

*Oncology and a time of crisis. Science, complexity, ethic values, and incertitude. An argumentative essay*_____

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Abstract

Who faces a neoplastic disease is more bewildered than in the past, in spite of the improvement of the possibility of cure and priority attributed to this subject by the health institutions and medicine, compared to few decades ago. Nevertheless, disorientation is increasing due to many factors, also beyond those of the scientific and welfare context of cancer and is related to the general background of crisis. The landscape of crisis involves the changes occurring in both epistemic and contextual values, and methodology of science at large, as well as those particular of the medical field, including oncology. The perceived loss of reliability of universal laws and the limits of general theories, in favor of the conception that elementary events concur to outcomes, makes the scientific appraisal more probabilistic than deterministic. This framework of “complexity” is characterized by non-linearity in the causal links, opacity of the investigated subject, and emergence of the phenomena we observe and analyze. In oncological medicine, the present deterministic “gold standard” of the random comparative trials, grounding the so-called evidence-based medicine (EBM), and the guidelines for clinical management - although being the most reliable resource - are critically considered. In fact, new “systems biology” approaches, based

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on big data analysis and advanced statistical methods, may bridge the gaps between the biological/pre-clinical and clinical investigations, hopefully allowing “precision” or “personalized medicine”. Artificial Intelligence is considered an indispensable tool to this regard. However, also this approach couldn’t effectively work without a sound, general theory on cancer, presently not at hand. Moreover, all of the above contexts suffer of the pressure of industry, interested in the economic impacts. On the other hand, the costs of cancer management, increasing at a higher rate compared to care results, motivate the health authorities to take physicians out of the personal professional and trust relationship with the patients. In this situation, oncologists have mainly to cooperate – often in a subordinate position - with bureaucratic professionals for the implementation of pre-established guidelines. As a consequence, patients are institutionalized and deprived of the reassuring presence of an entrusted doctor, thus experiencing enhancement of distress and solitude feelings. This connects with crisis in the social domain, defined as a strength that conquers autonomy without a manifest theory of itself, thus without a project, but with an impact capacity producing high perceivable effects. This existential landscape characterizes the present time as “the age of incertitude”. Complexity and uncertainty thus exist also in society. The social pact between individual and state (relinquishing of a part of freedoms by the former in exchange for security by the latter) is compromised, and the indeterminate nature of the crisis obscures any solution. The statements on the right to health are perceived as abstract formulations, generating mistrust in institutions and further distress. From the physicians’ point of view, this must not imply loss of responsibility, but even more so imposes a great ethic commitment. They must operate as best as they can, despite being aware that the desired effects could be vanished by context. This is a further subject to consider in the relationship between medicine and health institutions: the former must preserve its own statutory purposes of prevention and care of diseases in the best possible way, even if the inherent epistemic complexity and the contextual background makes this task more problematic than in the past. Indeed, medicine should cooperate with health institutions, developing the necessary attitudes given the present social background, but not in a subordinate role, as far as its intellectual and operative domains are concerned. Another factor of crisis must be considered, that is, communication. A diagnosis of cancer, an ominous event, induce to look for any glimmer of hope and entrusts false believes or pseudo-scientific results, because these appear easier to comprehend and promise clear-cut good results, compared to the scientific argumentations, hard to understand and expressed in terms of probability. The present cultural background of society is affected by the lack of humanistic education, that is, what grounds critical thinking. Biomedical researchers and physicians, sometimes suffering of the same deficiency, regrettably have also other faults, that is, defects in intellectual honesty such as egocentrism and self-reference that can generate mistrust in science on the long run. After examining

these items in the light of the available data and authoritative sources of the related literature, we reached the conclusion that a “new alliance” can be promoted between oncological science and society, based on “the humanism of science”. Improving intellectual honesty by the biomedical community, as well as critical thinking also in society is mandatory. This can be obtained with suitable educational programs in high school and university. Cultural empowerment, and a realistic approach to the epistemic and ethics issues on cancer may mitigate the related individual and social discomfort and - hypothetically - improve clinical outcomes through the increased patients’ compliance to therapy and prevention programs.

Key words: *Oncology, Complexity, Time of Crisis, Crisis in Science, Crisis in Medicine, Crisis and Society, Communication in Science, Communication in Medicine*

Introduction. The present landscape.

Presently, it is a sound data item that oncological medicine has achieved increasingly success-ful results over the last decades, due to the progress of medical research. However, this matter-of-fact should be quantitatively regarded in the light of statistics, from a critical point of view. The trend of the improvement of the 5-year overall survival (OS) rates for all cancers is less, in the first 15 years of the present century, compared to the last 25 of the former one.

Five-year OS rates, in fact, increased by 15 % from 1974 to 2001 in USA, for all cancers and in all ethnic groups ^[1], whereas a more far-reaching study, on a global scale, shows for the period from 2000 to 2014 an improvement of the age-standardized 5-year OS hardly approaching 5 %, with rare exceptions, for the most incident neoplasms, presumably representative of the impact of innovative diagnostic and therapeutic practices. The 5-year OS for breast carcinoma in Northern Europe and USA is unchanged over these 15 years.^[2] The two studies cannot be directly compared, due to the relevant differences in methodology and sample sizes, but the trend here considered clearly emerges, even if in coarse terms. The above remark should be framed taking in consideration the different growth in cost trends of cancer research, its products, and cancer care: the differential, for the two math functions, is less for results than for costs. (Figure 1).

This forethought is fundamental, when addressing the relationships between medical knowledge and society in general and also, ultimately, physicians and patients. In fact, as early as in 2011, a special oncology commission of *The Lancet* journal stated: “... *The cancer profession and industry should take responsibility and*

not accept a sub-standard evidence base and an ethos of very small benefit at whatever cost; rather, we need delivery of fair process and a real value from new technologies”, thus formally establishing the necessity of reliable and quantitative evaluations of health outcomes and costs, on the grounds of both equity and affordability.^[3] As a deviant and ominous consequence, many health institutions have equivocated these sacrosanct principles, in an interpretation that may be read as: “medicine is a too serious issue to be entrusted to physicians”, similar to the famous sentence on war by Georges Clemenceau (*La guerre! C'est une chose trop grave pour la confier à des militaires*). This conceptual drift ties also in misinterpretation of multidisciplinarity, that is, not in the correct sense of a cooperation among specialists in different medical and related scientific disciplines, but including instead bureaucracy and health politics professionals with an equal (or even higher-order status). More, health institutions declare as a statutory paradigm the centrality of patient, thus implicitly assuming the role of an impersonal deuteragonist for themselves.

However, from the point of view of patients, when they need cancer treatment, the perception of this complex and not fully understood situation is that their personal problem is just one - and not necessarily the most important - among other ones. Their incertitude and sense of loneliness is enhanced, as a result, shouldn't they have a main reference point in a trusted doctor inside the institution. This point will be addressed more in depth in a following section on the subject of medical responsibility: here we just underline that a medical doctor must be educated “to acquire leadership, teamwork, and communication skills” besides a medical scientific background.^[4] In fact, the medical profession is based not only on epistemic grounds: the present substantial evolution of sciences, not only in the biomedical field, requires a reflection on updating education regarding both purely scientific issues, and the contextual values of objectivity and intellectual honesty as well, to the purpose of correct relationships between science scholars and society.^[5]

On the other hand, there are many negative aspects of the widespread diffusion of too general, apodictic or uncontrolled information, or even false data concerning cancer that permeate people, and confuse those individuals whose general education is defective, in that lacking the development of critical sense. Firstly, confusion exists regarding the difference between the concepts of “welfare” and “health”. WHO and UNICEF, during the forty years since their first Conference in Alma-Ata (1978), to the last one held in Atama (2018), maintained the following statement: primary care and essential public health are the core of integrated health services, to be pursued through multisectoral policy and action, and empowerment of peoples and communities. Pope Francis, in his message on the occasion of the last conference, stated: “*Health is not a consumer*

good, but a universal right: let us unite our efforts so that health services are available to all” (Pope Francis - @ pontifex # Health ForAll). These affirmations, that are indisputable in the domain of ethics of values, nevertheless are relevant mainly insofar as meant directed to political authorities in terms of welfare improvement. Unfortunately, these statements may be manipulated on the grounds of affordability and opportunity, and objectivity may be often underevaluated or sidelined. On the other hand, when improvement of health is considered from a medical point of view, what is pursued is the absence of disease, that should be identified as a commitment to prevent and cure diseases under the epistemic perspectives of science, and the moral allegiance to the principles hinted at before (objectivity and intellectual honesty) besides personal responsibility.

The theme of objectivity deserves further consideration. According to The Stanford Encyclo-pedia of Philosophy: “*Scientific objectivity is a characteristic of scientific claims, methods and results. It expresses the idea that the claims, methods and results of science are not, or should not be influenced by particular perspectives, value commitments, community bias or personal interests, to name a few relevant factors. Objectivity is often considered as an ideal for scientific inquiry, as a good reason for valuing scientific knowledge, and as the basis of the authority of science in society*”.^[6] However, these authors recognize that presently the distinction between epistemic and non-epistemic values is strongly debated even within the official epistemological sphere. Nevertheless, we have to consider here the extreme “dark side of postmodernity” in the general framework of society, often taking hold against sound scientific disclosures and maintaining alternative and ontological confused point of views regarding genuineness, natural energy, narrative reports of empiric experiences, etc., and even trusting in questionable characters and believes borderline to witchcraft. Among these last misconceptions, is the use of the Cuban blue scorpion venom and shark cartilage against cancer. Sadly, some of other deviant tendencies have been uncritically considered by health institutions, on the grounds of political opportunities and a misunderstood interpretation of democracy. Examples are the Italian “Metodo Di Bella” for cancer therapy^[7] and the worldwide ideological movements against infectious diseases vaccinations^[8] and GMOs in agriculture.^[9]

Thus, the present landscape of the relationships between medicine (and science in general) and society is problematic due to the above factors, that further exacerbate the discomfort and incertitude of the oncological patients. In the present paper, we consider these issues to this regard, in the framework of crisis in sciences, society, and communication, with the aim to promote a cultural operation for basing appropriate strategies to be adopted for countering a tendency towards a decline in a fundamental aspect of our civilization.

Different rapidity of growth in cost trends of cancer care: the increase, for the two math functions, is less for results than for costs.

L. Pirtoli: 6th Organization Conference of the Tuscany Cancer Institute, 2011.

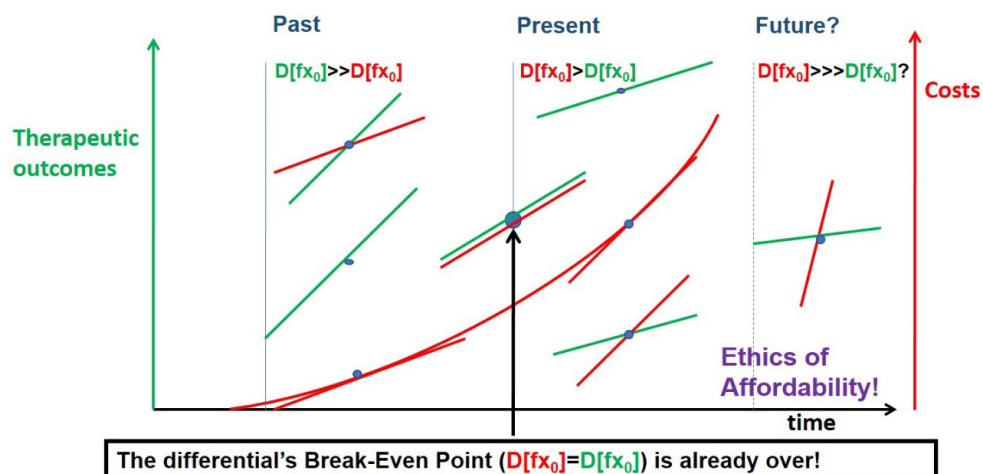


FIGURE 1. Different rapidity of growth in cost trends of cancer care.

The crisis in Science and Medicine

In a recent essay, ^[10] one of us (SZ) synthetically retraced the crisis of the fundamentals in the hard sciences, remarking that even Euclid has hesitated in applying his fifth postulate (regarding the unique parallelism of one straight lines with respect to another one lying on the same plane, up to infinite). Briefly, the first non-Euclidean geometry arose – in fact - when all the Euclid's postulates were deemed acceptable but the fifth one, thus admitting the possibility of an infinite number of parallel lines passing through a point external to another straight line (hyperbolic geometry). It must be remarked that this statement has anticipated the principle of denial of the insights, that is, their devaluation, even of those that Karl Popper included in “the context of discovery”. An insight, in fact, is just the beginning of a hypothetic-deductive process, which needs a factual demonstration through experiments (context of confirmation). Similarly, regarding mathematical sciences, the twentieth century started with a general loss of the reliability of intuitiveness, that had grounded the millennial issue of natural numbers, and the coming of a substantialistic conception of mathematics, that is, the set theory: a purely functional and relational vision of numbers. In physics, the turning point has come from the revision of the Newtonian mechanistic, and is focused on thermodynamics. This last domain,

in fact, doesn't refer to the mechanic energy of bodies (i.e.: kinetic energy) but deals with their inherent energy, due to molecular motion, that is, depending on physical quantities implying statistical values, somehow exiling of pure deterministically approachable relationships. The overall context of complexity in this field has been synthetized by Ilia Prigogine (a Nobel Prize-awarded scientist for studies on these issues) as follows: *“Mais dès le XIX siècle nous avons l'idée d'évolution, en biologie, en sociologie, et cette idée d'évolution domine le XX siècle ... mais qui dit évolution dit qu'il faut qu'il y ait une différence entre l'avant et l'après, qu'il ait apparition de nouveauté ou je dirais plutôt d'événement. En somme, je dirais que l'histoire intellectuelle de l'Occident a été dominée par le conflit entre la notion de loi et la notion d'événement”*.^[11]

Therefore, elementary and irreversible events cooperate for complex phenomena. Accordingly, the concept of evolution - since the Darwinian intuition, to the gene mutation-based present interpretation - dominates the realm of biology, entailing the passing of time, that is, before and after an impacting event. The recent, intellectual history of the western countries was ruled by the conflict between the notions of “universal law” and “event”. Presently, this last is prevailing in science at large, after the coming of quantum mechanics, which is inherently and uncompro-misingly probabilistic. Science becomes increasingly probabilistic and decreasingly deterministic, at the present time.

However, complex biological systems (included those addressed by cancer biology) are characterized by nonlinearity in the causal relationships, opacity regarding interpretation, and “emergence” of the functional phenomena we observe. Approaching complexity in biology entails both the context of discovery and that of confirmation (as we will deal with after in more detail) thus requiring in different situations the pure probabilistic and math modelling methodology for the observed and collected data, as well as the deterministic setting of experiments. Somebody maintains that in both cases the *a priori* of a hypothesis lying on a general theory is indispensable,^[12] but presently this concept is rarely contemplated as a general statement for research in bio-medicine, particularly in oncology.

As a matter of fact, in any case, the present gold standard of the medical community, as a reference for clinical practice, is Evidence Based Medicine. This definition was used by GH Guyatt thirty years ago in an editorial,^[13] in which he introduced the concept that medical practice should no longer be based on established authorities (e.g.: textbooks, senior lecturers or physicians) but instead on the critical appraisal of recent publications of relevant studies related to the particular clinical situation. In fact, this new approach was made possible, already at the time, by the availability of web access to medical literature data bases (MEDLINE in this report). This process was subsequently,

formally systematized for medical education purposes in a *JAMA* paper, authored on behalf of the Evidence-Based Medicine Working Group, established in the meanwhile. ^[14] Only later this approach was applied to clinical research, grounding the procedure of random comparative trials (RCTs) for innovative therapeutic disclosures versus the present standards of care. A less diffused implementation of RCTs was carried out for diagnostic tools, due to difficulty in selection of reliable endpoints and for ethic reason: there is a widely shared belief – perhaps questionable - that the most advanced diagnostic technology should be employed whenever available. Presently, the clinical guidelines of the preeminent medical associations indicate the “level of evidence” of the procedures, ranging from the lowest (case reports) to the highest ones (RCTs), placing in between the expert panels’ opinions and the retrospective studies. This pragmatic setting is successful and many outstanding results came from RCTs for therapeutic agents in oncology. However, the above framework for medical science doesn’t systematically include as a prerequisite the value of results from the pre-clinical research. At the present time, in fact, there is a huge quantity of drugs and other agents, shown as very promising after experimental studies in cell cultures, animal models and *in silico* elaborations, deserving clinical validations that cannot be accomplished, due to lack of funding in many cases. Thus, translational research from bench to bedside through RCTs is usually implemented when industry decides to support it, often following in-house, preclinical studies, and not necessarily due the perspectives of a high therapeutic effectiveness measured by reliable endpoints (OS or disease-free survival) but, e.g., progression-free survival, i.e.: the disease respond to therapy just as long as the drug is administered. That is, drug-centered, instead of patient-centered trials. Further, market prospects prevail: a small prognostic advantage, just beyond the limit of statistical significance in a very prevalent pathology, may be valued more than a great prognostic improvement in less frequent diseases, from an economic standpoint.

More, the RCT process is inherently reductionistic: the impact of the supposed “determinant” agent is tested in the clinical experiment, in the context of strict patient selection, methodology and endpoints. It may happen that the results are not coherent with the “real world” of the common clinical practice. Anyway, the process is labor-intensive, time-consuming and costly. The evidence for a better outcome, compared to the standard procedure, is achieved after a long-time lapse since patients’ recruitment.

Despite all this, the results of RCTs provide the best evidence on which medical practice can be based. However, by no means their deterministic approach is adequate to the increasing complexity of the bio-medical knowledge. An attempt to cope with the problem of complexity in cancer was proposed

by two eminent biomedical researchers at the transition to the present century.

^[15] Taking in account that previous research had shown that tumorigenesis is a multi-step process, during which multiple genetic alterations drive the malignant evolution of the cells, and that cancer incidence is age dependent, it was hypothesized that a limited number of rate-limiting stochastic events grounds the whole transformation, according to a previously developed model.

^[16] This hypothesis is reductionistic too, but Hanahan and Weinberger deemed it as formally coherent to the Darwinian evolutionism *“in which a succession of genetic changes, each conferring one or another type of growth advantage, leads to the progressive conversion of normal human cells into cancer cells”*. On these grounds, and considering in depth the evidences of the available body of scientific results at the time, they highlighted the convergence of known, genetically-driven, molecular mechanism into the famous “six hallmarks of cancer”, that is: self-sufficiency in growth signals; insensitivity to anti-growth signals; evading apoptosis; limitless replicative potential; sustained angiogenesis; tissue invasion and metastasis. The authors predicted that the improvement in definition of the genome-wide gene expression profile, during the coming twenty years since the formulation of their hypothesis, will allow a mechanistic knowledge of the cancer process on which mathematical modelling could predict prognosis and success of therapy according to the principles of rational sciences. Fourteen years later, instead, Weinberger admitted that the above theory has side-stepped the domain of signal transduction biochemistry, as well as tumor microenvironment (including immunity and inflammation), and also that the supervening age of “omics” (that is, besides genomics and transcriptomics: proteo-mics, epigenomics, kinomes, methylomes, glycomes, and matrisomes) could introduce engulfing amounts of data. This author pessimistically wondered about the possibility of achieving a mechanistic insight into such a complex system (systems biology) through computational algorithms, given that *“we lack the conceptual paradigm and computational strategies for dealing with this complexity”*.^[17] That is, a very similar point of view compared to that one expressed from a different domain (computer science) and a more general point of view on “big-data” by other authors,^[12] already quoted. Thus, we have yet to acknowledge the absence of a general theory on cancer, that might hamper the success of computational sciences in disentangling the “emergence” of neoplasia from its biologic complexity. In spite of these perplexities, once again, industry keeps an eye on this issue: an economic estimate of 150 billion euros was made in 2019 and reported by press organs, for the implementation of artificial intelligence (AI) in health programs within 2026. Thus, we should see anyhow the related impact in the oncological field, even if probably with the intellectual reserve already expressed for clinical experimentations. However, a pessimistic future vision seems not justified in

practical terms: a decreasing trend is presently shown in cancer-specific, age-adjusted mortality rate by a very recent epidemiologic study, with a substantial, progressive gain in averting cancer deaths since 1991 (more significant after 2000).^[18] This is mainly attributable to prevention, even if treatment breakthroughs have contributed, such as new drugs in hematological malignancies, together with the coming of immunotherapy and target therapy also in other tumors. The “traditional” strategy against loco-regionally confined cancers, based on surgery, radiotherapy, adjuvant or neo-adjuvant chemio-therapy, and hormone therapy, presently achieves definitive cure in many cases, that can be further improved by targeting actionable molecular mechanisms by monoclonal antibodies, tyrosine kinase inhibitors and other selective drugs. Moreover, even in advanced presentations traditional and innovative agents can obtain long-lasting survival rates without severe side-effects, making cancer a chronic disease in many of these patients. This is, e.g., the case of immunotherapy. Molecular target therapy still needs more reliable markers for prognostic prediction and selection of suitable patients, but biomedical research has made considerable advances in this field, even if precision (or personalized) medicine presently is not yet a full-accomplished goal. Resistance to inhibitors of the cellular growth ultimately develops, given the well-known ability of cancer cells to respond to chronic drug administration by adapting their signaling pathways,^[19] and due to the genomic instability, but also in this case some progress can be observed in recent results.

Ultimately, what the practitioner should keep in mind is that, in the vast majority of cancer patients, there is a reliable strategy for coping with their clinical situations, should it be aimed at a definitive cure or an effective, hopefully long-lasting achievement of a good quality of life, even if the “magic bullet” against cancer is not available. A sound and updated background of medical culture, experience, assertiveness and intellectual honesty, in relating with patients within a trusting relationship, are usually effective in containing anxiety by reducing uncertainty regarding the nature of their disease. A humanistic education is helpful in this context, and by no means a physician should behave and speak like a technocrat.

The crisis for Society, and Communication in Science and Medicine

In 1942, in the midst of the second world war, Albert Camus (a French writer and philosopher) wrote: *“Ce monde en lui-même n’est pas raisonnable, c’est tout ce qu’on en peut dire. Mais ce qui est absurde, c’est la confrontation de cet irrationnel et de ce désire éperdu de clarté.”*^[20] This existential landscape continues to dominate

the present time, that we could call “the era of incertitude”, a trait on which philosophers and sociologists converge. This characteristic is present at many levels, from the loss of the epistemic certitudes – previously considered – to the fall of metaphysic believes and the decline of any kind of transcendence. The concept of complexity covers the transformations also in the social, economic, and cultural fields, with the already mentioned features of absence of linearity in the causal relationships, opacity in assessing dynamics, and emergence of functional phenomena whose interpretation is very hard to achieve. Significant events may aggregate into “clusters”, with effects that can be additive, synergic, or even contrasting each other. Human actions sometimes generate relevant events, in good and evil according our present moral categories of civil solidarity, but are not absolute determinants of these consequences. However, from our point of view this doesn’t imply loss of responsibility, but instead – and even more so – imposes an even greater ethic commitment. It is not a trivial statement: any person must operate as best as she can, despite being aware that the desired effects could be vanished. As Max Gismondi wrote in a paper dealing with realism in political sciences: “*The ethics of responsibility requires one to take responsibility for one’s actions, ... knowing all the while that circumstances beyond one’s own control may alter the outcome and have unintended consequences*”.^[21] This world vision, like it or not, is the fundamentally tragic one that dominated the contemporary age since the half of the last century and – not paradoxically - enshrines the ethically correct action as aimed at positive purposes. Ideas and actions of more or less recent historical characters (such as some state leaders in the first half of the last century) have had a strong negative impact on their time, or subsequently. They have the responsibility of all the related consequences, even if synchronous or metachronous co-factors must be taken in account, without exempting them.

The present crisis, generally attributed to economic and financial factors traceable back to the interventions and responsibilities of identifiable persons, however, has acquired an imper-sonal historical substance that involves social and individual domains. As Zigmund Bauman (a distinguished sociologist and philosopher) maintained, this crisis is substantially a strength which gains autonomy without an appearing theory of itself, thus without a project, but with an impact that produces strongly perceivable effects.^[22] Complexity, uncertainty, and the lack of a general theory, thus exist also in social sciences. As a consequence, the fundamental social pact between individual and state (relinquishing of a part of freedoms by the former in exchange for security by the latter) is compromised, and the indeterminate nature of the crisis obscures any perspective of a solution. In this framework, the statements on the right to health addressed in the introductive paragraph of this paper may be perceived by people as abstract formulations, generating mistrust in institutions.

This is a further reason grounding the necessity to distinguish medicine from health institutions: the former must preserve its ontologic fundamentals, that is, its own statutory purposes of pursuing prevention and care of diseases in the best possible way, even if its present epistemic complexity and the contextual background makes this task more problematic than in the past. Indeed, medicine should cooperate with health institutions, developing the updated attitudes that are necessary, given the present social background, but not in a subordinate role, as far as the intellectual and the operative domains are concerned.

The role of communication is fundamental to this regard, including the related skills that should be the subject of particular bio-medical education programs. Atul Gawande, a surgeon and researcher in the field of public health, said: “Science . . . is a commitment to a systematic way of thinking, and allegiance to a way of building knowledge and explaining the universe through testing and factual observation. The thing is, that isn’t a normal way of thinking. It is unnatural and counterintuitive”.

^[23] In fact, when society keeps down the certitude of values because these are perceived as unreliable, it seems to get into a loss of critical thinking. “The tragedy may be not in Cassandra’s speaking, but in Troy’s inability to hear”, according to the Gawande’s speech. A diagnosis of cancer, that is generally understood as an ominous event, may induce to look for any glimmer of hope and entrust false believes or pseudo-scientific results, e.g., spread throughout the Web, because these appear easier to comprehend and promise clear-cut good results, compared to the scientific argumentation that, contrarily, is hard to understand. Moreover, the possible outcome of the disease is expressed in terms of probability, instead of certitude. The scientific community, including biomedical researchers and physicians, regretably has its faults in this scenario, that is, egocentrism and self-reference. Defects in intellectual honesty in reporting results of personal studies, emphasized beyond their real value in the context of public occasions like interviews, generate mistrust in science on the long run. Gundula Bosch, a philosopher involved in scientific education, maintained the importance of implementing “soft skills” when defining the educational curricula of researchers, in an recent editorial in *Nature*.^[5] She wrote that is important to “get students to reflect on the limits of science, and where science’s ability to do something competes with what scientists should do from a moral point of view”, and remarked “that researchers who are educated more broadly will do science more thoughtfully, with the result that other scientists, and society at large, will be able to rely on this work for a better, more rational world”.

Thus, the necessity exists to reevaluate on a realistic background intellectual honesty by science, including the biomedical field, and critical thinking by both scientists and society in general. This may ground a new alliance of medicine and society, intended to that Ilia Prigogine – already quoted – called “the humanism of science”.

Conclusions

In our argumentation we tried to focus on the main elements of crisis in science - with particular regard to the biomedicine and clinical aspects of oncology - and crisis in society, underlining the uncertainty aspects grounding both of them due to a common factor, that is, the demise of general principles and theories and the prevailing appearance of complexity in a deeply impacting occurrence, such as cancer, in the present individual and social existential landscape. The unfavorable dynamics of the improvement of outcomes versus costs for cancer management contributed to the subordination of medicine to the politic and bureaucratic establishment in health institutions, thus constraining the personal responsibility of physicians, who are deprived of the relationship of trust with patients, who suffer incertitude and sense of loneliness as consequences. This situation fits into a social background of disenchantment, due to the perception of the poor performance of the social pact, the indeterminate nature of the crisis and the lack of a reliable solution in sight for many existential problems, including cancer. Communication is presently inadequate in disentangling confounding elements, relevant for the distressing experience of cancer patients, that is, ambiguity in fields such as: welfare and health; epistemic and contextual values in science; methodology of the biomedical research; conflicts of interest in clinical studies, less-than-expected results in cancer care. All of the above converge into misinterpretation or even mystification of medical science.

After examining these items in the light of the available data and authoritative sources of the related literature, both in the biomedical and epistemological fields, we reached the conclusion that a “new alliance” can be promoted between oncological science and society, based on “the humanism of science”. That is, improving intellectual honesty by the biomedical community, as well as critical thinking of both sides, scientists and physicians, and society. This can be obtained on the grounds of suitable educational programs in high school and university, included in these last both science and humanistic departments’ teaching programs. An approach to the subject of cancer based on cultural empowerment, faced through a realistic approach to the related epistemic and ethics issues, may be effective in mitigating the related individual and social discomfort and - hypothetically - in improving clinical outcomes through the increased patients’ compliance to therapy and prevention programs.

References

1. Jemal A, R. Siegel, E. Ward, et al. (2006). *Cancer statistics 2006*. CA Cancer J. Clin, 56:106-130.
2. Allemani C, Matsuda T, Di Carlo V, et al. (2018). *Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): analysis of individual records for 37513025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries*. Lancet, 391:1023-75
3. Sullivan R, Peppercorn J, Sikora K, et al. (2011). *Delivering affordable cancer care in high-income countries*. Lancet Oncol, 12:933-80.
4. Quintero G. A. (2014). *Medical education and the healthcare system - why does the curriculum need to be reformed?* BMC Medicine 12:213. <http://www.biomedcentral.com/1741-7015/12/213>
5. Bosch G. (2018). *Train PhD students to be thinkers not just specialists*. Nature, 554:277
6. Reiss J, Sprenger J. 2017. *Scientific objectivity*. The Stanford Encyclopedia of Philosophy (Winter 2017 Edition), Edward N. Zalta (ed.).
7. Raschietti R, on behalf of the Italian Study Group for the Di Bella Multitherapy Trials. (1999). *Evaluation of an unconventional cancer treatment (the Di Bella multitherapy): results of phase II trials in Italy*. BMJ, 318:224-8
8. Browne M. (2018). *Epistemic divides and ontological confusions: The psychology of vaccine skepticism*. Human Vacc Immunother, 14:2540-2542
9. Kuntz M, (2012) *The postmodern assault on science. If all truths are equal, who cares what science has to say?* EMBO reports 13:885-889
10. Zacchini S, Pirtoli L. (2019). *Epistemologia e filosofia della cura per una "Nuova alleanza" in ambito medico-oncologico*. Complessità, 19:115-139
11. Prigogine I. (1992). *Vers un humanisme scientifique*, in: *Lezioni di Premi Nobel*, Gargano A (ed.), Istituto Italiano per gli studi filosofici. *Issued (Proceedings)*: Naples 2005, p. 105-118.
12. Coveney PV, Dougherty ER, Highfield RR. (2016). *Big data need big theory too* Phil Trans R Soc A, 374: 20160153
13. Guyatt G. H. (1991). *Evidence-based medicine*. ACP J Club, 114(s2): A16.
14. Evidence-Based Medicine Working Group. (1992). *Evidence-based medicine: a new approach to teaching the practice of medicine*. JAMA, 268:2420-2425
15. Hanahan D, Weinberger RA (2000). *The hallmarks of cancer*. Cell, 100:57-70
16. Renan MJ. (1993). *How many mutations are required for tumorigenesis? Implications from human cancer data* Mol Carcinogenesis, 7; 139-146
17. Weinberger RA. (2014). *Coming full circle-from endless complexity to simplicity and back again*. Cell, 157: 267 - 271
18. Siegel RL, Miller KD, Jemal A. (2020). *Cancer statistics 2020* CA Cancer J Clin 70:7-30
19. Logue JS, Morrison DK. (2012). *Complexity in the signaling network: insights from the use of targeted inhibitors in cancer therapy*. GenesDev 26:641-50
20. Camus A. (1942). *Le mythe de Sisyphe*. Gallimard, Paris
21. Gismondi M. (2004) *Tragedy, realism, and postmodernity: kulturpessimismus in the theories of Max Weber, E.H. Carr, Hans J. Morgetau, and Henry Kissinger*. Diplomacy and Statecraft ,15:435-464.
22. Bauman Z, Mauro E. (2015). *Babel*. Edizione Laterza, Roma-Bari
23. Gawande A. (2016). *The mistrust of science*. Commencement Address, California Institute of Technology. Issued: The New Yorker, June 10, 2016.

