of placebo in medicine.

**SECTION 1: CONCEPTS OF PLACEBO IN MEDICINE**

Perhaps intuition and just intuition only can give us the primary significance of placebo in medicine. It does not need much rational commitment to understand that placebo made its debut in medicine with notions typical of common forms of compassion like sympathy, care

and empathy. Common forms of compassion involve feeling for another. The common notion is that active compassion is the desire to alleviate another's suffering [1]. We are inclined to believe that in early medical practices, the desire to alleviate patients' sufferings perhaps did not preclude the notion to alleviate and to console. Substances or medical procedure both pharmacological and otherwise, active or not, were considered therapeutic if it alleviates and or consoles. Medical practitioners had the duty to cure but also a very important one to console. In view of these notions, one could infer that placebo as a medical therapy emanates from the approach to the medical practitioner's duty, which is to alleviate and console. Placebo practices therefore gained conceptual tractions being first understood as physician's duty in good faith; encouraged by patient's due expectations from the medical practitioner, the therapeutic results, and consequent researches and their unequivocal outcomes.

*1.1: Placebo: the physician's duty in good faith*

The Ancient Greek physician Hippocrates (460–370 BC), generally recognized as the father of Western medicine [2, 3], is said to have recommended to medical practitioners to cure sometimes, treat often, comfort always [4]. In the development of Western medicine,

Hippocrates' ideas and values found favour and dominant approval. The Hippocratic Oath, which is still sworn to today by all physicians [5], attests to his huge influence on conceptual approaches to medicine as well as on the important figures in the history of medical practice. For an instance, Ambroise Paré (1510–1590) reaffirmed that it was the physician's duty to cure occasionally, relieve often, console always [3]. Yet, parallel to the Hippocratic approach, Western medicine developed with significance given to compassionate or altruistic concerns for the 'neighbour'. This was implicit in the Middle Ages as the monastic traditions evolved, which meant that caring for the sick was inspired by the 'love thy neighbour' ideal of the Christian gospel [3]. Furthermore, the evolution of consolation approach to treatment logically consolidated in the idea that prescribing morale-boosting and pleasing remedies such as sugar pill and non-active pharmaceutical syrups are therapeutic. These morale-boosting therapies, while having no pharmacologically active ingredients, are believed to reassure and comfort the patient, albeit the patient is thought to be restored to health by the healing power of nature [6]. In the period running through the middle of 1500 and the early 1800, physicians and philosophers alike including Michel de Montaigne (1533 – 1597), Johann Nicolai Pechlin (1644 – 1706), John Dogulas (1721 – 1807), mostly upheld the notion of the healing power of nature, which in clearer conceptual expression tended to explain pain relief from the perspective of patient's expectations [7].

### 1.2: *Placebo: the patients' expectancy that matters*

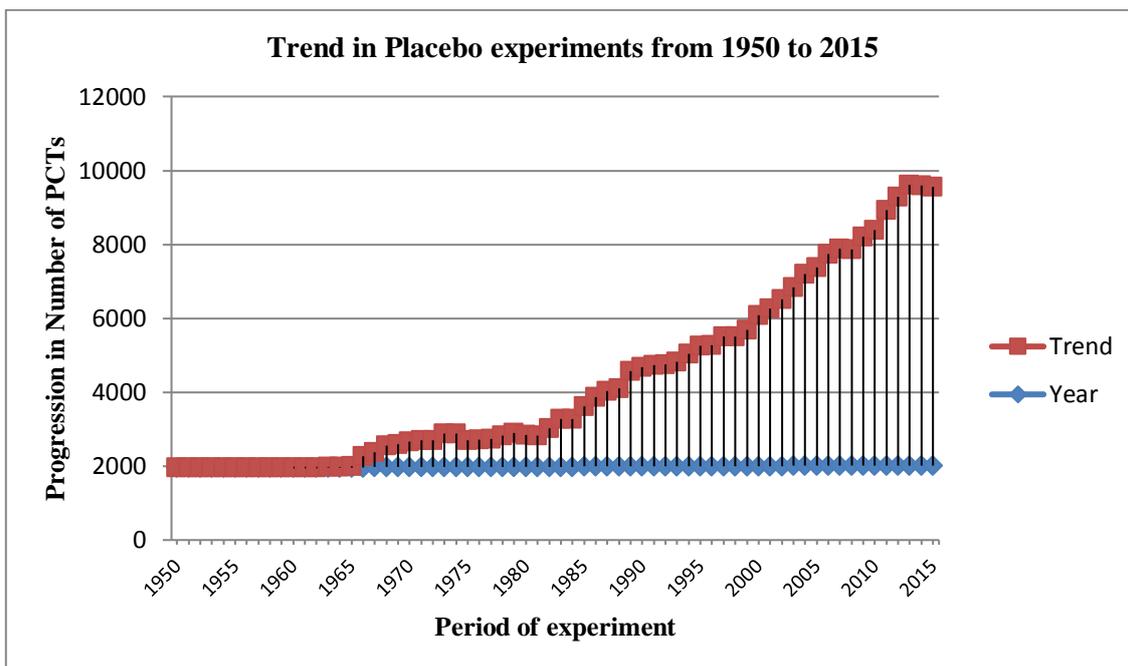
Long before modern medicine, the effect of the consoling approach to treatment was known. However, in recent history, this effect was connoted as 'placebo effect'. The placebo effect is traceable to conceptions of nature as primary healer, which has potency to cure diseases. Again, faith and hope and the cognitive expectancy of cure had been the bedrock of medications and their effectiveness. However, paradoxically this is not the case in placebo because with placebo, the substance is categorically known to be pharmacologically not potent for the health condition being treated. In other words, on the part of the medical practitioner, there is no belief nor cognitive expectancy that the substance will be 'pharmacologically' effective. There is however the important fact of confidence of patients in the skill of their physicians and the hopefulness that they feel while being treated. Studies have shown that since early 1700s, practices of placebo as part of the medical practitioner's duty, which arise from the perspective of Christian neighbourly love,

gradually changed from the faith-based perspective to the rational approach [3]. The rational approach stresses correctness of application and technicalities of procedures. Yet, neither trends in history, nor innovations in medicine seem to have fundamentally changed the continued favour of the concept of placebo as therapeutic.

Placebo remained effectual, perhaps because of the long standing concept that the eager confidence of the patient in the skill of his physician, and the firm expectation of relief by his means, has sometimes a wonderful efficiency in restoring health [8, 7]. Studies suggest that one explanation for placebo effect is that the hope of cure that the patient feels while being treated translates into a physiological surge of specific hormones and other biochemicals in the body. These then react to trigger therapeutic immune responses [9]. A particular class of hormones implied in these suggestions is the endorphins, which carry messages from the nervous system through the bloodstream to the endocrine and immune systems to induce the production and release of other biochemicals that contribute to healing [9]. It is possible to, then, argue that if all these inducements are naturally taking place, not as a result of the effectuality of a pharmacologically potent medication, but due to the patient's certain hope of cure which is effected in her/his belief in the medical practitioner's skills, placebo has a possibility of ethical justification for its therapeutic uses.

### 1.3: *Placebo: the Medical Research Tool*

The nature-healing concept implicit in placebo-effect was first demonstrated in 1799 by an English physician John Haygarth (1740–1827) [10]. Haygarth's perhaps first of what is today known as Placebo Controlled Trial (PCT) in medical research, was on a popular remedy of his time called Perkins-tractors. The Perkins-tractors are sort of metal rods supposed to relieve symptoms through the electromagnetic influence of the metal when applied on the body. Moved by the high cost of the metal rod, Haygarth prepared a comparative research with wooden-tractors. He treated 5 patients, using wooden-tractors. His results showed that 4 out of the 5 patients were relieved. The following day, on using Perkins-tractors, Haygarth obtained same result, which merely served to show that the high cost Perkins-tractors was unnecessary [11]. Since after Haygarth's experiment, boom of interest in similar subsequent experiments have been recorded.



**Fig. 1: Trend in Placebo Controlled Trials (PCT)**

PubMed publications from 1950 to 2015 show steady progression in placebo experiments over the years.

Though some of the experiments may be characterised by pragmatic belief in the natural forces that help healing in general, these experiments nonetheless imply a profound change in the concept of placebo in medicine. The increases shown in PCT trend in the use of placebo as research tool also added to increases in trusted diagnostic and medication possibilities. But PCT, the attractive trend of using placebo as research tool, together with the increasing trusted diagnostic and medication possibilities combine to influence current rationale for ethical valuation of placebo in medicine.

## SECTION 2: AVENUES AND CURRENT RATIONAL FOR ETHICAL VALUATION OF PLACEBO IN MEDICINE

In brief, considering its retrospective therapeutic purpose, placebo has grown morally vague and its mutating ethical dimension is being fostered in three basic viewpoints: the viewpoint that placebo is obsolescent due to increase in diagnostic and medication possibilities; the viewpoint that placebo is fraud and deception of patients; and the viewpoint that placebo use as medical research tool can be avoidable.

### 2.1: Placebo: the outdated therapeutic resource

In contemporary medical practice, the uses of placebo in medicine continue to enjoy high interests. There is however the fact that though interest in its clinical

therapeutic relevance is increasing (Fig. 1), placebo is often ironically mistaken to circumscribe an insignificant aspect of modern medical therapy. This happens largely due to changes in the notion and conception of placebo which we attempt to elucidate in this paper. First, since its early medical usage, placebo means more than a word or a terminology for a certain class of substance used in medication. It consists of a certain approach to medication that includes both the art of prescribing and the substance prescribed. The 1785 *New Medical Dictionary* defined placebo as a commonplace method or medicine [12], practically placing the prime importance in the art of prescribing rather than in the substance prescribed. Second, two forms of placebo use are therefore identifiable; namely placebo method and placebo substance. In the early medical usage, placebo weighed first and weighed more on the consoling (methodical) approach. The medical practitioner's gesture functioned as psycho-therapeutic cure. There was little consideration for what the substance of prescription was composed of. Today the concept of placebo tends to weigh more on the importance of the substance being prescribed. Accordingly, current dictionaries definitions of placebo emphasise on placebo - the 'substance'.

**Table 1: The overwhelming definition of placebo emphasising on ‘placebo as substance’****Some current definitions of Placebo**

	<b>(Dictionary.com, Web. 28 August 2017)</b>
(1)	1. A substance having no pharmacological effect but given to satisfy a patient who supposes it to be a medicine. 2. A substance having no pharmacological effect but administered as a control in testing experimentally or clinically the efficacy of a biologically active preparation.
	<b>(Collins English Dictionary, Web. 28 August 2017)</b>
(2)	1. An inactive substance or other sham form of therapy administered to a patient usually to compare its effect with those of a real drug or treatment, but sometimes for the psychological benefit to the patient through his believing he is receiving treatment. 2. Something said or done to please or humour another.
	<b>(The American Heritage Stedman’s Medical Dictionary, Web.28 August 2017)</b>
(3)	1. A substance containing no medication and prescribed or given to reinforce a patient’s expectation to get well. 2. An inactive substance or preparation used as a control in an experiment or test to determine the effectiveness of a medical drug.
	<b>(The American Heritage Science Dictionary, Web. 28 August 2017)</b>
(4)	A substance containing no medication and prescribed to reinforce a patient’s expectation of getting well or used as a control in a clinical research trial to determine the effectiveness of a potential new drug.
	<b>(The American Heritage New Dictionary of Cultural Literacy, Web. 28 August 2017)</b>
(5)	A substance containing no active drug, administered to a patient participating in a medical experiment as a control.
	<b>COBUILD Advanced English Dictionary (Web. 28 August 2017)</b>
(6)	A placebo is a substance with no effect that a doctor gives to a patient instead of a drug.
	<b>(Webster’s New World College Dictionary, (Web. 28 August 2017)</b>
(7)	1. The first antiphon of the vespers for the dead, beginning with the word placebo. 2. A harmless, unmedicated preparation given as a medicine merely to humour a patient, or used as a control in testing the efficacy of another medicated substance.
	<b>(Merriam-Webster Dictionary, Web. 28 August 2017)</b>
(8)	1a. A usually pharmacologically inert preparation prescribed more for the mental relief of the patient than for its actual effect on a disorder. 1b. An inert or innocuous substance used especially in controlled experiments testing the efficacy of another substance (such as a drug). 2. Something tending to soothe.

Implications of the swap of emphasis on weight of importance of placebo from the medical practitioner’s gesture of prescription to the technicalities of substance of prescription are clearly observable in the growing tendencies and trend in general medical practice. For instance, on one hand, the swap of emphasis appears to instil high trust in pharmaceuticals whilst diminishing active empathy in the patient-physician relationship. On the other hand, placebo use in medicine today, which emphasise the substance rather than practitioner’s gesture is being contested on three main grounds, namely: grounds of available substitutes in pharmacologically active medications; grounds of potential risk of placebo substances; and grounds of

patients’ awareness of their rights to enhanced and more efficient diagnostic treatment and cure.

#### 2.1.1: *Contestations on grounds of available substitutes in pharmacologically active medications*

The ethical question whether it is justifiable to expose patients to ineffective treatment with possible consequences of discomfort and risk when there are known effective treatments available underpins this contestation. However, it is instructive to consider this ethical question from the point of view of the use and implication of the terminology ‘placebo’ in both medical scientific and contemporary languages as has been clarified above in the dictionary definitions discussed. Where placebo stands only for inactive

medication substance, this question becomes relevant. It then implies that literally, the contestation is not only ethically legitimate, but also morally justified. Today, the ethical challenge for the use of placebo as therapy is the ambivalence on its implications for the medical practitioner's obligation to effective treatment. But grounds for any ethical valuation of placebo use can be particularly complex given that studies have shown that its uses in select cases may even be morally imperative [13]. This fact begs the argument to say then, that though placebo may not have known specific characterized effect on patient's condition, physicians of good conscience cannot conscientiously prescribe placebo without intuiting that the patient derives even uncertain, uncharacterized benefit from it. Thus, where the question raises ethical contestation of moral justification of placebo use, it is possible to argue the imperative of empathy in patient-physician relationship as sufficing for its medico-ethical value.

Recent studies seem to suggest that empathy is a critical factor in the clinical context. Empathy has been found to positively affect outcomes of both placebo treatments and bioactive treatments [14, 15]. In contemporary medical practices, there therefore necessarily arises such situation where the ethical dilemma of placebo, or if you like, the placebo-paradox places the practitioner in a moral miasma within which her/his ambivalence considers it unethical to use placebo, but equally unethical not to use something that is potent with positive outcomes, even if not from active pharmacological effect to the treatment. In this paradox, as long as the practitioner is conscientious, the placebo can find its ethical justification in the moral valuations with which the practitioner subscribes to in deciding on prescription or non-prescription [16].

#### 2.1.2: *Contestations on grounds of potential risks of placebo substances*

The contestations depend on a number of factors classifiable still according to types of placebo. For instance, today we make distinction between 'pure placebo' (substances with no pharmacological effect, e.g. sugar pills); and 'impure placebo' (substances with pharmacological effect but not on the condition being treated) [7, 17, 18].

Studies suggest that pure placebo could present risks of a certain odd phenomenon known as 'nocebo' effect. A nocebo effect is the opposite of placebo effect [19]. It is a negative symptom induced by the patient's own negative expectations [20]. Besides, it has long been suggested as well that even inactive placebo can have toxic effects in a substantial proportion, and that a

particularly serious possible side effect of even a harmless substance is dependency [21].

While the truth of the risks cannot be retained peculiar to pure placebo, it has as well been noted that the clearest danger lies in the gradual shift from pharmacologically inert placebos to more active ones [21]. Use of active placebo or impure placebo ranges from antibiotics to sedatives, analgesics, vitamins, etc. The risks of impure placebo include as an example the unnecessary prescription of antibiotics, which leads to antibiotic resistance that might affect not just the patient prescribed the medication, but a much broader group of seriously ill people [22]. Studies have noted that because impure placebos are often not recognized as such by practitioners, they remain at the fringe of many placebo-related debates, hence quietly absent from the discussions concerning policy and regulation [23]. Reasons for concern about placebo are rather the fact that safeguards are few or non-existent; as well as effective pressures – from drug companies, patients eager for cure and busy physicians eager for more medication whether it is needed or not. Given such pressures, the use of placebo can spread along a number of dimensions [21], and can, in this way unquestionably impact valuation of placebo and rationale for its ethical uses.

#### 2.1.3: *Contestations on grounds of the patient's rights to diagnosis and prognosis*

They largely depend on the conflict between the placebo mechanism often retained to involve necessary secrecy, and the rather growing idea that the individual has the right to give prior consent to, and even to refuse, what is proposed to him in the way of medical care. On one hand, the effectiveness of placebo has been claimed for many fields in medicine, such as surgery, psychiatry, primary care, cardiology, and elsewhere [24, 25, 26, 27, 13]. On the other hand, the very manner in which it can relieve suffering seems to depend on keeping the patient in the dark. The dilemma here becomes an apparent conflict between helping the patient and informing the patient about her/his condition [21]. However, it can be argued that in well considered clinical situations, the important fact of hopefulness for patients; the empathy in the patient-physician relationship or the act of invoking expectancy necessary for the placebo effect can induce the medical practitioner's justification for use of placebo even in secrecy. Nonetheless, dealing with patients' right to know cannot in practice be exercised without due regards for the myriad of proclamations, charters and bills on patients' rights to informed diagnosis and prognosis. Often, it does seem that these proclamations, bills and charters categorically rebuke

use of placebo in favour of patients' rights to know. Yet, in well considered situations, the bills and charters present no paradox between placebo and patient's rights to adequate information about their health situation. For an instance, in the Declaration on the Promotion of Patients' Rights in Europe, promulgated in Amsterdam 28-30 March 1994, Article 2.2. of the declaration make it explicit that:

Patients have the right to be fully informed about their health status, including the medical facts about their condition; about the proposed medical procedures, together with the potential risks and benefits of each procedure; about alternatives to the proposed procedure, including the effect of non-treatment; and about the diagnosis, prognosis and progress of treatment [28].

However, in this same declaration, from Article 2.5 and 2.6, could be deduced the resolution to a possible ethical dilemma between placebo use and the right of patients to information as pursued therein. Article 2.5 states that:

Patients have the right not to be informed, at their explicit request [28];

and Article 2.6 states that:

Patients have the right to choose who, if any one, should be informed on their behalf [28].

What these two articles perhaps more strongly affirm is the possibility of ethical valuation on the secrecy of placebo use in so far as the patient has acceded her/his right not to be informed through explicit consent. In this point of view, placebo effect in medicine, if it produces potent effect on the grounds of secrecy of patient's knowledge of placebo either as substance or gesture, cannot be utterly dismissed as unethical and unjustifiable therapy. One can argue further for specific conditions to apply in specific cases.

Furthermore, in considering patients' choice not to be informed about their diagnosis and prognosis, it is open to debate whether the patient in particular cases also gives her/his trust to the medical practitioners and in their approach/s by pharmacologically active or inactive prescriptions. This is a typical situation that highlights the perpetual contestations of placebo's indistinct ethical valuations. It is a situation that equally highlights limitations of conventional regulations and proclamations that derive from the remits of juridical rights in bringing clarity on this issue. Thus, notwithstanding regulations and proclamations set in the bills and charters, clinical and moral situations, which

present vagueness still arise. And, when notwithstanding guidelines and rules set in the bills and charters, clinical and moral situations still present vagueness, placebo use can either be exonerated or interpreted as fraud and deception of patients.

### 2.2: *Placebo: the 'pious fraud' but however fraud*

A very important aspect of the patient's rights is the right to honest medication; and, the ethical critique most frequently adduced against placebo is that in prescribing placebo, the medical practitioner merely deceives the patient. The argument is that whereas the patient wants effective treatment, she/he is deceived to receive a placebo instead [13]. Therefore, in a case where the medical practitioner fails to disclose to the patient about the pharmacological potency or non-potency of placebo, even though it has possibility of producing certain outcomes considered therapeutic, it amounts to dishonesty of medication, which is a violation of patients' right. The problem here is simply that a placebo is a substance provided to a patient, which is believed by the medical practitioner that it has no specific pharmacological effect on the condition being treated. Yet, it is delivered in the context of medical treatment [29]. This being the case, it is then difficult to adduce a valid argument to say that placebo given in the context of medical treatment is not deceptive, if and whereby the patient's entitlement to honest medication is not complied. Yet again, if such intentional and purposeful deception inherent in the use of placebo effect has no place in medicine, then placebo has no use in the treatment of patients [29].

On the one hand, criticisms against placebo use in medical treatment see it as unethical deception and therefore fraud [13, 29]. On the other hand, there is the argument that truth-telling and doctor-patient trust is important enough but the campaign against placebo is exaggerated. The argument that placebo is a fraud reclines on certain assumptions underpinned by the logic that it can only be through pharmacologically regulated procedural processes that the medical practitioner can offer therapeutic treatment for the patient's condition. But medical practitioners in their practices, intervene at different points and in varying degrees along the continuum of medical treatment through gestures like inspiring and boosting assurance through their presence and even mere touch, words of encouragement, offer of physical and emotional support, bringing clarity to anxiety, to mention just a few instances. Accordingly, it is then possible to contend that placebo is a deception only if we have to reduce the meaning of therapeutic treatment of the patient to merely the pursuit of procedural technicalities and use of pharmacologically

potent biomedical prescriptions [13]. While we argue that medical deception of patients is morally objectionable, we also highlight here the reality of practice where for instance, every time a doctor prescribes a medication and then adjusts his stethoscope on his shoulders while smiling at his patient, he is in fact harnessing just a little bit of that good of placebo effect [30, 31].

Though deception is morally objectionable, there are still lots of vagueness regarding issues for instance, of identifying conventional forms of placebo and how much deception is involved in such forms of placebo use. Besides, the concept of placebo deception – the *pious fraud* can be morally objectionable on grounds that placebo can be benevolent deception in circumstances where nothing else can be done or in psychogenic conditions where medication is not actually required [31]. In summary, although deception in medicine is generally wrong, as it tends to erode the trust between doctor and patient, the ethical duty to be honest is not absolute. Some moral goods, such as the avoidance of severe physical or emotional suffering and the preservation of life or long term autonomy, may override the *prima facie* duty not to deceive. Benignly intended deception by doctors may, in some cases, be morally acceptable [32].

### 2.3: Placebo: the avoidable medical research tool

There is growing controversy against the use of PCT as medical research tool. The argument is that PCT is a method of experimentation with humans. Hence, wherever and whenever PCT can be avoided, then it should be avoided. But the use of PCT in medical research shows no sign of relenting. New drugs, for example, are compared with placebos in order to distinguish the effects of the drug from chance events or effects associated with the mere administration of the drug. They can be tested in “blind” studies, in which the subjects do not know whether they are receiving the experimental drug or the placebos, and in “double blind” studies, in which neither the subjects nor the investigator know [21].

The PCT controversy follows a common contention that as a research approach PCT violates the therapeutic obligation of the medical practitioner to offer most favourable medical care. On one hand, in line with common conception from apparent validation from common sense and logic, the dominant ethical position on PCT is that whenever proven effective treatment exists for a given condition, it is unethical to test a new treatment for that condition against placebo [33]. This ethical position is the one favoured by World Medical Association (WMA) in its reversed Declaration of

Helsinki in the year 2000. Besides, current ethical stance seem to favour the push towards Active Control Equivalence Trial (ACET), which is also known as Non-inferiority Trials, and considered sufficient to establish efficacy on new therapies in many medical context. However, the European Agency for the Evaluation of Medical Products (EMA) and Committee for Proprietary Medical Products (CPMP) affirm that although the efficacy of some new medical products can be satisfactorily demonstrated without the use of a placebo, for others the judicious use of placebo remains essential to demonstrate their value [34]. The EMA/CPMP maintains that:

where medical products do exist for a given indication, active controlled trials are encouraged provided that a methodologically acceptable demonstration of efficacy and safety can be obtained. However, trials that seek to prove that a new agent and an active control have similar efficacy are inherently less reliable than trials that seek to prove the superiority of the new agent to a comparator, whether inactive or active. ...In some areas of medicine this lack of reliability means that it is only possible to obtain convincing scientific evidence of the efficacy of a new medicinal product by means of superiority trials [34].

Several studies point to the reversed Declaration of Helsinki and even its subsequent clarification note (October 2002) as having contributed to the confusion in the research world concerning how to assimilate and reconcile the roles of PCT and ACET, the two important tools developed to evaluate the efficacy of drugs [35,36,37]. While PCT involves superiority trial whereby, a new drug is tested against placebo; ACET involves a non-inferiority trial whereby, a new drug is tested against active treatment [36]. It has been observed that the ethical grounds for barring PCT could equally apply to ACET. Those who sustain PCT as unethical do so leaning on the Declaration of Helsinki, which affirm that in any medical study, every patient, including those of a control group if any, should be assured of the best proven diagnostic and therapeutic method [37].

The argument is that the requirement that all patients receive the best proven diagnostic and therapeutic method would bar not only placebo-controlled trials but also active control and historically controlled trials. When effective treatment exists, the patient receiving the investigational treatment instead of the established therapy is clearly not getting the best proven treatment [37]. Yet, provisions made to minimize the difficulties presented by the Declaration of Helsinki do not remove equivoques on PCT as a medical research tool. There persists a created ethical choice to be made between

avoiding PCT as against renouncing the role it plays in medical research. Some suggest that a superiority trial against a placebo is scientifically sound but ethically unacceptable, whereas a non-inferiority trial against active treatment is ethically sound but scientifically not reliable. But switching from a superiority type of trial with placebo to non-inferiority trial with an active control, is in practice switching from the violation of uncertainty principle to uncertainty of results – a true impasse living open the question, which is more unethical: to violate patient's rights or to produce results without scientific value [36]. Irrespective of the suggestion that use of a superiority trial design with an active control instead of placebo will satisfy scientific needs and expectations of patients [36], avoiding placebo as a medical research tool is not yet a road medical research is willingly ready to take. To the regards, the EMEA/CPMP affirms that:

Forbidding placebo-controlled trials in therapeutic areas where there are proven prophylactic, diagnostic or therapeutic methods would preclude obtaining reliable scientific evidence for the evaluation of new medicinal products, and be contrary to public health interest as there is a need for both new products and alternatives to existing medical products. ...Provided that conditions that ensure the ethical nature of placebo-controlled trials are clearly understood and implemented, it is the position of the CPMP and the EMEA that continued availability of placebo-controlled trials is necessary to satisfy public health needs [34].

Therefore, quite like a means justifiable by the end, placebo in medical research can continue to receive favourable ethical valuations inasmuch as it can still be justifiably trusted in its role.

## CONCLUSION

Placebo in medicine perhaps has suffered impressionistic prejudices in contemporary ethics and approach to understandings of contexts for its uses and justification. Doubtlessly, the concepts of placebo in medicine follow advancements in medicine and in turn innuendoes in its language uses. In its earlier use in medicine, placebo was conceptualised to be of beneficent value. In modern medicine, placebo presents ambiguities despite its relevance and persistent uses in medical practices and research.

With the advancement of pharmacology and push for evidence-based practices in medicine, regulatory technicalities become defining grounds for valuations of medical ethics. This development affected the uses and ethical justification for placebo in clinical medicine and in biomedical research. In this paper, our aim was to

bring critical insight to bear on the approach and the grounds warranting ethical valuation of placebo use in medicine today. Assessing if this aim has been achieved in this paper certainly depends on two underpinning standpoints we have tried to formulate regarding ethics of placebo in medicine. First, rationalising use of placebo from a medical ethics perspective would certainly mean that we examine understandings of contemporary justifications for scope and veracity of placebo use in medicine. Hence, the first step for ethical or moral evaluation of placebo in medicine must be to understand the main concepts that underline its current uses where its ethical concerns contextually emerge. Second, ethical or moral evaluations of placebo use in medicine cannot be based merely on its mutating concepts as that might amount to being shortsighted about the relevance placebo enjoys in medicine and its significance for the work the medical practitioner do. Hence, valuations of placebo use in medicine from the viewpoint of procedural technicalities of prescribing 'substance' is highly circumscriptive and discounts placebo 'art of gesture', which in its subliminal application contests grounds, can be considered a therapeutic resource.

We therefore conclude that overlooking the ethical dimensions of imperative conditions for placebo in medicine can be ethically unfair. Placebo persistently serve important role in medical practice as well as in medical innovations and research. It can still benefit from good and functional regulatory bodies to safeguard its role.

## REFERENCES

1. Jimenez, Sherlyn. 2009. Compassion. *The encyclopaedia of positive psychology*, 209-15.
2. Grammaticos, Philip C., and Aristidis Diamantis. 2008. Useful known and unknown views of the father of modern medicine, Hippocrates and his teacher Democritus. *Hell J Nucl Med* 11.1: 2-4.
3. Van den Brink, Erik, and Frits Koster. 2015. *Mindfulness-based Compassionate Living: A New Training Programme to Deepen Mindfulness with Heartfulness*. Routledge.
4. Taylor, Robert. 2010. Medical wisdom and doctoring: The art of 21st century practice. *Springer Science & Business Media*.

5. Miles, Steven H. 2005. *The Hippocratic Oath and the ethics of medicine*. Oxford University Press.
6. Wikipedia contributors. 2017. Placebo in history. *Wikipedia, the Free Encyclopedia*.
7. Jütte, Robert. 2013. The early history of the placebo." *Complementary therapies in medicine* 21.2:94-97.
8. Douglas, John. 1754. *The Criterion: Or, Miracles Examined with a View to Expose the Pretensions of Pagans and Papists*. Millar, 1A.
9. Placebo and Placebo effect. 2017. *Kennedy institute of Ethics*.
10. Booth, Christopher. 2005. The rod of Aesculapios: John Haygarth (1740–1827) and Perkins' metallic tractors. *Journal of medical biography* 13.3: 155-161.
11. Haygarth, John. 1800. *Of the Imagination: As a Cause and as a Cure of Disorders of the Body; Exemplified by Fictitious Tractors, and Epidemical Convulsions.* decipimur Specie. "Hor. Read to the Literary and Philosophical Society of Bath. By John Haygarth, MDFRS Lond. And Edinb. Of the Royal Medical Society at Edinburgh, and of the American Academy of Arts and Sciences. R. Cruttwell.
12. Motherby, George. 1785. *A New Medical Dictionary. The Second Edition Enlarged and Corrected*. J. Johnson.
13. Lichtenberg, Pesach, Uriel Heresco-Levy, and Uriel Nitzan. 2004. The ethics of the placebo in clinical practice. *Journal of Medical Ethics* 30.6: 551-554.
14. Kaptchuk, Ted J., et al. 2008. Components of placebo effect: randomised controlled trial in patients with irritable bowel syndrome. *Bmj* 336.7651: 999-1003.
15. Braga-Simões, João, Patrício Soares Costa, and John Yaphe. 2017. Placebo prescription and empathy of the physician: A cross-sectional study. *European Journal of General Practice* 23.1: 98-104.
16. Newman, David H. 2009. *Hippocrates' shadow*. Simon and Schuster.
17. Shapiro, Arthur K., and Louis A. Morris. 1978. The placebo effect in medical and psychological therapies. *Handbook of psychotherapy and behaviour change* 2: 369-409.
18. Linde, Klaus, Margrit Fässler, and Karin Meissner. 2011. Placebo interventions, placebo effects and clinical practice. *Philosophical Transactions of the Royal Society of London B. Biological Sciences* 366.1572: 1905-1912.
19. Kennedy, Walter P. 1961. The nocebo reaction. *Medical world* 95: 203-205.
20. Häuser, Winfried, Ernil Hansen, and Paul Enck. 2012. Nocebo phenomena in medicine: their relevance in everyday clinical practice. *Deutsches Ärzteblatt International* 109.26: 459.
21. Bok, Sissela. 1974. The ethics of giving placebos. *Scientific American* 231.5: 17-23.
22. Merkes, Monika. 2017. Using placebo in medical practice – an ethical conundrum. Web. 28 August.
23. Harris, Cory S., and Amir Raz. 2012. Deliberate use of placebos in clinical practice: what we really know. *Journal of medical ethics* 38.7: 406-407.
24. Johnson, Alan G. 1994. Surgery as a placebo. *The Lancet* 344.8930: 1140-1142.
25. Laporte, Joan-Ramon, and Albert Figueras. 1994. Placebo effects in psychiatry. *The Lancet* 344.8931: 1206-1209.
26. Thomas, K B. 1994. The placebo in general practice. *The Lancet* 344.8929: 1066-1067.
27. Bienenfeld, Laura, William Frishman, and Stephen Glasser. 1996. The placebo effect in cardiovascular disease. *American heart journal* 132.6: 1207-1221.
28. World Health Organization. 1994. A declaration on the promotion of patients' rights in Europe. *Copenhagen: WHO Regional Office for Europe*.
29. Rorty, Mary V, and Lorry Frankel R. 2009. The paradoxical placebo. *The American Journal of Bioethics* 9.12: 17-20.
30. Jospe, Michael. 1978. *The placebo effect in healing*. Lexington Books.
31. Sharma, RK. 2017. Placebo – Historical Background and its Role in Medicine, Web. 10 July 2017.

32. Sokol, Daniel K. 2007. Can deceiving patients be morally acceptable? *British Medical Journal* 334.7601: 984.
33. Miller, Franklin G., and Howard Brody. 2002. What makes placebo-controlled trials unethical? *The American Journal of Bioethics* 2.2: 3-9.
34. Committee for Proprietary Medicinal Products. 2001. EMEA/CPMP Position statement on the use of placebo in clinical trials with regard to the revised Declaration of Helsinki.
35. Batra, Sadhvi, and Jeremy Howick. 2017. Empirical evidence against placebo controls. *Journal of Medical Ethics*, 2016.
36. Spławiński, Jacek, and Jerzy Kuźniar. 2004. Clinical trials: active control vs placebo—what is ethical? *Science and engineering ethics* 10.1: 73-79.
37. Temple, Robert, and Susan S. Ellenberg. 2000. Placebo-controlled trials and active-control trials in the evaluation of new treatments. Part 1: ethical and scientific issues. *Annals of internal medicine* 133.6: 455-463