T

Placing Trust in Medicine by Dealing with Its Uncertainty

Francesca Marin

1. *The need for a triple pattern*

This paper promotes the idea of mutual dependence between trust, medicine and uncertainty, and critically analyzes those approaches that either partially recognize such interdependence or propose a misrepresented view of medicine in terms of its relationship with uncertainty, negatively affecting trust in medicine. Indeed, on the one hand, nowadays the trust-medicine dyad is sometimes recognized without the acknowledgment of the medicine-uncertainty dyad, or vice versa. In other words, the role of trust in medical practice and the presence of uncertainty in medicine could be approached as issues which are unrelated to each other. In this way, the process of planning to promote trust in medicine and strategies for responding to medical uncertainty might be separately addressed. On the other hand, intolerance or even a refusal of medical uncertainty could affect trust in medicine because, by considering medicine itself as a science and a practice characterized by full certainty, claims of infallibility on the one side, and suspicions as well as incredulity on the other, might be fostered.

In order to avoid all these reductive views and to promote a well-placed trust in medicine, the paper's aim is to argue for the need for a change from a dual scheme, i.e. trust-medicine or medicine-uncertainty, to a triple pattern, that is, the trust-medicine-uncertainty interdependency. This is a particularly innovative proposal because, as it will be argued in the next paragraph, the scientific literature does not seem to have examined the trust-medicine-uncertainty pattern in depth. Indeed, although there are some exceptions[1],

[1] For example, see K. Armstrong, *If You Can't Beat It, Join It: Uncertainty and Trust in*

 DOI: 10.4454/teoria.v39i1.58

the debate has been more concerned with analyzing the twofold dyad mentioned above, i.e. trust-medicine and uncertainty-medicine. In this way, the role of trust in the medical context and the implications of uncertainty for both the clinical encounter and healthcare systems have been addressed. Although relevant, these contributions to the debate seem to have failed in acknowledging the trust-medicine-uncertainty interdependency, leading one to consider any effort to hide or eliminate medical uncertainty as a particularly promising strategy to promote trust in medicine.

The first part of the paper aims to critically analyze this strategy, not only by asserting that medical uncertainty cannot be completely removed, but also by arguing that there is a kind of irreducible uncertainty that typifies the nature of medicine as a science and a practice. This is an intrinsic uncertainty due to the epistemological status of medicine that cannot be confused with other forms of medical uncertainties, such as those arising from personal factors or limits of available medical knowledge. This is why the main forms of medical uncertainty will firstly be distinguished and facing one of them, intrinsic uncertainty, will secondly turn out to be a necessary condition for *well-placed trust in medicine*. This approach will be suggested by exploring the main consequences arising from the unwillingness to acknowledge and tolerate intrinsic medical uncertainty. In particular, examples of *misplaced trust in medicine* due to considering medicine as an absolutely certain scientific knowledge[2] and *misplaced distrust in medicine* as a result of an antiscientific view of medical knowledge will be discussed.

In the second part of the paper, the need to promote trust in medicine by dealing with its uncertainty will prove to be particularly urgent. Strictly speaking, the words "evidence" and "precision", which are abundantly used in the era of evidence-based medicine and precision medicine, could erroneously suggest a high degree of certainty and thus obscure the irreducible

Medicine, in «Annals of Internal Medicine», 168 (2018), n. 11, pp. 818-819; J.B. Imber, *How Navigating Uncertainty Motivates Trust in Medicine*, in «AMA Journal of Ethics», 19 (2017), n. 4, pp. 391-398.

[2] This view is usually based on the so-called "scientism", which rests on a problematic epistemological tenet. According to this tenet, only science can provide a successful explanation of the reality so much so that «scientific inquiry is our only genuine source of knowledge; all other alleged forms of knowledge (e.g., ordinary perception, *a priori* knowledge and introspection) are either reducible in principle to scientific knowledge or illegitimate». M. De Caro, *Realism, Common Sense, and Science*, in «The Monist», 98 (2015), pp. 197-214, p. 203. For an in-depth critical analysis of scientism and for a more inclusive approach to nature than any provided by the natural sciences, see M. De Caro, D. Macarthur (eds), *Naturalism in Question*, Harvard University Press, Cambridge (MA) 2004.

uncertainty of medicine. Actually, advances in these fields, rather than diminishing medical uncertainty, are contributing to its increase and even generating new kinds of uncertainties. After providing some examples about this topic, it will be argued that adequately promoting the expansion of medical knowledge means further justifying the trust-medicine-uncertainty interdependency. In other words, it means acknowledging that the triple pattern proposed in this paper is advantageous, and no less than necessary.

2. *A twofold dyad: trust-medicine and uncertainty-medicine*

The crucial role of trust in medical practice has long been recognized, and reasons to encourage mutually trusting relationships in medical context have been addressed. For instance, the phenomenological approach to the clinical encounter proposed by Edmund Pellegrino stresses that being ill means experiencing a particular vulnerable state as well as being forced to seek assistance from and to trust another person, i.e. the health professional, who holds the balance of the power by having the necessary knowledge and competences to heal[3]. As a consequence, strategies for building trust are both requisite responses to the patient's vulnerability and efforts to reduce the inequality of knowledge and skills that characterizes any relation with professionals, and consequently the patient-physician relationship as well[4].

Besides being required by the nature of the clinical encounter, interpersonal trust is also rightly considered one of the most important contributors to effective care. In medical settings, trusting attitudes such as loyalty, willingness to listen, truthful communication, and empathy usually result in improved health outcomes. Actually, good health care requires trust in medical institutions and health care systems as well, so much so that organizational aspects, such as availability of and accessibility to health care services, are likely to affect trust in one's doctor and, conversely, a trusting patient-physician relationship may enhance institutional trust[5].

[3] E.D. Pellegrino, *Toward a Reconstruction of Medical Morality: The Primacy of the Act of Profession and the Fact of Illness*, in R. Bulger, J. McGovern (eds), *Physician and Philosopher. The Philosophical Foundation of Medicine: Essays by Dr. Edmund Pellegrino*, Carden Jennings Publishing, Charlottesville 2001, pp. 18-36.

[4] Cfr. C.C. Clark, *Trust in Medicine*, in «Journal of Medicine and Philosophy», 27 (2002), n. 1, pp. 11-29.

[5] J. Saunders, *Trust and Mistrust Between Patients and Doctors*, in T. Schramme, S. Edwards (eds), *Handbook of the Philosophy of Medicine*, Springer, Dordrecht 2017, pp. 487-502.

These considerations explain why strengthening trust in medical science and practice is a primary goal. Nevertheless, in order to achieve such a purpose, it seems necessary to come to terms with another feature of medicine, its uncertainty, which has long been addressed within scientific literature. Indeed, both the philosophy of medicine and medical sociology have analyzed the medicine-uncertainty dyad, examining sources and implications of medical uncertainty for the clinical encounter[6] as well as for healthcare systems[7]. Uncertainty related to, for example, diagnosis and outcome is generally uncomfortable for those involved in the clinical decision-making process. Indeed, such uncertainty might instill further vulnerability in the patient and evoke a sense of helplessness in the physician. As a consequence, questions have been raised about whether and how uncertainty should be communicated[8] as well as whether and how physicians should be trained for uncertainty[9]. Furthermore, inappropriate responses to uncertainty might have a negative impact on the quality and cost-effectiveness of healthcare system, for example leading to unnecessary diagnostic tests or treatments.

[6] M.S. Henry, *Uncertainty, Responsibility, and the Evolution of the Physician/Patient Relationship*, in «Journal of Medical Ethics», 32 (2006), pp. 321-323.

[7] R.L. Logan, P.J. Scott, *Uncertainty in Clinical Practice: Implications for Quality and Costs of Health Care*, in «Lancet», 347 (1996), pp. 595-598.

[8] P.K. Han, *Conceptual, Methodological, and Ethical Problems in Communicating Uncertainty in Clinical Evidence*, in «Medical Care Research and Review», 70 (2013), 1 Suppl., pp. 14-36. Many qualitative studies have investigated this topic, obtaining non-homogenous results about the disclosure of uncertainty by physicians and patient satisfaction deriving from such disclosure. For example, Braddock and colleagues reported that during the informed consent process, physicians shared uncertainty with their patients in only 5% of the clinical encounters. See C.H. Braddock, K.A. Edwards, N.M. Hasenberg *et al.*, *Informed Decision Making in Outpatient Practice: Time to Get Back to Basics*, in «JAMA», 282 (1999), pp. 2313-2320. In contrast, in a more recent audiotape study, physicians made verbal expressions of uncertainty in 71% of clinic visits. Cr. G.H. Gordon, S.K. Joos, J. Byrne, *Physician Expressions of Uncertainty During Patient Encounters*, in «Patient Education and Counseling», 40 (2000), pp. 59-65. Furthermore, in the study conducted by Gordon, an increase has been registered in patient satisfaction with physician expression of uncertainty. Nevertheless, another study focused on therapeutic uncertainty has shown that patient satisfaction ratings were highest when no uncertainty was shared by the physician. See C.G. Johnson, J.C. Levenkron, A.L. Suchman *et al.*, *Does Physician Uncertainty Affect Patient Satisfaction?*, in «Journal of General Internal Medicine», 3 (1988), pp. 144-149. The results of the same study have confirmed that patient satisfaction is influenced by the manner in which uncertainty is conveyed and resolved by the physician.

[9] For opposite views on this issue, see R.C. Fox, *Training for Uncertainty*, in R.K. Merton, G. Reader, P.L. Kendall (eds), *The Student-Physician. Introductory Studies in the Sociology of Medical Education*, Harvard University Press, Cambridge 1957, pp. 207-241 and P. Atkinson, *Training for Certainty*, in «Social Science & Medicine», 19 (1984), n. 9, pp. 949-956.

All these considerations might suggest the idea that efforts to hide or remove medical uncertainty are a particularly promising strategy to promote trust in medicine. As it will be argued later, in addition to being unattainable given that medical uncertainty cannot be completely eliminated, such a project is disadvantageous because it deprives medicine of its proper nature and could lead to the decline of the authoritativeness of medical knowledge.

3. *The main kinds of uncertainty in medicine*

Quoting David Eddy, «uncertainty creeps into medical practice through every pore» so much so that the patient-physician relationship could be described as "a chain of uncertainty"[10]. From achieving more knowledge about a patient's condition to selecting and following a treatment plan, there are several links of uncertainty that vary depending on who performs the procedure and upon whom it is performed. These are what Eric Beresford has defined as "personal sources of uncertainty[11] alluding to both patient factors and physician aspects. Among the former, for example, there are biological variability, variable responses to treatment, partial presentation of symptoms to the physician, access to other sources of information, and even incompetence or inability to make wishes known. Diagnostic, prognostic and therapeutic uncertainty might be further emphasized by physician factors, such as bias, personal ignorance, poor communication skills, and intolerance to acknowledge the actual limits of medical information[12]. Furthermore, medical practice is characterized both by what Beresford has called "conceptual uncertainty", which occurs when applying abstract criteria (i.e. treatment guidelines or risk classifications) to particular patients, and by «uncertainty arising from health-care management and delivery, related to the complexity of systems involving a myriad of healthcare professionals that need to be coordinated, managed, and regulated»[13].

[10] D.M. Eddy, *Variations in Physician Practice: The Role of Uncertainty*, in «Health Affairs», 3 (1984), pp. 74-89, p. 75.

[11] E.B. Beresford, *Uncertainty and the Shaping of Medical Decisions*, in «Hastings Center Report», 21 (1991), n. 4, pp. 6-11.

[12] T. Dhawale, L.M. Steuten, H.J. Deeg, *Uncertainty of Physicians and Patients in Medical Decision Making*, in «Biology of Blood and Marrow Transplantation», 23 (2017), pp. 865-869 (in particular, p. 867).

[13] A.J.E. Seely, *Embracing the Certainty of Uncertainty. Implications for Health Care and Research*, in «Perspectives in Biology and Medicine», 56 (2013), n. 1, p. 68. For further types of

In addition to personal and conceptual uncertainties as well as to those originated by healthcare systems, there is a kind of uncertainty due to limitations in currently available medical knowledge and thus based on a scientific data deficit. This is the so-called "technical or informational uncertainty", which is expected to be reduced by the continuous progress in medical research. Nevertheless, the legitimate goal of acquiring additional knowledge cannot be rooted in the belief that this acquisition will totally remove medical uncertainty. Such a belief is unfounded not only because medical practice is confronted with the complexity and the singularity of the particular on a daily basis, but also because medicine is marked by an "irreducible or intrinsic uncertainty". Being a science and a practice, medicine discloses an alterable character given that medical knowledge and competences are all, at least in principle, revisable and no physician's mind is a blank slate or *tabula rasa*, but rather "a mind of a physician". Quoting Dario Antiseri, «behind a physician's eyes and hands there is a *mind of a doctor* and this *mind of a doctor* is laden with theories, expectations, experiences, mistakes already made by himself and by other physicians, technical devices, therapeutic theories, solved (and unsolved) clinical cases»[14]. The previous points are, as already mentioned, open to revision. As a consequence, intrinsic uncertainty is an essential characteristic of medicine and is an inevitable companion of medical practice.

It must be noted that the acknowledgment of this hallmark of medicine is not in conflict with any effort to decrease informational uncertainty. Not only is intrinsic uncertainty different from informational uncertainty, but also accepting the former as an inherent feature of medicine is a necessary condition for fostering our desire to reduce the deficit in current medical knowledge[15] as well as for being willing to minimize medical uncertainty. In order to examine this point in depth, some epistemological considerations regarding scientific knowledge are required. Although the following notes might initially appear misplaced, they will later reveal themselves to be an argument that justifies the need for the triple pattern proposed in this paper.

medical uncertainty, see P.K.J. Han, W.M.P. Klein, N.K. Arora, *Varieties of Uncertainty in Health Care: A Conceptual Taxonomy*, in «Medical Decision Making», 31 (2011), n. 6, pp. 828-838.

[14] D. Antiseri, *Epistemologia contemporanea e logica della diagnosi clinica*, in P. Giaretta, A. Moretto, G.F. Gensini, M. Trabucchi (eds), *Filosofia della medicina. Metodo, modelli, cura ed errori*, il Mulino, Bologna 2009, pp. 75-104, p. 81 (my translation).

[15] Although softer, a similar argument has been proposed by Seely when stating that «accepting intrinsic uncertainty is complementary to our desire to reduce and quantify informational uncertainty». A.J.E. Seely, *art. cit.*, p. 67.

4. *Toward a well-placed trust in medicine*

By its nature, scientific enterprise is revisable and historical evidence confirms this aspect so much so that scientific theories are likely to be, in Popper's terms, falsified or, better, superseded by other scientific theories. As a consequence, the acquisition of further knowledge in any scientific field must be supported by the acknowledgement that no area of scientific knowledge is characterized by a degree of absolute or apodictic certainty. In fact, any assertion or theory that would present itself as a totally irrefutable or incontrovertible knowledge could not be considered as a scientific statement[16]. The revisable character of scientific enterprise unavoidably assigns to any content of science a certain degree of uncertainty. Due to the particular nature of science, this is an uncertainty that, although modifiable, is ineradicable.

It is important to note that the certainty of such uncertainty does not question the authoritativeness of scientific knowledge. On the contrary, it is properly the source of this uncertainty, that is, the revisability of scientific knowledge, which makes science an authoritative form of knowledge. Indeed, such revisability characterizes the slow "march of science"[17], but does not invalidate the truth of scientific knowledge: although scientific truth is temporary precisely because it is revisable, it is however a scientific truth by being evidence-based as well as partially or entirely accredited by the scientific community. Furthermore, the revisable character of scientific enterprise can firstly guarantee an even more in-depth knowledge of reality, and secondly, impede that any scientific theory exclusively auto-confirms itself.

Applying these considerations to medicine, we can say that what is often considered as a failure of medicine or its Achilles' heel, that is, its irreducible uncertainty and thus its continual process of revision, assigns to medical knowledge the status of scientific knowledge. In other words, it is precisely this fickle aspect which is the greatest strength of medicine because it makes medicine an authoritative form of knowledge. This explains why acknowledging the medical intrinsic uncertainty means recognizing the epistemological status of medicine and differentiating such uncertainty from personal, conceptual and informational uncertainties is the starting point for dealing with medical uncertainty and being willing to reduce it.

[16] Cfr. E. Agazzi, *Scientific Objectivity and Its Context*, Springer, London 2014, p. 411.

[17] L. Rosenbaum, *The March of Science - The True Story*, in «The New England Journal of Medicine», 377 (2017), n. 2, pp. 188-191.

Indeed, any effort in this direction should consider a complete removal of intrinsic uncertainty to be not only impossible, but also disadvantageous or even undesirable because it would lead to the decline of medicine and of the authoritativeness of medical knowledge.

Accepting this conclusion means adopting an approach for the promotion of trust in medicine that is not aimed to deny or hide intrinsic uncertainty, but rather to acknowledge and value it. To specify, this is an approach that encourages us to put trust in medicine by precisely facing and embracing its intrinsic uncertainty. Such encouragement is rooted in the trust-medicine-uncertainty interdependence because it does not simply address the twofold dyad, that is, the crucial role of trust in medical context and the ubiquitous presence of uncertainty in medical practice, but also considers uncertainty as a fundamental aspect of the epistemological status of medicine, whose presence guarantees well-placed trust in medicine.

5. *Misplaced trust vs misplaced distrust in medicine*

By analyzing medical uncertainty and in particular the kind of uncertainty that intrinsically characterizes medicine as a science and a practice, the link between the revisability of scientific knowledge and the authoritativeness of science has been addressed. Nowadays this link is not easily recognized and accepted, so much so that a sort of intolerance toward the revisability of medical knowledge is still widespread not only in the public opinion, but also within a part of the scientific community. This intolerant attitude could assign the highest degree of certainty and absoluteness to medical knowledge, misunderstanding the proper nature of medicine and leading to unquestioning trust in medicine.

Besides offering an epistemologically problematic scenario, this misplaced trust in medicine affects medical practice and raises many ethical issues. Firstly, if medical knowledge is considered as the only knowledge deserving of the name "scientific knowledge", a standardized approach to disease could be proposed, reducing the human body to a completely quantifiable reality as well as determining any status of health exclusively on the basis of objective parameters. In this way, our body might be considered as a mere extended physical substance (*Körper*), underestimating the subjective experience of our corporeity (*Leib*)[18], and personal valua-

[18] In this respect, see E. Dahl, C. Falke, T.E. Eriksen (eds), *Phenomenology of the Broken*

tions regarding our health status could be totally excluded. Secondly, efforts to consider or even to present medical knowledge as an absolutely certain form of knowledge usually result in a claim for infallibility and in a search for the highest degree of certainty. To specify, on the one hand, denying or hiding medical intrinsic uncertainty could increase the degree of patient expectations and create new demands towards medicine. On the other hand, an unwillingness or incapacity to accept intrinsic uncertainty could lead to a physician's maladaptive responses to uncertainty, such as anxiety, obsession with finding the right answer, and reluctance to disclose uncertainty for fear of projecting ignorance or failure to patients[19].

Further problematic issues arise when the revisability of scientific knowledge is recognized but the authoritativeness of science is questioned or, in the worst case, denied. When dismissing scientific consensus, perceptions of corruption are usually invoked. Unfortunately, stories of scientific misreporting (such as exaggeration of the conclusions drawn from research and unpublished negative findings)[20], conflicts of interest with pharmaceutical industry and political meddling are, although rare, sadly true. Nevertheless, doubts, suspicions and skepticism are often unwarranted, and an antiscientific view of medical knowledge is also due to an intolerance of medical uncertainty. Indeed, it is precisely this fickle aspect of medicine that generally leads people to distrust medical data and guidelines, for example by resorting to alternative medicines. In this way, the authoritativeness of medical knowledge is usually superseded by emotions, personal beliefs and pseudoscientific conspiracies whose misjudged statements are easily shared and exponentially amplified by social platforms. It's no coincidence that the Oxford Dictionaries declared "post-truth" as the international Word of the Year for 2016, defining it as an adjective «relating to or denoting circumstances in which objective facts are less influential in shaping public opinion than appeals to emotion and personal belief»[21].

Body, Routledge, London 2018; R.T. Jensen, D. Moran (eds), *The Phenomenology of Embodied Subjectivity*, Dordrecht, Springer 2013; S. Gallagher, D. Zahavi, *The Phenomenological Mind. An Introduction to Philosophy of Mind and Cognitive Science*, Routledge, London 2012[2].

[19] A.L. Simpkin, R.M. Schwartzstein, *Tolerating Uncertainty - The Next Medical Revolution?*, in «The New England Journal of Medicine», 375 (2016), n. 18, pp. 1713-1715.

[20] For some misleading conclusions drawn from health-related research, see P. Sumner, S. Vivian-Griffiths, J. Boivin *et al.*, *The Association Between Exaggeration in Health Related Science News and Academic Press Releases: retrospective Observation Study*, in «British Medical Journal», 349 (2014), https://www.bmj.com/content/bmj/349/bmj.g7015.full.pdf.

[21] https://en.oxforddictionaries.com/word-of-the-year/word-of-the-year-2016.

Passively accepting to live in a post-truth era means dangerously impeding the spread of evidence-based data and calling into question the strength of rational arguments. When dealing with health-related issues, this tendency is potentially harmful both for the individual and for society because in general fake news, fallacies, inconsistent beliefs and scams about unsubstantiated treatments spread useless, and even worse, dangerous practices, usually for commercial purposes or for making money easily. This risk is further exacerbated by the advancement of Information and Communication Technologies (ICT). Indeed, through the use of search engines, users may be subjected to the so-called "information bubble phenomena", that is, being isolated in a universe of information algorithmically created on the basis of users' location, personal preferences and past click-behavior[22].

The weakest people, such as teenagers and the elderly, as well as those who uncritically use search engines and social networks, are more likely to be exposed to misinformation in the medical field and prone to the information bubble. Their searching on the internet could be exploited by ICT companies, for example for displaying advertisements of selected goods or unsubstantiated therapies during users' future online browsing, which might appear to vulnerable people as "the solution" to their problems.

To sum up, living in a digital and post-truth era where it is becoming increasingly necessary to verify truthfulness and the quality of information, it is more reasonable to sustain the slow "march of science" and accept the revisability of scientific knowledge than to be damaged by unverified or false information. In fact, as sadly confirmed by the news, a believed lie (for example believing that cancer might be cured with sodium bicarbonate) can cause irreversible injury, and, in the worst-case scenario, lead to death. As a consequence, questioning medical knowledge although there is a reasonable evidence for trustworthiness, and at the same time unquestioning non-authoritative opinions as well as untrustworthiness information obtained in the internet or shared by social platforms, is a real paradox. Even more, it is proof of an irresponsible behavior that leads to misplaced distrust in medicine and has negative health implications for the individual and for society[23].

[22] For the main ethical issues raised by the diffusion of ICT, cfr. National Committee for Bioethics, *Information and Communication Technologies and Big Data: Bioethical Issues*, 25 November 2016, http://bioetica.governo.it/media/3207/p124_2016_information-techonolgies-and-big-data_en.pdf (in particular, pp. 13-16).

[23] In this respect, the decrease in immunization coverage is a good example because the tendency to defer or refuse vaccinations has consequences at an individual and collective level, for example invalidating the protection of vulnerable people, including those who cannot be

6. *The risk of the boomerang effect*

At this point, the following question could be raised: what should medicine do in order to solve the "Cassandra problem", that is, to face «unwarranted suspicion and misjudged refusal to trust, even where there is adequate – if inevitably imperfect – evidence of trustworthiness» with regard to medical knowledge[24]? Surely, the adequate promotion of competence criteria is required in order to acknowledge and accept its peculiar traits. For example, differently from the power of prophecy possessed by the mythological figure of Cassandra, medical competence is not a gift, but rather the result of an endless studying and training process. This is why not everyone can be considered an expert in medicine, although medical knowledge might be obtained, at least in principle, by all. In other words, competence criteria show an inherent selective character and not all different opinions on scientific matters are equally valuable. Medical competence assigns a stronger force to experts' opinions, which are however called to be continuously discussed within the medical scientific community. Once again, it is precisely the revisability of medical knowledge and, in parallel, intrinsic uncertainty in medicine that guarantee the authoritativeness of expert medical opinions and competences.

The question that has been proposed at the beginning of this paragraph could thus be reformulated in the following terms: what should medicine do in order to show that medical knowledge is not absolute but, despite the presence of intrinsic uncertainty, is nonetheless characterized by a certain degree of certainty? When illustrating both discoveries in the medical field and medical advances that are expected for the future, a careful selection and use of words by the medical scientific community would be a good starting point. Terms should not be ambiguous, for example, suggesting the highest degree of certainty and thus obscuring the irreducible uncertainty of medicine. Actually, some words currently used in the era of evidence-based medicine (EBM) and precision medicine (PM) would seem to assign a fully scientific character to medicine. For example, at first glance, "evi-

vaccinated for health reasons. A greater personal and social responsibility should thus be assumed, and falsehoods regarding vaccines (such as the scientifically unfounded idea that vaccination triggers autism) should be dispelled.

[24] O. O'Neill, *Autonomy and Trust in Bioethics*, Cambridge University Press, Cambridge 2005[3], pp. 141-142 (quotation is at p. 141). In Greek mythology, Cassandra was a daughter of Priam, the King of Troy, who received the gift of prophecy from Apollo. Nevertheless, when Cassandra refused Apollo's love, he condemned her to never be believed to the extent that, despite her trustworthiness, her prophecy regarding the fall and destruction of Troy went unheeded.

dence" could be considered as an absolute category, entirely free of context[25]. In this way, in reference to EBM's main instruments, i.e. clinical practice guidelines and research protocols, EBM might be erroneously expected to rely on indisputable facts. Besides, "evidence" derives from the Latin *evidentia* which means vividness or clearness; when literally translated into other languages this word can mainly lead one to consider scientific evidence as an irrefutable form of knowledge. For instance, the literal Italian translation of "evidence", which is "evidenza", alludes to something that cannot be questioned or denied precisely because of its clearness.

The previous remarks do not intend to question the contribution of EBM[26]. Information obtained by randomized controlled trials (RCTs), and systematic reviews of RCTs as well, regarding the efficacy and safety of healthcare interventions provides clinical practice guidelines, such as step-by-step instructions and estimates of the treatment outcomes, usually helping to reach medical decisions. Moreover, adequate communication of evidence results to patients can lead to a more shared decision-making process because, for example, statistical data may enhance patients' participation in the context of discussing risk. Nevertheless, the evidence provided by EBM concerning the effectiveness of interventions might obscure the intrinsic uncertainty of medicine because, at first glance, the word "evidence" alludes to something that is indisputably evident, and thus totally certain.

Similar considerations can be made for the word "precision" because, especially in the colloquial sense, it «implies a high degree of certainty of an outcome, as in "precision-guided missile" or "at what precise time will you arrive?»[27]. The terminological ambiguity seems to be further emphasized by the emerging concept of systems medicine, which is often promoted as "P4 medicine" (predictive, preventive, personalized and participatory) and conveys advances in genetic research towards PM[28]. Indeed, focused on the

[25] This risk has been addressed, for example, by the Canadian Health Services Research Foundation within a document that summarizes the results of a workshop held in 2005 and focused on scientific evidence. See Canadian Health Services Research Foundation, *Weighing Up the Evidence. Making Evidence-Informed Guidance Accurate, Achievable, and Acceptable*, January 2006, https://www.cfhi-fcass.ca/migrated/pdf/weighing_up_the_evidence_e.pdf.

[26] For the main advantages of EBM methods, see W. Rogers, K. Hutchison, *Evidence-Based Medicine in Theory and Practice: Epistemological and Normative Issues*, in Schramme, Edwards (eds.), *Handbook of the Philosophy of Medicine*, cit., pp. 851-872 (in particular, pp. 852-857).

[27] D.J. Hunter, *Uncertainty in the Era of Precision Medicine*, in «The New England Journal of Medicine», 375 (2016), n. 8, p. 711.

[28] For an overview of advances in the field of PM as well as of their implications, see H.-P. Deigner, M. Kohl (eds), *Precision Medicine: Tools and Quantitative Approaches*, Academic Press,

intersection of three factors, i.e. individual variations in genes, environmental interactions and influence of lifestyle, the four Ps are associated with promises of a forthcoming revolution in medicine[29]. Systems medicine pledges to provide predictive assessments, that is, individual health risk information relating to potential future genetic diseases, and thus to facilitate prevention, personalize medicine and motivate people to change their health-related behavior, reducing the risk of the disease's onset[30].

By illustrating medicine as a scientific enterprise able to achieve these goals in the short or long term, a boomerang effect could occur. The four Ps might present medicine itself as a science and a practice characterized by full certainty, fostering in this way claims of infallibility by the individual and society on the one hand, and suspicions as well as incredulity on the other hand. In other words, such a boomerang effect might negatively affect the trust-medicine dyad because medicine itself could lead to a refusal of its epistemological status or paradoxically contribute to a decrease in its authoritativeness, respectively promoting displaced trust and displaced distrust in medicine.

7. *The certainty of increasing uncertainty*

Beyond the words that are chosen to illustrate medical advances, benefits of EBM and developments in genetic testing technology could constitute

Amsterdam 2018; M. Verma, D. Barh (eds), *Progress and Challenges in Precision Medicine*, Academic Press, London 2017.

[29] Cfr. L. Hood, R. Balling, C. Auffray, *Revolutionizing Medicine in the 21st Century through Systems Medicine*, in «Biotechnology Journal», 7 (2012), n. 8, pp. 992-1001. See also M. Flores, G. Glusman, K. Brogaard, N.D. Price, L. Hood, *P4 Medicine: How Systems Medicine Will Transform the Healthcare Sector and Society*, in «Personalized Medicine», 10 (2013), n. 6, pp. 565-576.

[30] In this respect, the growing diffusion of direct-to-consumer (DTC) genetic susceptibility tests should not be underestimated. This kind of testing can be purchased at increasingly reduced prices and gives everyone the possibility to obtain health risk information without the guidance or supervision of healthcare providers or genetic counselors. It is not possible to discuss here the main problematic issues raised by these tests. The following remark is only mentioned as related to the focus of this paper. Although research is ongoing, genetic susceptibility testing has limited predictive power because it carries a degree of uncertainty as to whether a disease will develop, when it will develop and how severe it will be. The use of DTC genetic susceptibility tests usually increases the problem of managing the impact of this uncertainty. Indeed, without specialized knowledge of genetics and the involvement of healthcare professionals, misinterpretation of test results may occur and entail unjustified negative feelings, such as anxiety and depression. For an in-depth analysis of the main ethical issues of DTC genetic susceptibility tests as well as of their implications for healthcare systems, see F. Marin, *Putting Health in the Marketplace. Ethical Issues about Providing Online Health Risk Information*, «Medicina e Morale», 66 (2017), n. 1, pp. 31-43.

themselves a proof that a decrease, or even an elimination, of uncertainty is really possible. For example, considering the ability of well-designed RCTs to inform medical practice and to guide the decision-making process as well as the current possibility to scan and compare entire genomes, a reduction of medical uncertainty may intuitively be expected in EBM and PM.

Actually, advances in these fields, rather than diminishing medical uncertainty, are contributing to its increase and even generating new varieties of uncertainties. Indeed, as regards EBM, it has been shown that, given the increased reliance on information technologies and epidemiology, research protocols and evidence-based guidelines generate new kinds of uncertainties. For example, through in-depth interviews with pediatric residents from two medical programs about their experiences with EBM, Stefan Timmermans and Alison Angell have addressed a new form of uncertainty, named "research-based uncertainty"[31]. Some of the interviewees felt uncomfortable in conducting literature searches or evaluating protocols and guidelines, while others felt unsure in distinguishing a good sample from a bad one as well as in differentiating statistical significance from confidence intervals.

A greater set of biomedical and epidemiological variables is offered by PM as well[32]. Indeed, quoting Lily Hoffman-Andrews, «the wonderful promise of expanding testing has, in practice, run into the frustrating reality of a greater burden of uncertain results»[33]. For example, when reviewing thousands of variants obtained by exome sequencing, clinicians and laboratory personnel deal with many variants of uncertain significance (VUSs) and have to decide whether to omit or include them[34]. When encountering VUSs, troublesome questions concern the care relationship as well because genetics professionals and clinicians are asked whether and how to disclose these variants to the patient and how to manage their impact[35].

[31] S. Timmermans, A. Angell, *Evidence-Based Medicine, Clinical Uncertainty, and Learning to Doctor*, in «Journal of Health and Social Behaviour», 42 (2001), n. 4, pp. 342–359 (in particular, pp. 348-349). A reworked version of this article is chapter 5 of a book that Stefan Timmermans has written with Marc Berg. See S. Timmermans, M. Berg, *The Gold Standard: The Challenge of Evidence-Based Medicine and Standardization in Health Care*, Temple University Press, Philadelphia 2003, pp. 142-165.

[32] D.J. Hunter, *art. cit.*, pp. 711-713.

[33] L. Hoffman-Andrews, *The Known Unknown: The Challenges of Genetic Variants of Uncertain Significance in Clinical Practice*, in «Journal of Law and the Biosciences», 2017, pp. 648-657 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5965500/pdf/lsx038.pdf), quotation is at p. 649.

[34] S. Timmermans, C. Tietbohl, E. Skaperdas, *Narrating Uncertainty: Variants of Uncertain Significance (VUS) in Clinical Exome Sequencing*, in «BioSocieties», 12 (2017), n. 3, pp. 439-458.

[35] See K. Barlow-Stewart, *The Certainty of Uncertainty in Genomic Medicine: Managing the Challenge*, in «Journal of Healthcare Communication», 3 (2018), n. 3, p. 37.

As a consequence, although the expansion of medical knowledge is expected to reduce informational uncertainty, the certainty of increasing medical uncertainty is confirmed properly by medical progress and technological innovations. This is why, nowadays, dealing with the medicine-uncertainty dyad requires greater tolerance of uncertainty and further strategies to face new kinds of uncertainties derived by medical advances.

8. *Conclusions: from a twofold dyad to a triple pattern*

This paper has not merely addressed the crucial role of trust in medical practice and the ubiquitous presence of uncertainty in medicine, as tends to happen in scientific literature; rather, it has gone further by showing that several problematic issues arise when the trust-medicine dyad is recognized without the acknowledgment of the medicine-uncertainty dyad, or vice versa. Indeed, displaced trust and displaced distrust in medicine occur when respectively considering medical knowledge as an absolutely certain knowledge and refusing uncertainty as an inherent feature of medicine. In this way, the main thesis of the paper has been justified, that trust in medicine is well-placed when the trust-medicine-uncertainty interdependency is fully recognized and adequately valued.

The triple pattern proposed in these pages is particularly advantageous for the following reasons. Firstly, it adds value to the epistemological status of medicine because intrinsic uncertainty is proof of the revisable character of medical enterprise, and such revisability guarantees a well-placed trust in medicine. Secondly, the promotion of the trust-medicine-uncertainty interdependency involves healthcare professionals, patients, mass media, and society in general. Indeed, everyone is called to recognize the authoritativeness of medical knowledge and competence criteria as well as to paradoxically appreciate episodes of dissent within the scientific community as proof of the revisability of medicine. Thirdly, the triple pattern proposes a sort of balancing between certainty and uncertainty. By admitting irreducible uncertainty in medicine, the authoritativeness of medical knowledge as well as the contribution of medical-technological progress are not questioned and at the same time an overestimation of uncertainty does not occur. Instead, the interdependency mentioned above denies the ascription of a fully scientific character to medicine on one side, and an antiscientific view of medical knowledge on the other side.

As far as the final point is concerned, is must be noted that balancing

certainty and uncertainty avoids a twofold risk. On the one hand, absolutizing certainty leads healthcare professionals to take less responsibility for their actions, negatively affecting the patient's health. On the other hand, an overemphasis on uncertainty leads to over-responsibility, questioning any plan of care on behalf of the patient. In this way, medicine as a science and a practice is dangerously considered as a world which is neither white nor black. Actually, the certainty of uncertainty makes medicine a gray-scale space[36] toward which, as it has been argued in this paper, trust can be well-placed by precisely dealing with medical uncertainty. In other words, adequately facing the challenges posed by this grey-scale scenario means recognizing and promoting the trust-medicine-uncertainty interdependence.

Abstract

The paper does not merely address the crucial role of trust in medical practice and the ubiquitous presence of uncertainty in medicine, as tends to happen in scientific literature; rather, it goes further by showing that problematic issues arise when the trust-medicine dyad is recognized without the acknowledgment of the medicine-uncertainty dyad, or vice versa. Firstly, it is argued that the trust-medicine-uncertainty interdependency is necessary because there is a kind of irreducible uncertainty due to the epistemological status of medicine, whose presence guarantees well-placed trust in medicine. *In this respect, examples of* misplaced trust in medicine *due to considering medicine as an absolutely certain scientific knowledge and* misplaced distrust in medicine *as a result of an antiscientific view of medical knowledge are discussed. Secondly, the need for a triple pattern is proved to be urgent because medical advances, rather than diminishing medical uncertainty, are contributing to its increase and even generating new kinds of uncertainties.*

Keywords: trust; medical practice; medical uncertainty; evidence-based medicine; precision medicine.

Francesca Marin
Università degli Studi di Padova
francesca.marin@unipd.it

[36] A.L. Simpkin, R.M. Schwartzstein, *art. cit.*, p. 1714.