Special issue

Incidental findings and the right not to know in clinical setting: Constitutional perspectives

Alessia-Ottavia Cozzi*

ABSTRACT: Next generation sequencing (NGS) induces frequent discoveries of incidental findings. This means that, during the sequencing, primary information concerning the alteration in gene for which the sequencing test was ordered goes with other information on different alterations. This problem is first faced by laboratories, followed by clinicians. The core question is whether to inform patients of those alterations. The first part of this paper overviews the guidelines adopted by the scientific community to set incidental findings. References are made to the 2016 European Guidelines for Diagnostic NGS, U.S. Recommendations adopted in 2013 and revised twice, in 2015 and in 2016, Italian Report of Bioethics Committee of 2016, and French Guidelines on secondary findings related to cancer gene of 2018. The second part of this paper discusses the rationale of "the right not to know" and analyses two main frameworks: autonomy and privacy. An attempt is made to consider the issue through different constitutional backgrounds: the U.S. and French notion of autonomy and freedom, and the Italian constitutional background. This paper argues that the right not to know is a negative right comprising a denial, but whose exercise requires positive obligations from clinicians to fulfil an effective and conscious choice. Recalling a famous U.S. debate on negative and positive liberty, a synthesis of the two sides could be managed through a procedural setting of consent, including information about family members. In this sense, the right not to know refers to a constitutional pattern of principles that is not limited to self-determination but entails solidarity and responsibility.

KEYWORDS: Incidental findings; Genome sequencing; Autonomy; Privacy; Negative and positive liberties

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* *Assistant Professor in Public Law (rtd b), Department of Law, University of Udine. Mail: alessiaottavia.cozzi@uniud.it.* *I am grateful to Dr. Flavio Faletra, Geneticist and expert in Medical Genetics at the Research Institute for Motherhood and Childhood, IRCCS materno infantile Burlo Garofolo, Trieste, for the great help in collecting and analysing scientific articles on the issue. I remain responsible for any mistake. The article was peer-reviewed by the editorial committee.*

framework – 10. *(continue)* The right not to know under Italian constitutional law – 11. The positive side of the right not to know: Consent – 12. Conclusions: Double consent as a nudge.

1. Introduction

"The right not to know" questions some deeply rooted principles underlying constitutionalism – the idea to change our lives through human will and action. The evolution of technology and science faces borders, where knowledge refusal, at the given state of understanding and depending on intimate and private beliefs, probably is the best chance to organise a worthy life. Concurrently, such an intimate decision is inextricably intertwined with others, family members whose relation could be good or bad, as always in life. This paper argues that exercising "the right not to know" reflects autonomy but refuses isolation and calls for solidarity and responsibility. In this framework, there is a positive obligation of public authorities to set appropriate measures through which everyone can manage his faith and expectations for how his life is supposed to be.

This paper explores incidental findings in a clinical setting. Managing them raises different problems in both clinics and research, and even if the borders between research and clinic are increasingly blurring, we concentrate only on clinical aspects.[1] Also, this paper does not discuss issues concerning minors and third parties other than family members.

[1] The main differences between incidental findings in clinical and research settings are as follows: genome sequencing for clinical diagnosis primarily entails protecting the individual patient's health, so an examination ordered for clinical reasons involves evaluations on prevention or treatment; the interests of others, particularly family members, are much more compelling in clinical practise than in research activity; genomic analysis performed for health research sometimes lacks the same sensitivity and quality criteria (depth and coverage) as that performed in a healthcare context. The main point for incidental findings in research seems to be the opportunity or duty of recontact, depending on the scale of the study, the object - rare diseases or not - and the formula of initial consent. See J. VIBERG, M.G. HANSSON, S. LANGENSKIÖLD, P. SEGERDAHL, *Incidental Findings: The Time Is not yet Ripe for a Policy for Biobanks*, in D. MASCALZONI (ed.), *Ethics, Law and Governance of Biobanking*, Heidelberg, 2015, 121-131, and, in Italian literature, M. TOMASI, *Genetica e Costituzione*. *Esercizi di eguaglianza, solidarietà e responsabilità*, Napoli, 2019, 245 ff. On the right not to know in research, S. M. WOLF, J. PARADISE, C. CAGA-ANAN, *The Law of Incidental Findings in Human Subjects Research: Establishing Researchers' Duties*, in *Journal of Law, Medicine and Ethics*, 36, 2, 2008, 361-383; B.M. KNOPPERS, *From the Right to Know to the Right Not to Know*, in *Journal of Law, Medicine and Ethics*, special issue no. 1, 2014, 1-10, who notes that "no return" policies adopted by large population genome studies, for example, P3G, on 23 national biobanks, have been integrated with new options of consent upon recontact of participants, because the increasing use of WGS caused the discovery of unsolicited information such as rare mutations or clinically significant incidental findings, blurring the distinction between research and clinical contexts. Nevertheless, the borders between research and clinics in the matter still exist. See *European Society of Human Genetics' Guidelines for diagnostic next-generation sequencing*, in *European Journal of Human Genetics*, 24, 2016, 2-5, 5, on "Distinction between Research and Diagnostic", Statements no. 32-38. Recently, the American College of Medical Genetics and Genomics gave a statement to forbid using their clinical recommendations for incidental findings for general population screening because any of the ACMG SF v2.0 genes, as quoted later, have uncertain penetrance when identified in asymptomatic individuals (e.g. SCN5A and Brugada syndrome). In the absence of penetrance data that can only be obtained through robust genotype-phenotype correlation, the medical ethical principle of nonmaleficence should dominate, in *The use of ACMG secondary findings recommendations for general population screening: a policy statement of the American College of Medical*

The first part of this paper overviews current guidelines and recommendations adopted by the scientific community to set incidental findings. References are made to the 2016 European Guidelines for Diagnostic Next Generation Sequencing (NGS), U.S. *Recommendations* adopted in 2013 and revised twice, in 2015 and in 2016, Italian Report of Bioethics Committee of 2016, and French *Guidelines* on secondary finding related to cancer gene of 2018. A comparison is made on the procedures adopted to define the guidelines and to their content by considering clinicians' viewpoints (types of variations and actionability) and patients' viewpoints (right not to know). In this first part we will use both the acronyms IFs, incidental findings, present in the Italian Report, and SFs, secondary findings, where U.S. *Guidelines* since the 2015 version and French *Guidelines* refer specifically to secondary findings, as we will better explain later.

The second part of this paper discusses the rationale of "the right not to know" by analysing two main frameworks having a great echo between scholars: autonomy and privacy. Subsequently, an attempt is made to consider the issue through different constitutional backgrounds: the U.S. and French notion of autonomy and freedom, and the Italian constitutional framework. Constitutional traditions are relevant because the clinician–patient relationship mirrors an individual's position in society and the relation with power. The common tread chosen is the negative and positive way "the right not to know" is framed. The two aspects, in our opinion, do not create dichotomy, but coexistence – the positive side setting the condition to fulfil the negative one. Hence, this paper argues that "the right not to know" is a negative right comprising a denial, but whose exercise requires positive obligations from clinicians to fulfil an effective and conscious choice. Recalling a famous U.S. debate on negative and positive liberty, synthesising the two sides could be managed through a procedural setting of consent, including information about family members. In this sense, "the right not to know" refers to a constitutional pattern of principles that is not limited to self-determination but entails solidarity and responsibility.

2. Incidental findings in clinical setting: A scientific overview

Next Generation Sequencing[2] and the increasing use of multi-panel analysis in clinical practise to discover genes responsible for main diseases induces frequent discoveries of incidental findings. This means that, during the sequencing, primary information concerning the alteration in gene for which the sequencing test was ordered goes with other information on different alterations. Geneticists

Genetics and Genomics (ACMG), in *Genetics in Medicine*, 2019 (21), 1467-1468, and the ongoing debate that followed. In contrast, French *Guidelines*, as quoted later, 1736, 1738, concern both somatic analyses performed in healthcare context for research, and the provided consent forms too. For a recent example of management in research, see le dossier *Comment donner suite aux découvertes fortuites significatives. Lignes directrices sur l'application de l'article 3.4 EPTC* 2 (2018), *Group consultative en éthique de la recherche*, 2019, in https://ethics.gc.ca/fra/incidental_findings.html.

[2] See the introduction of European Society of Human Genetics' Guidelines for diagnostic next-generation sequencing: "Next generation sequencing (NGS) allows for the fast generation of thousands to millions of base pairs of DNA sequence of an individual patient. The relatively fast emergence and the great success of these technologies in research herald a new era in genetic diagnostics. However, the new technologies bring challenges, both at the technical and in terms of data management, as well as for the interpretation of the results and for counselling", cit., 2.

usually divide IFs into different categories: fortuitous or secondary. Fortuitous findings are completely unexpected, accidental and non-predictable results, while secondary findings are predictable results, i.e. they can be expected as a part of the results, even if they are unrelated to the primary research of alteration.[3] The problem is first faced by laboratories, followed by clinicians. The core question is whether to inform patients of those alterations.

IFs are well known in the fields of medicine other than genetics. For example, radiographs for a particular anatomical focus can report abnormal findings in regions not indicated as the primary reason for investigation. Although it is generally argued that there is a right of the patient to know this information and a duty of the clinician to report them to protect the patient's health, the same pattern may not be suitable for genome IFs. Many differences exist between radiographic images and genetic information regarding predictability of the information and interpretation, both technically and clinically.[4] Furthermore, patient could avoid obtaining genetic information for many reasons. Learning to be at risk of genetic disease may induce anxiety, depression, changes in self-image, reduced capacity to organise the future or even stigmatisation and discrimination.[5] Moreover, the desire for ignorance could rely on economic and social conditions, concerns about the costs of therapies, or the fear of being a burden to others.

Few recommendations have been adopted in Europe to manage IFs, and scientific publications have shown variabilities in European practices for transmitting incidental information both from laboratories to clinicians and from clinicians to the patient. A need for common guidelines emerged to help molecular laboratories and clinician physicians harmonise their practice, particularly for cancer-related genes, and to assure equal access and uniform service across Europe.[6]

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[3] We will see later that U.S. *Guidelines* and French *Guidelines* refer to secondary findings, while the Italian Bioethics Committee use the term "incidental findings" because it is common in international debate: Report *Gestione degli "incidental findings" nelle indagini genomiche con le nuove piattaforme tecnologiche*, 17 marzo 2016, http://bioetica.governo.it/media/1803/p123_2016_incidental_findings_it.pdf, 11, note no. 23.

[4] See French *Guidelines for reporting secondary findings of genome sequencing in cancer gene: the SFMPP recommendations*, in *European Journal of Human Genetics,* 26, 2018, 1732-1742, spec. 1737, admitting that the sensitivity of variant detection may vary among genes according to the coverage and depth of the sequencing process. Thus, the coverage and depth at the position of the gene of interest *will differ from that of genes secondarily and deliberately studied*. This concern could induce misinterpretation of the results by the clinician and/or the patient, such as the absence of a pathogenic variant in secondarily studied genes. Therefore, the French *Guidelines* suggest reporting the conditions of sequencing and analysis of secondary data if it differs from that of the primary data. Similarly, see European Society of Human Genetics' Guidelines, cit., "The implications of diagnostic test based on NGS depend on the procedures, platforms, filtering processes and data storage used in the laboratory. It is crucial that the referring physician is fully informed about the limitations and possible unfortunate effects of a genetic testing".

[5] R. CHADWICK, *The Philosophy of the Right to Know and the Right Not to Know*, in R. CHADWICK, M. LEVITT, D. SHICKLE (eds.), *The Right to Know and the Right Not to Know. Genetic Privacy and Responsibility*, Cambridge, 1997, 13-22, spec. 18.

[6] French *Guidelines*, cit., 1733, quoting D. F. VEARS, K. SENECAL, P. BORRY, *Reporting practices for unsolicited and secondary findings from next-generation sequencing technologies: Perspectives of laboratory personnel*, in *Human Mutation*, 38, 2017, 905-911, for variability in transmitting information from laboratories to clinicians, and J. Y. HEHIR-KWA, M. CLAUSTRES, R. J. HASTINGS, C. VAN RAVENSWAAIJ-ARTS, G. CHRISTENHUSZ, M. GENUARDI et al., *Towards a European consensus for reporting incidental findings during clinical NGS testing*, in *European Journal of Human Genetics*, 23, 2015, 1601-1606, from clinicians to patients. For the need of common guidelines, see C. G. VAN EL, M. C. CORNEL, P. BORRY, R. J. HASTINGS, F. FELLMANN, S. V. HODGSON et al., *Whole-genome sequencing in*

Here the issue is addressed by analysing different sets of recommendations adopted in the U.S., Italy, France and at the European level by the European Society of Human Genetics. It will be useful to start from the European level, which demonstrates a lack of common vision for IFs. The 2016 European Society's Guidelines on Diagnostic NGS recognise that the main implication of a diagnostic test based on NGS is the chance of unsolicited and secondary findings. To face the problem, under the paragraph "Informed consent and information to the patient and clinician", Statement no. 9 suggested focusing on the gene panel under investigation because the chance of unsolicited findings in a gene panel is very low and mainly depends on the genes involved. However, if the unsolicited information occurs, *choice is given to each laboratory, institute or to authorities at the national level*, *whether patients are offered opt-in, opt-out options* to get additional information. The only recommendation is that laboratories disclose the chance of unsolicited findings and set up "unsolicited and secondary finding protocols", which must agree with the decision of an ethical committee. Each protocol should specify whether unsolicited findings are reported and, in that case, provide for pre-test genetic counselling, including a discussion on both expected results and the potential for unsolicited and secondary findings, local policies assuring clear dissemination for patients.[7] Overall, adopting opt-in and opt-out policies on IFs is discretionary. A definitive settlement of the interests at stake has not been established, and the balance between the task to report and the desire of the patient remains open. We will see that this setting has been discussed at the national level on both sides of the Atlantic.

3. U.S., Italian and French Guidelines on disclosing secondary findings: Scope of application and working procedures

After a strong scientific debate in 2013, the American College of Medical Genetics and Genomics adopted guidelines (in the following, U.S. *Guidelines*) concerning secondary findings.[8] For their organic and influential attempt to set the issue, U.S. *Guidelines* induced discussion in the scientific

healthcare: Recommendations of the European Society of Human Genetics, in *European Journal of Human Genetics*, 21, 2013, 580-584, and M. CLAUSTRES, V. KOZICH, E. DEQUEKER, B. FOWLER, J.Y. HEHIR-KWA, K. MILLER et al., *Recommendations for reporting results of diagnostic genetic testing (biochemical, cytogenetic and molecular genetic)*, in *European Journal of Human Genetics*, 22, 2014, 160-170. Many governments have drawn up plans to develop and generalise the use of large-scale genetic analysis, such as the UK (100,000 Genomes Project), Iceland, Estonia (Estonian Genome Project), France (Genomic Medicine France 2025), The Netherlands (Genome of The Netherlands Project), and Germany (National Genome Research Network). In this dynamic, it is likely that IFs become frequent and a harmonisation of practices to better care for the patient has become necessary.

[7] *European Society of Human Genetics' Guidelines*, cit., 3-4, Statements no. 10, 11 and 12, under "Informed consent and information to the patient and clinician"; under "Reporting": all pathogenic (class 5) and likely pathogenic (class 3) variants have to be reported. Whether or not Unclassified Variants (UVs. class 3) are reported will depend on local practice, which has to be clear for the laboratory scientist and the referring clinician. Statement no. 29 re-clarifies that laboratories should have a clearly defined protocol for addressing unsolicited and secondary findings before launching test.

[8] *ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing*, published on 20 June 2013, in *Genetics in Medicine*, 15, 7, 2013, 565-574, so called ACMG SF v1.0 or "ACMG 56".

community. They have been revised in 2015[9] and 2016[10] and, in the last version, they listed 59 medically actionable genes recommended for return in clinical genomic sequencing (four genes were added to the first list and one removed).

In Europe, no common approach was observed. In Italy, since 2007 the Italian Data Protection Authority gave general provisions on genetic data processing for clinical and research purposes. The aim of this regulation, as defined by the Italian Data Protection Code, was to govern all stages of genetic data processing, from the initial information, to consent, communication and dissemination. The problem of unexpected results was addressed within the more general definition of data processing.[11] In 2016, the National Committee for Bioethics followed the American debate, adopting a specific *Report on Management of Incidental Findings in genomic sequencings with new technological platforms*. As U.S. *Guidelines*, to define IFs, the Committee referred to the 2013 report of the Presidential Commission for the Study of Bioethical Issues, which divided the findings into primary (related to the primary investigation), secondary (anticipable results, so results that the sequencing is looking for) and discovery (non-anticipable results, fortuitous).[12]

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[9] *ACMG policy statement: Updated recommendations regarding analysis and reporting of secondary findings in clinical genome-scale sequencing*, in *Genetics in Medicine*, 17, 1, 2015, 68-69.

[10] *Recommendations for reporting of secondary findings in clinical exome and genome sequencing, 2016 update (ACMG SF v2.0): A policy statement of the American College of Medical Genetics and Genomics*, published on 17 November 2016, in *Genetics in Medicine*, 19, 2, 2017, 249-255, so called ACMG SF v2.0 or "ACMG 59". Original version of 2013 uses the term "incidental findings". In 2015 the *Recommendations* were first revised, adopting the term "secondary findings" "because these genes are intentionally being analysed, as opposed to genetic variations found incidentally or accidentally"; the shift in terminology, it is said, also maintained consistency with a recommendation by Presidential Commission on Bioethical Issues, C. WEINER, *Anticipate and communicate: Ethical management of incidental and secondary findings in the clinical, research, and direct-to-consumer contexts*, December 2013*, Report of the Presidential Commission for the Study of Bioethical Issues*, in *American Journal of Epidemiology*, 180, 2014, 562-564.

[11] The Italian Data Protection Authority ("Garante per la Privacy", DPA in the following) is an independent administrative authority established by law no. 675 of 31 December 1996 and regulated subsequently by the Personal Data Protection Code, Legislative Decree no. 196 of 30 June 2003. Before the entry into force of the EU Data Protection Regulation no. 2016/679, the processing of genetic data under Italian law was governed by a so called "general authorisation" issued by the DPA, pursuant to Art. 90 of Legislative Decree no. 196 of 2003, under which the requirements and conditions laid down in the authorisation were the only cases in which processing was allowed. The position and force of the authorisation in the hierarchy of sources gave rise to a wide-ranging debate concerning its assimilation to the law. The first version of the general authorisation dates back to 2007 and was significantly amended in 2011, with renewals up to 2016 (www.garanteprivacy.it/web/guest/home/docweb/-/docweb-display/docweb/5803688). As will be seen in more detail below, one of the most significant changes introduced since 2011 concerned precisely the possibility of allowing the processing of genetic data carried out to protect the health of family members without the consent of the data subject, and the disclosure to family members of genetic data indispensable to prevent harm to their health. Legislative Decree no. 101 of 10 August 2018 amended the Code and established that the Italian DPA is the supervisory authority responsible for monitoring application of the EU General Data Protection Regulation, pursuant to its Art. 51. The general authorisation no. 8 of 2016 has been replaced by the no. 146 of 2019, www.garanteprivacy.it/home/docweb/-/docweb-display/docweb/9124510 (last visited on 19 April 2021).

[12] Report *Gestione degli "incidental findings" nelle indagini genomiche con le nuove piattaforme tecnologiche*, 17 marzo 2016, cit.; the Italian National Committee of Bioethics refers to statements of its previous report of 2010, adopted together with the National Committee for Biosecurity, Biotechnologies and Life Sciences, *Test*

An attempt to generalise secondary findings in genome sequencing has been made in France. In 2017, the French Society for Predictive and Personalised Medicine (*Société Française de Médecine Prédictive et Personnalisée*, SFMPP in the following) organised *ad hoc* working groups to identify secondary findings (*données secondaires*) implications and treatments, and in 2018, the French *Guidelines* were published (in the following also SFMPP *Recommendations*).[13] They were expressed regarding an extensive European genome project and aimed at providing a first step towards standardised guidelines in France and all Europe.

We will focus briefly on the scope of application and the procedure of adoption of the U.S., French *Guidelines* and the Italian Bioethics Committee's Report.

Concerning the scope of application, all documents aim at giving indications, without limiting or substituting the judgment of the clinician, whose adherence to recommendations is voluntary. The U.S. *Guidelines* self-define as an "educational resource", and both U.S. and French text refer to the professional, clinical and ethical evaluation of the practitioner, depending on the specific clinical circumstances presented by the individual patient.[14]

Regarding the adoption procedure, the Italian Report, due to the composition and tasks of the Bioethics Committee, does not enter detailed discussion on the type of genetic variations, while the U.S. and French *Guidelines* are the results of a participatory procedure, between the medical community in the U.S., and more extensively between clinicians, experts in bioethics, philosophers, sociologists and lawyers in France, both aiming at classifying variations and their management. In detail, the U.S. list of pathogenic variations was composed following a bottom-up process. The Secondary Findings Working Group (SFWG) created by ACMG and other colleagues collected information in a nomination form. Completed forms were reviewed in a study section-like model and by another working group. Each form was presented in an SFWG meeting or conference called by the submitter or a designee and discussed. After discussion, SFWG members voted on whether to accept the submitter's recommendation. Nominations recommended by the SFWG were sent to ACMG Board of Directors with a summary of the SFWG discussion, voting outcome, and a recommendation for the suggested change to the SF minimum list.

In France, from June 2016 to May 2017, the SFMPP established a working group of 47 experts to elaborate guidelines for managing SFs for cancer-related genes. The experts were divided into two subgroups regarding ethical and legal questions and medical expertise. The ethical and legal group comprised 17 members, psychologists, sociologists, ethicists, methodologists, lawyers and members of patients' associations, to elaborate general recommendations on information related to patients

genetici di suscettibilità e medicina personalizzata, in http://bioetica.governo.it/media/4045/test-genetici-sulla-suscettibilita.pdf, confirming the distinction between research and clinical activity, and the distinction between minors and adults.

[13] See *Guidelines for reporting secondary findings of genome sequencing in cancer gene: The SFMPP recommendations*, in *European Journal of Human Genetics,* 26, 2018, 1732-1742.

[14] *ACMG SF v2.0*, cit., 249; the *SFMPP Recommendations*, cit., 1739: "The present recommendations are not meant to substitute for the clinical and ethical judgement of clinician, but they are proposed as a basis for reflection to help with the prescription and the results of the genomic analyses in a homogeneous way. These recommendations are not a substitute for a personal bibliographic watch that is an integral part of the clinician's work in a context of continuous improvement of medical knowledge due to the variety of cancer-predisposition syndromes and the technical complexity […]".

and consent, and to provide informed consent forms and information media tools. The medical expertise group comprised 30 members, oncologists, clinical geneticists, molecular biologists, and cancer gene experts, who provided independent evaluation and classification of cancer genes for cancer risk and actionability.[15] To homogenise the results, evaluation criteria were designed on the models of the ACMG, with the aim of creating a common global standard. Both U.S. and French *Guidelines* are presented as provisional text, calling for updates and research on the list of variations and psychological impact of returning SFs.

4. *(continue)* and contents: Types of variations and actionability, the clinician's viewpoint

As we said, due to the composition and tasks of the National Bioethics Committee, the Italian Report did not aim at distinguishing types of variations, while both U.S. and French *Recommendations* included a detailed list of variants. Both considered differences in genetic variations: pathogenic (causative) mutations, polymorphisms, variations that can be found also in healthy people. Both *recommended restricting the report of SFs to pathogenic variations*, providing a list considered "minimal", and open to regular update.[16]

Moreover, both rely on the concept of *actionability* (*données secondaires actionnables* in French) or clinical utility. We will see that actionability is the comet guiding clinicians' perspective.

Broadly speaking, utility measures the personal benefit that someone has from an intervention, outcome, product or process, and medical clinical utility describes the relevance and usefulness of an intervention in patient care.[17] The meaning of "clinical utility" adopted by both U.S. and French *Guidelines* refers to the existence of preventive measures or treatments.[18] Since 2013, the U.S.

[15] In detail, the ethical and legal group comprised three psychologists, one sociologist, four ethicists, two methodologists, four lawyers and three representatives of patient associations (BRCA France, the Vaincre les Maladies Lysosomales association and the Association pour la Prévention, Traitement Etude des Polyposes Familiales); the medical group eight oncologists, eleven clinical geneticists, three molecular biologists and eight cancer gene experts.

[16] See the *SFMPP Recommendations*, cit., 1739. *ACMG SF v2.0*, cit., 251, adopting the classification of variants in S. RICHARDS, N. AZIZ, S. BALE ET AL., *ACMG Laboratory Quality Assurance Committee. Standards and guidelines for the interpretation of sequence variants: A joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology*, in *Genetics in Medicine*, 17, 2015, 405-424.

[17] L. J. LESKO, I. ZINEH, S.-M. HUANG, *What Is Clinical Utility and Why Should We Care?*, in *Clinical Pharmacology & Therapeutics*, 88, 6, 2010, 729-733.

[18] It seems useful to quote *ACMG SF v2.0* on actionability: "Initially, medical actionability was evaluated according to a semiquantitative metric that included the following major adjudication criteria: severity of disease/nature of the health threat; likelihood of the disease/health threat materializing (i.e., penetrance); efficacy of specific intervention(s); and overall strength of the current knowledge base about the gene/condition. In July 2015, a fifth criterion was added: acceptability of the proposed intervention based on its risks and benefits. The SFWG acknowledged the inherent subjectivity and difficulty of rating any given intervention as it applies to an individual but voted unanimously in favour of adding this fifth criterion". An example on evaluation of a pathogenic variation could be read in the same *Guidelines*, concerning genes added to the original list: ATP7B is associated with autosomal-recessive Wilson disease (MIM 277900). Morbidity among homozygotes directly correlates with copper deposition in the liver, brain, and eye. The disease is progressive, and, if left untreated, premature death is likely. In some cases, liver failure may be the presenting

Recommendations admitted that there was much to be learned about disease predictability from genomic testing, particularly in asymptomatic individuals. A debate occurred between some arguing that IFs should not be reported at all in clinical sequencing until there is strong evidence of benefit, and others advocating that variations in any all disease-associated genes could be medically useful and should be reported. The working group admitted that there was insufficient evidence about benefits, risks and costs of disclosure to make evidence-based recommendations, a consensus on the listed variations having been found on clinical experience largely from patients with symptoms or positive family histories. The conclusion was that: "Given the low prior probability that an individual has a monogenic disorder that could be identified incidentally through exome or genome sequencing, we recommended that only variants with a higher likelihood of causing disease should be reported as IFs although we recognise that there are limited data available in many cases to make this assessment". So, the minimal list was limited to variants "where there is strong evidence of high probability of severe adverse medical outcomes that can be prevented or ameliorated by existing modalities".[19] In this sense, actionability is the leading principle driving IFs information, and it mirrors the bioethics principle of benefit, *bienfaisance*, in French.[20]

French *Guidelines* also define actionability as availability of screening or prevention strategies, risk evaluation (severity, penetrance and age of disease onset), and level of evidence from published data. Under these criteria, genes have been divided into three classes and 60 genes were listed in class 1, as actionable pathogenic variants.[21] There is an important overlap between the ACMG and SFMPP lists of actionable genes concerning cancer, except for one or two additional genes classified as class 1.

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sign. Given its long recognition as a Mendelian disorder, it is reasonable to consider Wilson disease to be at least relatively highly penetrant. Expressivity is variable. Treatment for Wilson disease involves administration copper chelating agents and/or zinc to block intestinal absorption of copper; treatment is extremely effective when administered prior to the onset of symptoms. Sanger sequencing of the ATP7B gene is considered confirmatory in asymptomatic patients. In symptomatic patients, in addition to Sanger sequencing, the results of serum ceruloplasmin, serum copper concentration and 14-hour urine copper excretion can be diagnostic. The ClinGen Actionability scoring process generated a high actionability score of 10/12 for copper chelation and zinc therapy in the treatment of ATP7B-associated liver disease and/or neuropsychiatric disease. Based on this evidence, the SFWG voted unanimously to add ATP7B to the SF list for the recessive state in which two KP/EP variants are detected in trans through GS. The benefit principle is also based on the recent ACGM, *Patient re-contact after revision of genomic test results: Points to consider—A statement of the American College of Medical Genetics and Genomics*, in *Genetics in Medicine*, 21, 4, 2019, 769-771.

[19] AMGC, *Incidental findings in clinical genomics: A clarification* in *Genetics in Medicine*,15, 8, 2013, 664-666, developing considerations of 2013 *AMGC SF v1.0*, cit.

[20] Three conditions should exist to have benefit: discovery must be scientifically validated; it could be meaningful for the patient health; and there exist a therapy or a preventive behaviour. For general references, see M. TOMASI, *Genetica e Costituzione*, cit., 33-35.

[21] In detail, for class 1 genes (n = 36), delivering the information on SFs was *recommended*; for class 2 genes (n = 5), delivering the information remained *questionable* because genes include significant risk and detection/prevention possibilities, but the literature data or level of evidence seems too low to measure the real benefit of an intervention in an asymptomatic context; and for class 3 genes (n = 19), delivering the information on SFs was *unrecommended* because of the moderate risk of cancer and/or prevention or limited or non-existent therapeutic possibilities.

Overall, for clarity, in both U.S. and French *Guidelines*, disclosing secondary findings is now recommended, but not binding, for actionable pathogenic variants, taking advantage of the patient's health. In contrast, a pathogenic variation of an incurable disease will be uncommunicated. The same is true for variations of uncertain or unknown significance, whose evidence should not be given to the practitioner (first step) or the patient (second step), because it can involve misinterpretation in the results, being unnecessary for the patient's healthcare.[22]

In Italy, the Data Protection Authority general authorisation no. 8 of 2016 adopted the narrow concept of clinical utility, defining unexpected findings in the context of genetic testing *consent* and *communication* as those that "represent a concrete and direct benefit in terms of therapy or prevention or awareness of reproductive choices".[23] But the Italian Committee of Bioethics Report, as a soft law source specifically focusing to incidental findings, adopted a different way. First, as we anticipated, the Report did not refer to an explicit list of variations, as cancer-associated genes. Second, the Committee adopted a smoother and descriptive approach, illustrating different meanings of clinical utility, the traditional stricter view, present in the U.S. *Guidelines* and in the following French ones, where there are preventive measures or treatment, and a broader sense, including wider considerations on situations of non-immediate interventions, or non-existing treatment or non-pathogenic information. This broader meaning of clinical utility implies a corresponding wider assessment of benefits and risks, involving the patient, family or third-person interests, and concerning all decisions where a choice can occur, like reproductive choices, assurance schemes, or other planning of life. From this perspective, all information concerning an opportunity of choice may be reported. The Committee observed that there is a general agreement in the literature on disclosure of actionable findings, while communication of uncertain results or results with no prevention or treatment available is discussed. In the end, the Committee *suggests leaving to the patient, during pre-test and post-test counselling, the choice whether to have information and the kind of information*, i.e. only pathogenic variations or even variations related to untreatable disease. In contrast, the Committee agrees that unknown variations or variations with uncertain significance should not be reported.[24] By this way, an extensive discretionary is given to the patient, while a relatively less intense duty of qualification of clinical utility remains to the doctor.

[22] See also AMCG, *Incidental findings in clinical genomics: A clarification*, cit.: "We agree that variants of unknown significance, variants associated with low or unknown penetrance, and variants associated with disorders not currently amenable to intervention should not be reported". For incidental findings of unknown significance, the SFMMP works assessed that additional follow-up tests or procedures could be risky and costly.

[23] Italian Data Protection general authorisation no. 8 of 2016, cit., par. 6, and now in the same way no. 146 of 2019, par. 4.5. sub 3.

[24] Report *Gestione degli "incidental findings"*, cit., 18: "si rispetti, nella acquisizione del consenso informato, il diritto all'autodeterminazione del paziente e pertanto sia lasciata al consultando, una volta che ha compreso la differenza tra le diverse tipologie degli IF, la scelta di decidere quali risultati conoscere. Il paziente deve essere libero di scegliere se rifiutare le informazioni sugli IF, oppure ricevere solo informazioni relative alle patologie prevenibili o trattabili, o ancora conoscere anche i dati che riguardano condizioni patologiche al momento non prevenibili né curabili", and note no. 39 on uncertain variations: "Non è opportuno invece comunicare le varianti di significato incerto, né le suscettibilità per i motivi già ricordati". In sum, there is a difference between the strict clinical utility for consent and communication of the DPA general authorisation and the broad clinical utility of the Bioethics Committee's Report, where the first is a mandatory source and the second is not. This is a symptom of the lack of clarity and sensitivity on this issue. For the sake of completeness, the

Clearly, statements on actionability or clinical utility, and their consequences on information, put the attention on clinicians' duties and tasks. Now, it is necessary to investigate the guidelines from the patient's viewpoint, and the U.S. debate has been significant again.

5. *(continue)* the patient's viewpoint: The uncertainty of information

From the patient's viewpoint, the U.S. original version of *Guidelines* in 2013 recommended a *mandatory disclosure of actionable secondary findings*, but this statement was revised in 2015, in a relatively short time. Starting from the beginning, in 2013 the working group recognised that denying a preference whether to receive information may be seen to violate existing ethical norms regarding the patient's autonomy and the "right not to know" genetic risk information. However, they felt that "clinicians and laboratory personnel have *a fiduciary duty to prevent harm* by warning patients and their families about certain IFs and that this principle supersedes concerns about autonomy, just as it does in the reporting of IFs elsewhere in medical practice".[25] In detail, the debate on reporting IFs was presented as follows: While genetic libertarians believe that patients have the right to full and complete accounting of all possible risks conveyed by both established and novel variants, or even variants of unknown significance in disease genes, genetic empiricists believe that there is insufficient evidence about the penetrance of most pathogenic variants in the general population to warrant the sharing of any IFs, and that it is irresponsible to create the psychological burdens of being a "patient in waiting" or to expose patients to iatrogenic harm of possibly unnecessary surveillance or diagnostic testing.[26] The fair balance comprised precisely reporting only the listed variations, without seeking preference from the patient and family. So, the duty to protect health prevails when results convey the near certainty of an adverse yet potentially preventable medical outcome. Not returning under these conditions was considered unethical.[27]

DPA general authorisation no. 8 of 2016 and the ongoing no. 146 of 2019 both refer to an extensive meaning of utility in another stage of data processing, during the pre and post-test genetic counselling. The counsellor is called upon to help the person concerned to independently take the most appropriate decisions, taking into account genetic risk, family aspirations and ethical and religious principles, to achieve the best possible adaptation to the disease (see par. 4.4. of the ongoing authorisation).

[25] *ACMG SF v1.0*, continuing: "whenever clinical sequencing is ordered, the ordering clinician should discuss with the patient the possibility of incidental findings, and that laboratories seek and report findings from the list described in the [list] without reference to patient preferences. Patients have the right to decline clinical sequencing if they judge the risks of possible discovery of incidental findings to outweigh the benefits of testing".

[26] *ACMG SF v1.0*, quoting J. M. KWON, R. D. STEINER, *I'm fine; I'm just waiting for my disease: The new and growing class of presymptomatic patients*, in *Neurology*, 77, 6, 2011, 522-523.

[27] AMCG, *Incidental findings in clinical genomics: A clarification*, cit.: "The rationale for our recommendations was that failure to report a laboratory test result conveying the near certainty of an adverse yet potentially preventable medical outcome would be unethical. A common objection to this recommendation has been that some genetic test results *might not be predictive* of disease, either because of incomplete penetrance or because of the occurrence of variants of unknown significance. The recommendations, however, explicitly focus only on unequivocally pathogenic mutations in genes in which pathogenic variants lead to disease with very high probability and cases in which evidence strongly supports the benefits of early intervention. We

Three points should be clarified. First, the 2013 U.S. *Guidelines* version clearly explained that concern and uncertainty surrounding IFs depend on a lack of empiric data, both on predictability and patients' behaviours. Second, this position plainly rejected genetic "exceptionalism", recalling that reporting IFs is a form of screening that had a long history in clinical medicine, where disease to one system could call for other systems' testing in multisystem diseases.[28] Third, it relied strongly on the clinical-patient relationship. The patient has already been presented to the medical care system and has been evaluated by a clinician who is familiar with the patient's conditions and family history. The clinician-patient interaction is the appropriate place for extensively evaluating the opportunity of a specific genetic testing, and for explaining and discussing IFs eventuality.[29] Patients' opt-out option is not completely denied in this pattern, but is conceived at the beginning of the procedure. The patient, conscious of the possibility of extra findings, declines clinical sequencing if the risks of possible incidental discoveries outweigh the benefits of testing.

Refusing opt-in opt-out induced a controversial debate.[30] In 2015, the *Guidelines* were first revised, introducing the possibility to decline SFs through "the right not to know". The version of 2016

agree that variants of unknown significance, variants associated with low or unknown penetrance, and variants associated with disorders not currently amenable to intervention should not be reported".

[28] *ACMG SF v1.0*, "When patients complain of symptoms in the digestive system, the well-trained physician examines cardiac and respiratory systems as well, both for clues to a multisystem disease and to incidentally discover any unrelated signs. When radiographs are read for a particular anatomical focus, the radiologist scans the entire radiograph and also reports on abnormal findings in regions not indicated as the primary reason for the study. In these situations, the patient has already presented to the medical care system, has been evaluated and is under the care of a clinician […]".

[29] See also AMCG, *Incidental findings in clinical genomics: A clarification*, cit., where the clinician, and his or her consultant, i.e. clinical geneticists, is the point of reference for ordering and returning laboratory tests: "It is expected that the clinician will contextualize these findings to the clinical circumstances (e.g., the nature of ongoing clinical problems, knowledge of personal and family history, patient preferences), and the provider and patient will participate in a shared decision-making process regarding the return of results. This is similar to the shared decision-making that is undertaken by patients and physicians: whenever complex medical testing is contemplated, patients are informed that data generated from such tests can reveal unexpected results". A strong concern is expressed on direct-to-consumer testing, where patients directly receive results from laboratories, but "Patients who seek out their laboratory test results independent of their healthcare providers have made their own choice about learning these results".

[30] See A. TOWNSEND, F. ROUSSEAU, J. FRIEDMAN, S. ADAM, Z. LOHN, P. BIRCH, *Autonomy and the patient's 'not to know' in clinical whole-genomic sequencing*, in *European Journal of Human Genetics*, 22, 2014, 6-11, questioning constructively the obligation to return IFs because of paternalism, predicating upon "the physician as gatekeeper" model, instead of the "patient as partner" or "patient as gatekeeper" models. They broadly rely on autonomy in Andorno sense, following in this paper, arguing that a chance must be offered in all pre-test and post-test counselling and the choice cannot be presumed, but must be activated by the patient. The position is based on a focus group study, whose participants strongly supported the right to decline information: "Individuals may have valid reasons for not knowing results. The "objective" clinical utility of knowledge may have very different meaning "subjectively" for patient regarding its relevance and manageability for them; all things considered, they simply may make an informed choice not to have the information disclosed to them. The impact that all genetic information has on the individual, including psychological, social and financial consequences or harms, needs to be reconsidered by clinicians at all stages of disclosure". In contrast, for further critics to "the right not to know" as an autonomy based right, because the right to refuse medical treatment is doubtful and with the aim to protect vulnerable people from the risk to decline medically

confirms this solution and is stated as follows: An additional *modification to the original policy included offering an option to opt out of receiving SFs for individuals undergoing clinical genomic sequencing (GS).* This revision was due, in part, to results from a survey of ACMG members in which more than 80% of respondents supported an option for patients undergoing GS to decline SF analysis following appropriate counselling. In conclusion, for U.S. *Guidelines* now informed consent is necessary and reporting of secondary findings is optional.

Similarly, the issue has been deeply discussed during the French SFMPP works as well, and many doubts have arisen. The French working groups considered that genomic consent rules did not adequately fit with the disclosure of secondary findings from genome sequencing, nether under Art. L. 1111-4 *Code de la santé*, inspired by Art. 5 Oviedo Convention, nor as the informed consent under the *Loi Bioètique*. Art. 5 Oviedo Convention, in particular, may not be suitable with SFs because there is no "intervention", neither "act", nor "treatment". Moreover, there is no well-established, but only possible information. Again, predictability is one of the main problems. The disease is uncertain, but possible. It depends not only on the genome, but also on lifestyle, environment or other external factors. The quantity and quality of information have also been questioned because the lack of knowledge could depend on the scarcity of data, but even their large amount can be a problem, making their interpretation unclear and doubtful. Therefore, informed consent, as provided in general for genomic testing, may be unsuitable *per se* for the communication of secondary findings. The working groups questioned, in the end, the practical possibility of a right to know or not to know, because the object of knowledge is too uncertain and undefinable.

Ethically, four alternatives were discussed concerning the degree of disclosure, assuming autonomy in the meaning of making a life lived according to each own project: first, to be always informed (*être prévenu systématiquement*), expression of the principle of absolute autonomy, i.e. the right to know everything (*droit de tout connaître*); second, to be informed of relevant information (*être prévenu avec les informations pertinentes*), mirroring the principle of controlled autonomy depending on the relevance of data; third, not to be informed, unless the relevant information is strongly validated or clinical assistance is very recommended, mirroring again the principle of controlled autonomy, but focusing on a significant loss of chance; fourth, not to be informed at all. During the works, it has been specified that all alternatives imply a certain degree of paternalism, either in the obligation to know, as the only way to make choices and worthily organise life, or in completely avoiding knowledge, assuming that the patient could not understand the choice or to bear the pain. Finally, spoiling the end of the story, French *Guidelines* opt for a model of partial disclosure, admitting "the right not to know" of the patient as a central feature and adopting a new formula called "double consent", which dissociates the announcement of primary findings from SFs, as we will illustrate later.[31]

significant information, B.B. BERKMAN, S.C. HULL, L.G. BIESECKER, *Scrutinizing the Right Not to Know*, in *The American Journal of Bioethics*, 15, 7, 2015, 17-19.

[31] See the presentation *Consentement éclairé et aspects éthiques* of Ms. Michèle Anahory, lawyer, during the works of SFMMP working groups, available at https://www.sfmpp.org/2019/01/31/recommandations-de-la-sfmpp-sur-les-donnees-secondaires/ until November 2019. In January 2021, videos and power points were unavailable anymore. All mistakes reporting the contents are in my responsibility.

The Italian Bioethics Committee also referred to "the right not to know", and the report on IFs deeply discussed its rationale relying on the results of a Canadian Symposium held in Spring 2014.[32] The Committee identified three main meanings of autonomy as the source of the right to decline information: first, the protection from interferences of others in the most personal choices, requesting policies that enforce individual liberties, including "the right not to know" health data; second, autonomy as control by a rational agent of all circumstances of life, to make responsible and organised choices, and here there is no room for "the right not to know", lack of information preventing any rational decision,[33] third, "veridicity" in Hans Jonas words in the seventies, facing biomedical innovations, i.e. the right to find his own way of life and to shape the future. This last position supports a moral right to ignorance about the future, for example, for genetic diseases where no treatment is available, to remain free in determining the sense of self. However, these different theoretical models, in the Committee's opinion, did not help find a concrete solution if the patient had not expressed any will about being informed or not. Hence, the Committee referred to another theoretical scheme, Laurie's approach to privacy, which we will deeply analyse in the next paragraph. Finally, the Italian Committee, as we mentioned before, recognised centrality to self-determination, assigning priority to pre-test and post-test counselling with support of psychological expertise, and stating the existence of the right to choose whether to be informed and on which pathogenic results, actionable and non-actionable.[34]

Collectively, the U.S. *Guidelines* recommend the reporting as secondary findings of known or expected pathogenic variants and do not recommend reporting variants of uncertain significance or associated with disorders not currently amenable to intervention. The focus is mainly on SFs related to monogenic disorders for which there is a higher likelihood of causing the disease, i.e. evidence of clinical utility. Since 2015, informed consent is necessary, and reporting SFs is optional.

Similarly, French *Guidelines* of 2018 suggest reporting only pathogenic variations and clearly assure an opt-in opt-out option to patient, adopting the procedural approach of "double consent". In this way, for the French too, the knowledge of secondary findings is limited to variations where validated screening or prevention strategies are available, is optional, even if recommended, and it depends on the will of patient to know or not to know.

The Italian Bioethics Committee suggested that laboratories should store secondary findings, including non-known variations; centrality should be given to self-determination of the patient

[32] *From the Right to Know to the Right not to Know*, Special Issue in *Journal of Law, Medicine and Ethics*, 42, 1, 2014, *Special Issue,* 1-6.

[33] Report *Gestione degli "incidental findings"*, cit., 16, referring to J. HARRIS, K. KEYWOOD, *Ignorance, Information and Autonomy*, in *Theoretical Medicine*, 22, 5, 2001, 415-436.

[34] Report *Gestione degli "incidental findings"*, cit., 18. There is a sort of contradiction in the Report. In the previous part, concerning the different rationales of autonomy, the Committee observed that the interest and/or right not to know should be protected to the greatest extension. Later, it is said that being not absolute, the right can be limited, depending on factual circumstances, to protect other interests, that the Committee do not explicitly mention, in a case-by-case evaluation. In that context, said the Committee, it is not possible to completely avoid discretionary because *it is in the last resort to clinicians, or researchers, with the help of consultants, decide to 'exceptions', relying on the kind of information at stake*. Overall, while great relevance is given to the patient's choice by letting him to decide the kind of pathogenic variations to be known, the final decision is left to practitioners without any clear guideline.

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through consent, leaving him the choice to select which variations to know, pathogenic with clear clinical utility or pathogenic without available treatment. The difference from U.S. and French conclusions is consistent, involving non-actionable pathogenic variations.[35] In contrast, all recommendations refuse reporting and communication of unknown variations.

6. The right not to know: Legal basis and conceptual objections

The overruling of U.S. *Guidelines* from a mandatory disclosure of secondary findings concerning pathogenic variations to an optional choice, from 2013 to 2015, is a clear symptom of the very sensitivity of the issue and the complexity of the interests involved. The same impression comes from the French debate on the suitability of traditional informed consent because of the uncertainty of information itself. For the patient, now all guidelines clearly refer to the so-called right not to know. Despite the incertitude and the intense debate, "the right not to know" in health matters has a clear legal basis in international law. It dates to 1997 in both the UNESCO Declaration on the Human Genome and Human Rights, Art. 5.c, and in the Oviedo Convention on Human Right and Biomedicine, Art. 10.2.[36] The Oviedo Additional Protocol concerning Genetic Testing for Health Purpose, entered into force recently, on 1 July 2018, protects the wish of a person undergoing a genetic test not to be informed.[37] Under both the Oviedo Convention and its Protocol, the right to know or not to know is part of the right to respect private life. Also, a right to decline information is provided by many domestic legislations, and recently by Italian law on consent and non-resuscitation orders too, no. 219 of 2017.[38] Prior to this law, as we mentioned, rules were provided for under the Italian Data Protection Authority authorisation, with the specific task of regulating the processing of genetic data.

[35] *Gestione degli "incidental findings" nelle indagini genomiche con le nuove piattaforme tecnologiche*, cit., 18.

[36] "2. Everyone is entitled to know any information collected about his or her health. However, the wishes of individuals not to be so informed shall be observed. 3. In exceptional cases, restrictions may be placed by law on the exercise of the rights contained in paragraph 2 in the interests of the patient". The right not to know is recognised also in international clinical guideline, the *World Medical Association Declaration on the Rights of the Patient* of 1981, revised in 1995, Art. 7.d: "the patient has the right not to be informed on his/her explicit request, unless required for the protection of another person's life", and the *World Health Organisation Guidelines on Ethical Issues in Medical Genetics and the Provision of Genetic Services* of 1997, Table 7: "the wish of individual and families not to know genetic information, including test results, should be respected, except in testing of new born babies or children for treatable conditions".

[37] "2. Everyone undergoing a genetic test is entitled to know any information collected about his or her health derived from this test. The conclusions drawn from the test shall be accessible to the person concerned in a comprehensible form. 3. The wish of a person not to be informed shall be respected. 4. In exceptional cases, restrictions may be placed by law on the exercise of the rights contained in paragraphs 2 and 3 above in the interests of the person concerned".

[38] Art. 3 It. law no. 219 of 2017: "Ogni persona ha il diritto di conoscere le proprie condizioni di salute e di essere informata in modo completo, aggiornato e a lei comprensibile riguardo alla diagnosi, alla prognosi, ai benefici e ai rischi degli accertamenti diagnostici e dei trattamenti sanitari indicati, nonché riguardo alle possibili alternative e alle conseguenze dell'eventuale rifiuto del trattamento sanitario e dell'accertamento diagnostico o della rinuncia ai medesimi. Può rifiutare in tutto o in parte di ricevere le informazioni ovvero indicare i familiari o una persona di sua fiducia incaricati di riceverle e di esprimere il consenso in sua vece se il paziente lo vuole. Il rifiuto o la rinuncia alle informazioni e l'eventuale indicazione di un incaricato sono registrati nella cartella clinica e nel fascicolo sanitario elettronico […]".

For what is relevant here, this authorisation referred to secondary discoveries, stipulating that the information resulting from a genetic testing to be provided to the data subject included among the results the "unexpected news" and stating that the data subject was required to declare whether or not he wanted to know the results, including the unexpected one.[39] Differently, Italian law no. 219 of 2017 does not explicitly concern genetic testing but gives a general framework on consent and the substantive values it embodies. Perhaps terms like "informed consent", "diagnostic assessment", or "treatment", under this law, could not be suitable for genetic information, thereby raising the same concerns of the French debate resumed before. But we assume that the general framework provided by this law, giving centrality to the trusty clinical-patient relation, to dignity and self-determination of the patient and decisional autonomy and expertise of the practitioner, is broad enough to apply to genetic testing too. Moreover, we consider that IFs returning policies move rapidly, depending on increasing evidence-based data both on predictability of information and on psychological impact, so that, at this time, a more specific legislation may not be appropriate, while an adjustment based on clinical guidelines regularly updated, and hopefully standardised across Europe, seems desirable.

Despite these legal references, as we have seen, the clinical, ethical, and legal debate on IFs concentrated on the acceptability of a "not to know" pretension. Whole-genome sequencing has dramatically broadened the scope of available information.[40] Nevertheless, the general lines of the debate about the *rationale* of the right not to know have not significantly changed. Therefore, it seems useful to illustrate them.

The relation between the right to know or not to know and genetic information has been explored since the 2000s.[41] Literature specified that "the right not to know" one's genetic status raised several objections. Preliminarily, this right goes strongly against the trend of claiming, affirming and widening the right *to know* health information by patients, which has been fundamental to re-define the modern doctor-patient relationship. More generally, politically and philosophically, the right to remain in ignorance seems contrary to the desire to know, as a feature that distinguishes humans from other animals, and to the capability of knowledge as a prerequisite for decision, that is, at the foundation of legal rights since the Enlightenment.

Further, if we leave aside, for a moment, the issue of health information, from a constitutional perspective the right *to know* has been questioned by American law scholars since the 1960s as a

[39] See the DPA general authorisation no. 8 of 2016, cit., par. 5, lett. b) on unexpected results; par. 6, second sentence, on informed consent: "the person concerned is required to state whether or not he or she wishes to know the results of the examination or research, including any unexpected information concerning him or her, if it represents a concrete and direct benefit for the person concerned in terms of treatment or prevention or awareness of reproductive choices". The regulation is remained the same under the ongoing DPA authorisation no. 146 of 2019, par. 4.3 on *Information*, including unexpected news among the attainable results, par. 4.5, *sub* 3, on *Consent*, par. 4.6. on *Communication and dissemination of data*, under which: "the results of genetic testing must be communicated to the person concerned also in accordance with his or her declaration of willingness to know or not to know such events and, where necessary, together with appropriate genetic counselling" (our translation from Italian).

[40] B.M. KNOPPERS, *From the Right to Know to the Right Not to Know*, in *Journal of Law, Medicine and Ethics*, special issue 42, 1, 2014, 1-10, 6, who argues that the question now is not whether to return results, but how much information should be returned.

[41] For general references, R. CHADWICK, M. LEVITT, D. SHICKLE (eds.), *The Right to Know and the Right Not to Know. Genetic Privacy and Responsibility*, Cambridge, 2014 (second edition revised of the first dating 1997).

basic principle for democracy, referring it to the freedom of press and the public to acquire and share information on government and the exercise of public powers. Certainly, the context highly differs, but it is to say how *knowledge* is perceived as a stronghold, perhaps the most important, for democracy in Western societies.[42] Notably, even in that context, the right to know, as part of the liberty of expression, also covered a personal intimate position, essential to personal fulfilment. It is a significant method for seeking the truth, or at least for seeking the better answer, as it has been said.[43] In addition, in that context "the right not to know" emerged as the other side of the right to know, particularly in the meaning of not to be forced to receive communication. However, concurrently, it was relevant in narrower cases, much less significant for democracy than the right to know ones.[44]

Overall, knowledge seems to be the essence of human life. This is perfectly described in the famous words that the Italian poet Dante gave to Ulisse: "Fatti non foste a viver come bruti ma per seguir virtute e canoscenza"[45] [Consider your origin: you were not born to live like brutes, but to follow virtues and knowledge]. However, going back to health information, there are other objections to "the right not to know". It would undermine the relationship between doctor and patient, hindering the duty to disclose health information to the patient and returning to the paternalistic approach by which doctors are restricted to tell the truth, to supposedly protect the patient from harm. Moreover, "the right not to know" would be in contrast to the values of solidarity and responsibility, preventing the possibility of giving vital information to family members, in opposition to the relational nature of genetic information with relatives.[46]

[42] See for example in the U.S. debate, T. I. EMERSON, *Legal Foundations of the Right to Know*, in *Washington University Law Quarterly*, 1, 1976, 1-24, lecture delivered on March 3, 1976, during the Symposium *The First Amendment and the Right to Know*, discussing a constitutional theory and workable operating rules to anchor the right to know, an emerging constitutional right, in the U.S. Constitution. The A. opens the paper quoting a letter from James Madison to W.T. Barry, August 4, 1822, in *9 Writings of James Madison 103* (G. Hurst ed. 1910): "A popular government, without popular information or the means of acquiring it, is but a prologue to a farce or a tragedy; or perhaps both. Knowledge will forever govern ignorance. And people who mean to be their own governors, must arm themselves with the power knowledge gives".

[43] T.I. EMERSON, *op. cit.*, 2, 4: "Moreover, the right to know serves the same function in our society as the right to communicate. It is essential to personal self-fulfilment. It is a significant method for seeking the truth, or at least for seeking the better answer. It is necessary for collective decision-making in a democratic society. And it is vital as a mechanism for effectuating social change without resort to violence or undue coercion". Personal fulfilment is considered an important aspect because "our society moves further and further towards conformity and depersonalization".

[44] See T.I. EMERSON, *op. cit.*, 22-23, for whom the right not to know is a limit of the right to know, but much less meaningful than another opposite right, the right to privacy. While privacy needs the application of complex balancing theories, the right not to know, in U.S. Supreme Court case law at that time, refers to "simple" cases on the refusal to listen to music and broadcasting during bus travels, or to receive mails from anonymous senders. In general, concluded the A., the conflict is between the right not to know and the right to communicate, rather than the right to know.

[45] Dante Inferno, Canto ventiseiesimo, vv. 112-120.

[46] There would be also a practical impossibility of the right not to know, and a logical contradiction, because "in the very process of asking "Do you want to know whether you are at risk…?", the geneticist has already made the essence of the information known", in D.C. WERTZ, J.C. FLETCHER, *Privacy and Disclosure in Medical Genetics Examined in an Ethics of Care*, in *Bioethics*, 5, 3, 1991, 212-232, 221. The argument is fascinating, but seems

7. Theoretical frameworks between autonomy and privacy

Despite the referred objections, as we have seen, the right to refuse health information has a specific legal basis in international law, and in domestic law too, including now in Italian law. Different rationales of the right have been proposed to describe its nature and substance. We limit our analysis to two theoretical frameworks, which have had a great echo in the debate: "the right not to know" as an expression of autonomy and as an expression of privacy. The first thesis has been argued by Roberto Andorno. Against the argument that ignorance affects autonomy, preventing any choice and control,[47] Andorno argues that "the right not to know" is part of autonomy itself, understood as self-determination, mirroring the basic bioethical principle for which everyone should be free to make choices regarding health information. It is part of autonomy, without any paternalism, because the decision is in the patient's hands and does not come from abroad.[48] Autonomy is presented as the immediate source of the right, but the substantive interest protected in the end is psychological integrity, through the possibility to avoid the harmful effects of genetic information.[49] In Andorno's description, this right relies on an active approach from two perspectives. First, the opportunity of a choice is given to the patient. Second, the expression of will from the patient, being an explicit choice, is required[50]. Unlike, the privacy framework excludes the disclosure of information even if the patient has not explicitly expressed his or her will. This seems to be the main difference between the two frameworks, as we will see now.

The second framework, supported by Graeme Laurie, argues that "the right not to know" is not a right in itself, but an interference to privacy. While the framing paradigm of autonomy is choice, the framing paradigm of privacy is non-interference. More deeply, for Laurie, the ethical and legal basis of "the right not to know" is rooted in a "psychological spatial privacy, to the aim of safeguarding "one's own sense of the self".[51] The point is that spatial privacy should protect the patient even if no explicit choice has been made to assure that unsolicited revelations are prevented.

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invalid, because prior explanation of the possibility to find something does not say anything about the final output; so the effectiveness of the right relies, as always happens, on when and how information is given.

[47] For example, J. HARRIS, K. KEYWOOD, *Ignorance, Information and Autonomy*, cit, 415-436.

[48] R. ANDORNO, *The right not to know: An autonomy based approach*, in *Journal of Medical Ethics*, 30, 2004, 435-440, spec. 436, who refers this meaning of autonomy also to German legal literature, as part of the "right to informational self-determination" ["Recht auf informationelle Selbstbestimmung"].

[49] R. ANDORNO, cit., 436, recalling the oldest principle of medical clinics "first, do not harm" – "Primus non nocere," and the modern "principle of non-maleficence," including patient's psychological integrity.

[50] R. ANDORNO, cit., relies also on normative indications: The *European Convention on Human Rights and Biomedicine*, Art. 10.2, the UNESCO *Universal Declaration on the Human Genome and Human Rights*, Art. 5.c, as well as the WMA *Declaration on the Right of the Patient*, Art. 7.d, and the WHO *Guidelines on Ethical Issues in Medical Genetics and the Provision of Genetic Services*, Table 7, all require an explicit choice to the functioning of the right not to know.

[51] See G. LAURIE, *In defence of ignorance; genetic information and the right not to know*, in *European Journal of Health Law*, 6, 1999, 119-132; ID, *Protecting and promoting privacy in an uncertain world: Further defences of ignorance and the right not to know*, *ivi*, 7, 2000, 185-191; ID, *Challenging medical-legal norms. The role of autonomy, confidentiality, and privacy in protecting individual and familial group rights in genetic information*, in *Journal of Legal Medicine*, 22, 2001, 1-54; ID, *Genetic privacy. A Challenge to medico-legal norms*, Cambridge, 2000, 259, references made by R. ANDORNO, *op. cit.*, notes 30-36. See also ID, *Privacy and the right not to know:*

Collectively, the autonomy and privacy framework both protect the same substantive position, psychological integrity, and both admit that autonomy and privacy often overlap. Also, as Andorno himself noted, unsolicited information directly *interferes* with psychological integrity, passing by the choice on knowledge. However, the two theoretical frameworks differ in differentiating between general rule and exceptions. Under the privacy approach, non-interference is the rule, so that information becomes the exception. However, this effect, in Andorno's opinion, subverts the clinician's duty of disclosure principle. In fact, under the autonomy framework, the rule remains that the patient has the right to know his or her health status and that an alternative should be offered to him or her, if to have information or to remain in ignorance.[52] Non-information as a rule breaks this pattern. Overall, for the autonomy approach, "the right not to know" cannot be presumed but should be "activated" by the explicit will of the person.

Alternatively, it is true that the language of privacy has resonance with the ways that Western legal systems frame the interests involved.[53] Laurie recalls the "penumbra" definition of privacy in the U.S. Supreme Court case law on abortion and reproductive choices,[54] and, in Europe, the Strasbourg Court case law on Art. 8, par. 1, ECHR concerning respect for private and family life . But, the theoretical framework of Laurie's spatial privacy differs in reality from the ECHR interpretation. It is not the case here to deeply analyse the case law on 8 ECHR. It is enough to say that respect for private life under Art. 8 ECHR covers, depending on the circumstances of the case, personal autonomy, physical and psychological integrity, individual's psychological wellbeing and dignity.[55]

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a plea for conceptual clarity, in R. CHADWICK, M. LEVITT, D. SHICKLE (eds.), *The Right to Know and the Right Not to Know. Genetic Privacy and Responsibility*, cit., 38-51.

[52] R. ANDORNO, *op. cit.*, stresses that to determine which right should prevail will depend on the circumstances of each case, but law and ethics need rules to operate coherently. The right to know too, since its origin, had a positive shape. See T. I. EMERSON, cit., 2, for whom the right to know focuses on the affirmative aspects of the first amendment and the system of freedom of expression, the negative right to be free of government interferences being partial, meaning that the right is entitled to support by legislation or other affirmative government action.

[53] G. LAURIE, *Recognizing the Right Not to Know: Conceptual, Professional, and Legal Implications*, in *Journal of Law, Medicine and Ethics*, special issue 42, 1, 2014, 53-63, spec. 57.

[54] It is well known that privacy has different meanings, depending on each normative background and legal tradition. In a very general manner, at the origin U.S. privacy referred to a spatial dimension: it was intended to protect a *zone* of privacy within which the individual is protected against any intrusion from any rule or practise, public or private. Actually, the U.S. Supreme Court ruled on the constitutional foundation of consent under the *due process* clause of XIV Amendment on the grounds of a common law rule rooted in history and traditions, which considers forced medication as a battery. See R.R. FADEN, T.L. BEAUCHAMP, *A History and Theory of Informed Consent*, New York, Oxford, 1986, 120 ff., and, in Italian literature, C. CASONATO, *Introduzione al biodiritto*, Torino, 3rd ed., 2012, 160 ff. To question the right not to know, B.B. BERKMAN, S.C. HULL, L.G. BIESECKER, *Scrutinizing the Right Not to Know*, cit., 17, argue that the *Cruzan v. Director* case, 1990, concerning hydration and nutrition, related to bodily integrity, and cannot be extended to psychological integrity, falling outside the scope the XIV Amendment.

[55] See for all P. VAN DIJK, F. VAN HOOF, A. VAN RIJN, L. ZWAAK, *Theory and Practise of the European Convention on Human Rights*, 5th ed., Cambridge, Antwerp, Portland, 2018, 667-734. A recent summary of the case law is available in the Guide on Article 8 of the European Convention on Human Rights, dated 31.8.2020, at https://www.echr.coe.int/documents/guide_art_8_eng.pdf. The case law is divided in three categories: (i) a person's physical, psychological, or moral integrity, (ii) his privacy and (iii) his identity and autonomy. Under the first one, the rights protected include, among others, wellbeing and dignity (*Beizaras and Levickas v. Lithuania*,

Now, the Laurie's notion of space and preemptive non-interference fits with the original meaning of privacy, as undue home invasion from unlawful house searches or other police activities. It entails a negative obligation of abstention by public powers. However, the evolution of ECHR privacy, even concerning personal and intimate aspects of personality, has given increasingly importance to the so-called positive obligations.[56] Applicants claim a violation of eight ECHRs because of omissions by national authorities. Their quest is for an intervention of State at different levels, legislative, administrative or in practise, to put in place conditions to effectively develop their intimate expectations. It is also true that the opposition between negative and positive obligations is a false one, because negative obligations can easily be restated as positive obligations, and vice versa, and all rights can just as readily be described as having correlative obligations that are both positive and negative.[57] Anyway, the concept of positive obligation emphasises that standing is not enough for public authorities to respect rights.

Thus, in our opinion, Laurie's approach seems less convincing for two reasons. First, it recalls the ancient model of privacy as a duty of abstention from undue invasions but overshadows the positive duty of intervention implied in "the right not to know". For the good intention to avoid unsolicited information, it overlooks the complexity of positive and negative behaviours which are required by this right. Second, the "spatial privacy approach" seems to place the patient in a previous condition of isolation, supposing a pre-emptive opposition to intervention and, in some way, leaving him alone. Intervention as an assumed intrusion recalls an authoritarian, vertical model, while the doctor-patient relationship developed through years tends to a horizontal model, inspired by mutual trust. Further, if an unsolicited information is given, or a problem arises about sharing information or not,

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§117), personality development (*Von Hannover v. Germany* (no. 2) [GC], §95), physical and psychological integrity (*Söderman v. Sweden*, [GC], §80), relations with other human beings (*Couderc and Hachette Filipacchi Associés v. France* [GC], §83), the protection of personal data (*M.L. and W.W. v. Germany*, §87) and a person's image (*Reklos and Davourlis v. Greece*, §38). The ECHR ruled for the first time that the notion of private life covered the physical and moral integrity of the person in *X and Y v. the Netherlands*, 26 March 1985, §22, concerning the sexual assault of a mentally disabled sixteen-year old girl and the absence of criminal law provisions to provide her with effective and practical protection. Since this first case, the Court has held that the authorities' *positive obligations*—in some cases under Articles 2 or 3 ECHR*,* and in other instances under Article 8 taken alone or in combination with Article 3—may include a *duty to maintain and apply in practice an adequate legal framework affording protection*.

[56] See for all A.R. MOWBRAY, *The Development of Positive Obligations under the European Convention on Human Rights by the European Court of Human Rights*, London, 2004; M. KLATT, *Positive Obligations under the European Convention on Human Rights*, in *Zeitschrift für ausländisches öfentliches Recht und Völkerrecht = Heidelberg Journal of International Law*, 71, 4, 2011, 691-718, discussing positive and negative obligations and the principle of proportionality under Alexy theories. The main reasons why the negative wording of ECHR has been rephrased in positive terms are the overcome of the distinction between first generation, civil and political rights, and second generation, social rights, a pure passive approach to human rights being insufficient due to the complexity of our society, and indivisibility emerging under day-by-day situations; the need for effectiveness, especially after the reform of 1998 on individual applications; the main critics to this evolution rely on the lack of democratic accountability of the ECtHR, in. B. DICKINSON, *Positive Obligations and the European Court of Human Rights*, in *Northern Ireland Legal Quarterly*, *Special Issue*, 61, 3, 2010, 203-208, collecting the acts of a workshop on positive obligations in ECHR case law held in the Human Rights Centre of the School of Law at Queen's University Belfast, 24 March 2010.

[57] B. DICKINSON, *op. cit.*, 203.

probably a movement which breaks individual "separateness" has already happened and maybe it has been caused by the patient himself, because he or she has already made access to healthcare. Therefore, the question is how public authorities should manage the situation to let the patient, whose separateness has already been infringed, enjoy his or her right to refuse information. Overall, the spatial privacy approach, as mere abstention, contrary to the ECtHR case law, underestimates all conditions, tasks and duties required to make a right effective, which is at the core of Art. 8 ECHR interpretation.

Another debate on "the right not to know" concerns the effectiveness of freedom and the possibility of coercion. Briefly, criticism of the autonomy approach could be formulated considering that people are not always free to decide according to their real interests, because various forms of coercion, in a more or less explicit way, may interfere and press their will. We will see now that the effectiveness of freedom occupies the debate on negative or positive liberties.

8. Constitutional background between negative and positive liberty

It is well known that BioLaw shows a strong trans-nationality due to the cross-communication of scientists and the growing importance of international instruments, legally binding and non-binding. Scientific research is naturally cross-border, and its permeability implies a dilution of the distance between different constitutional cultures and a weakening of borders between common law and civil law systems. However, concurrently, there are certain "constitutional features" that depend on history, tradition, doctrine and practise. An attempt is made to analyse whether different approaches to set the right to know or not to know secondary findings could be justified by different constitutional cultures. The second part of this paper addresses this issue.

The relatively fast shifting of U.S. *Guidelines* on secondary findings from mandatory to optional disclosure, from 2013 to 2015, and the recognition of the right not to know, seem to put greater emphasis on autonomy of the patient as the only relevant principle at stake. As a first impression, this interpretation could rely on the primacy of personal liberty in the U.S. constitutional tradition, mistrusting government and public authorities' intervention affecting individual choices. This pattern comes after the origins of American society, where the smallholders refused positive interventions from authorities, finding a consensus on the core values of individual capacity, property and limitation of powers.[58] However, the strong emphasis which the first version of U.S. *Recommendations* put on the fiduciary duty of care and the clinician's obligation to prevent harm, to justify a mandatory disclosure, shows that this first impression is false.

Also, scholars' in-depth analysis has demonstrated that American constitutional tradition cannot be reduced to liberty as an isolated right from different perspectives.[59] First, American tradition is

[58] On the role of property as a model to describe personal rights, see later in the text.

[59] A. DI MARTINO, *La doppia dimensione dei diritti fondamentali*, in V. BALDINI (ed.), *Cos'è un diritto fondamentale*, Atti del Convegno Annuale di Cassino, 10–11 giugno 2016, Napoli, 2017, 123-158, spec. 136-142, and extensively in *Gruppodipisa.it*, no. 2 of 2016, who compares German, American and Italian constitutional backgrounds on rights and duties, using as a starting point the relation between individual dimension and institutional dimension, i.e. the institutional and organisational measures giving substance to rights, where the term "dimension" is taken from German constitutional interpretation. On Republican liberty see also I. CARTER,

pervaded by republicanism, which refers to common good, political participation and protection of liberties through the rule of law. Second, the U.S. Supreme Court case law, while discovering fundamental rights through the due process clause of the XIV Amendment, often refers to liberty and justice or, in more recent cases, ruled on freedoms that require a positive intervention of the State, for example, on the same-sex couple marriage.[60] Then, to give place to autonomy and personal development, public authorities must engage and adopt organisational measures. The same "positive" background is involved in the debate on privacy, if understood not only as a duty of abstention, but also as a duty of protection, to create and assure a place for freedom of choice despite different social and economic conditions. Third, different American constitutional theories associate rights and autonomy to responsibility, considering the promotional role played by the State.[61] Finally, concerning social rights, it has been demonstrated that they cannot be differentiated from civil rights regarding the costs and engagement of public authorities because even civil rights protection needs public expence and organisational measures.

This agrees with the American debate on the negative or positive meaning of liberty. The debate became stronger between social and political philosophers after the famous distinction defended by Isaiah Berlin in 1950s.[62] It has been demonstrated that many aspects of negative and positive liberty overlap, so that the distinction is not theoretically clear, but remains useful in a descriptive sense, at least to map different theories of liberty. Negative liberty, here, means the absence of obstacles or constraints, and usually refers to the absence of voluntary, intentional actions of others. Positive liberty is the possibility of acting, having control of one's life and realisation of one's purposes. Thus, positive liberty can be understood as self-realisation or self-determination. The concept gives relevance not only to external voluntary interventions of others, but also to internal barriers which could influence one's behaviour, for example ignorance, or fear, admitting interventions of the State to make the individual effectively free, interventions not normally allowed by a liberal conception.[63] As we said, the distinction has a descriptive meaning more than a prescriptive one. Libertarian and egalitarian in many cases overlap, giving different meanings to the constraint of freedom, where libertarians count as a restriction of freedom those brought about intentionally, being subject to the arbitrary will of another, and egalitarians endorse a broader conception of constraints as unintended obstacles, including economic forces, social conditions, poverty, instruction or other factors which

Positive and Negative Liberty, in *Stanford Encyclopedia of Philosophy*, in *plato.stanford.edu*, first published on February 27, 2003; last revision August 2, 2016, 5.

[60] A. DI MARTINO, quoted above.

[61] Compare the literature concerning a duty of protection of State, in A. DI MARTINO, cit., 28, who observes that a general category as the *Schutzpflichten* lacks in American tradition, but many Authors found a duty of protection principle rooted in the common law and translated into States' Constitutions.

[62] I. BERLIN, *Two Concepts of Liberty*, in I. BERLIN, *Four Essays on Liberty*, London, 1969, new edition in 2002.

[63] For a full discussion of Berlin's theory and scholars' different positions, I. CARTER, *Positive and Negative Liberty*, cit., devoting an extensive analysis to G. McCallum's "one concept of liberty" theory, in 1967, following F. Oppenheim studies in the 1950s., for whom the dichotomy between "freedom from" and "freedom to" is a false one and always refer to a triadic relation between three things, an agent, certain preventing conditions, and certain doings or becoming from agent, so that each theorist could be considered a supporter of the negative or positive one depending on the viewpoint. In sum "it is conceptually and historically misleading to divide theorists into two camps, a negative liberal one and a positive non-liberal one".

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are external, but also the presence of abilities, of capabilities, both influencing the internal sense of self and self-realisation.[64] These nuances lead us to a similar coexistence between negative and positive sides of liberty in the Italian constitutional framework.

9. Consent and the right of self-determination in the Italian constitutional framework

In the French legal system, free and informed consent is considered an expression of human dignity.[65] In Italian system, consent is usually described as a component of the right to self-determination.[66] This right is not explicitly mentioned under the Italian Constitution. Nevertheless, since the 1990s, the Italian Constitutional Court (ItCC) held that self-determination is a constitutional right. It could be useful to describe briefly how this right has been woven into Italian basic norms. The story of self-determination is like the current of a river, born as part of its natural flow, and then perceived as a single stream. Its origin is peculiar both because of the sources and the meaning. Starting from the sources, self-determination has always been strictly related to consent. Initially, consent was required by deontological sources, literature and justice, but not by law. In this way, rules for practise and a case-by-case approach lay the foundations of consent. As we have seen, only in 2017 has a general law on consent entered into force, turning the case-law principles into a legislative written text.

Regarding the meaning, self-determination was discovered by the ItCC as part of the right to health protected by Art. 32 It. Const. The Italian constitutional right to health is a very complex figure. It could be described, as the Italian constitutional scholars say, like a figure with different dimensions.[67] It comprehends liberties and duties, individual rights and general interests. Briefly, the constitutional right to health means freedom to choose if and how to seek treatments and, at the opposite, freedom not to seek treatment and to refuse them. Concurrently, health entails a typical social right, the right to access healthcare and to benefit from medical treatment. In other systems, the right to health could be framed differently. For example, it has been observed that the EU Charter of Fundamental Rights properly guarantees the freedom side and the social side under different articles.[68] Nevertheless, despite the different formulation, these two dimensions, the freedom to

[64] On types and sources of constraints in liberal and egalitarian theories and their nuances, and on the ambiguity of term "external" as the source of obstacles, I. CARTER, cit., 8, 9.

[65] Fr. Conseil Constitutionnel, 24 July 1994: "*le devoir d'information est un principe à valeur constitutionnelle et trouve son fondement dans l'exigence du respect du principe constitutionnel de la sauvegarde de la dignité de la personne humaine*".

[66] For a complete bibliography on informed consent, M. TOMASI, *Genetica e Costituzione*, cit., 38-39, note 82.

[67] Constitutional rights are described within dimensions in P. RIDOLA, *Diritti fondamentali. Un'introduzione*, Torino, 2006.

[68] A. CARMINATI, *Libertà di cura e autonomia del medico. Profili costituzionali*, Bari, 2018, 55-56, referring to Art. 3.2, *Right to the integrity of the person*, Title I, *Dignity*, for the right to consent: "1. Everyone has the right to respect for his or her physical and mental integrity. 2. In the fields of medicine and biology, the following must be respected in particular: (a) the free and informed consent of the person concerned, according to the procedures laid down by law […]", in which consent is part of the integrity of the body; Art. 35, *Healthcare*: "Everyone has the right of access to preventive healthcare and the right to benefit from medical treatment

choose treatments and the right to obtain them, are inevitably interconnected. The freedom dimension may be void if medical treatments are inaccessible, for example, because they are expensive. Liberty could be formally affirmed, but it is denied if choices are unaffordable.[69] Then, in the Italian constitutional framework, social rights to healthcare and healthcare organisations in general are strictly connected to the freedom dimension. A clear symptom of this interconnection lies in the wording of Art. 32 It. Const., which guarantees free medical care to the indigent. Also, under Art. 32 It. Const. health is a general interest and entails the obligation to behave under the law to achieve collective health. A typical example of health as a collective interest are mandatory vaccinations.[70]

Under this framework, ItCC found the basis for the right to self-determination. It has been discovered as a current in the health river, and it has become a single stream. Precisely, the right to self-determination has been derived from the second paragraph of Art. 32 It. Const. "No one may be obliged to undergo any health treatment except under the law". A consent to treatments should be necessary, to possibly refuse them.[71] Then, as a single stream, self-determination became an autonomous right in the ItCC case law.[72] This evolution had important consequences. While the meaning of heath extended moving from the organic functionality of the body to psychological

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under the conditions established by national laws and practices. A high level of human health protection shall be ensured in the definition and implementation of all the Union's policies and activities".

[69] B. PEZZINI, *Il diritto alla salute. Profili costituzionali*, in *Diritto e società*, 1985, 42-43.

[70] For a distinction between mandatory obligations and coactive obligations in ItCC case law concerning Art. 32 It. Const., on health, and Art. 13 It. Const., on personal liberty and integrity of the body, M. CARTABIA, *La giurisprudenza costituzionale relativa all'art. 32, secondo comma, della Costituzione italiana*, in *Quad. cost.*, no. 2, 2012, 455-465, spec. 456-460.

[71] E. ROSSI, *Profili giuridici del consenso informato: i fondamenti costituzionali e gli ambiti di applicazione*, in *Rivistaaic.it*, 2011, 6, who describes consent like a hinge between the negative dimension and the positive dimension of the right to health, i.e., the negative right to refuse actions of third parties causing damages and the positive right to ask for assistance and access to healthcare; in details, if mandatory medical treatments must be imposed only by law, all other treatments are voluntary, thus conditioned to consent. G.U. RESCIGNO, *Dal diritto di rifiutare un determinato trattamento sanitaria secondo l'art. 32, c. 2, Cost., al principio di autodeterminazione intorno alla propria vita*, in *Diritto pubblico*, 2008, 85 ff., spec. 91, insists on the fact that, to allow refusal, consent must be informed, i.e. imply a clear and qualified information. On the obligation of a qualified information as an essential attribute of consent, B. PEZZINI, *Il diritto alla salute. Profili costituzionali*, cit., 42-43. Following S. RODOTÀ, *Il nuovo habeas corpus: la persona costituzionalizzata e la sua autodeterminazione*, in S. RODOTÀ, M. TALLACCHINI (eds.), *Ambito e fonti del Biodiritto*, in S. RODOTÀ, P. ZATTI (eds.), *Trattato di Biodiritto*, Milano, 2010, 177, Art. 32.2 introduced a sort of new *habeas corpus*, parallel to the protection of physical integrity under Art. 13 It. Const. For these and more references, see A. CARMINATI, *Libertà di cura e autonomia del medico. Profili costituzionali*, cit., 24 ff., who emphasises that self-determination, and consent, is part of the right to physical integrity of our own body, protected by Art. 13 It. Const.

[72] Self-determination was born "in the shadow" of the right to health and the two proceeded together as travel companions for A. SANTOSUOSSO, *Autodeterminazione e diritto alla salute. Da compagni di viaggio a difficili conviventi*, in *Notizie di Politeia*, 1997, 27 ff. The leading cases are ItCC no. 438 of 2008 and no. 253 of 2009. In no. 438 of 2008 the independence of self-determination from health became clear. The autonomy of self-determination is evident in the case law of civil courts concerning medical treatments, where failure to collect consent, as an infringement of the right to self-determination, gives cause for compensation claims *per se*. On the relation between science and law in ItCC case law under a comparative perspective, deeply S. PENASA, *Presupposti scientifici delle leggi e giudizio di costituzionalità: spunti dal diritto comparato*, in M. D'AMICO, F. BIONDI (eds.), *La Corte costituzionale e i fatti: istruttoria ed effetti delle decisioni*, Milano, 2018, 255-269.

integrity, self-determination now comprehends personal aspects such as sexual identity, religious beliefs, different views on the beginning of life, education, self-development, the meaning of social relationships, and solidarity. Informed consent is in a way the bridge between the health river and the single stream of self-determination, giving protection to the whole complex of subjective aspirations and emotions that the physical dimension evokes.[73] Overall, a subjective perception of health emerged, parallel to its objective meaning.

10. *(continue)* The right not to know under Italian constitutional law

The question is whether the described constitutional framework fits with the challenges of secondary findings. Certainly, express reference made by Art. 32.2 It. Const. to the right to refuse treatments, combined with the constitutional right to self-determination, offers a secured, stable foundation to "the right not to know", as a negative expression of liberty. Italian Law no. 219 of 2017, under Art. 1, *Informed consent*, par. 3 states that every person "can refuse all or part of information or designate family members or a person of trust to receive them and give consent if this is the will of the patient".

However, the only anchor of self-determination may not be enough to set the issue. As the scholars have already demonstrated, genome information implies a strong relation between the individual and those who belong to the same family line. Genome holds messages that project the person back to the past and forward to the future horizontally and vertically.[74] So, the genome does not go along an individual dimension, but a relational dimension. This understanding has significant consequences in organising genomic information between the single person and the other family member. Then, a self-determination model that focuses on the individual as an isolated subject seems not to consider all the interests involved.

We could rephrase the problem from another constitutional viewpoint. If we select consent and the right to self-determination as the only parameter driving the right to know or not to know secondary findings, the risk is to approach the issue using a model like a very ancient freedom, the right to property. In this sense too, Italian constitutional evolution could be useful. Since the sixties of the past century the relation between each person and his or her body was questioned. The traditional paradigm, emerging from the liberal approach, considered this relation regarding property. The right of property was the model on which is still based, for example, Italian Civil Code of 1942, Art. 5, forbidding acts of disposition of his own body causing a permanent reduction of physical integrity, or opposing the law, public order or common decency. This model recalls dominion and all powers to use and abuse things within the limits of the law. After the entry into force of the Italian Constitution in 1948, many years passed before lawyers and judges finally changed paradigm. In the sixties of nineteen centuries, a joint reflection was undertaken between civil law and constitutional law scholars, and the result was a re-definition of this relation of person to his or her body regarding

[73] A. CARMINATI, *Libertà di cura e autonomia del medico. Profili costituzionali*, cit., 34.
[74] M. TOMASI, *Genetica e Costituzione*, cit., 14-15, 229 ff.

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responsibility and solidarity towards others.[75] Art. 2 It. Const. associates the inviolable rights of each human and the fundamental duties of solidarity. Art. 3 It. Const. recognises equal social dignity, and states that it is the duty of the Republic to remove those obstacles of an economic or social nature that constrain the freedom and equality of citizens, thereby impeding the full development of the human person and the effective participation in the political, economic and social organisation. Overall, freedom and equality both design the path of self-realisation and personal achievement in a relational context, associating freedom to solidarity and responsibility.[76] This seems to be the complete set of parameters fitting with genetics and the issue of secondary findings. In this sense, two interrelated positive aspects of "the right not to know" emerge, the first concerning the protection of family members, as we said, and the second dealing with the obligations to make the freedom of choice effective, regarding consent.

10. Right not to know and family members

We have seen in the first part of this paper that one of the main objections to "the right not to know" concerns responsibility towards others, first family members. Clarification should be made on the meaning of family. Certainly, family entails bloodline. Somehow genetics moves the concept of family counter current, focusing on bloody "natural" family, whose human relationship could lack affection and common will, while legal and constitutional protection has evolved concerning the social meaning of family. Definitively, due to the hereditary nature of genes, genetic information is relevant to relatives. So relatives could entail the same health risks and should have the possibility to access available health remedies, and to change way of life and behaviours as well.[77] Also, family comprehends, under constitutional meaning, spouses or partners, whose involvement could be opportune for example in reproductive choices, opening strong questions on the protection of future children.[78] Here we leave aside the situation of spouses and partners and we limit our analysis to the bloodline family. Both from a theoretical viewpoint and in practise, "the right not to know" cannot supersede the rights of family members.

In the autonomy approach mentioned above, the right to refuse knowledge is not absolute. As a relative right, it should be restricted when disclosure to the individual is necessary to avoid serious

[75] R. ROMBOLI, *La libertà di disporre del proprio corpo: art. 5*, in *Commentario del Codice civile Scialoja-Branca*, Roma, 1988; ID. (ed.), U. BRESCIA, A. PIZZORUSSO, *Atti di disposizione del proprio corpo*, Pisa, 2007, collecting the acts of the third joint seminar of the Doctoral School of Private Law and the Doctoral School of Constitutional Justice and Fundamental Rights. See more broadly, P. VERONESI, *Il corpo e la costituzione*, *Concretezza dei casi e astrattezza della norma*, Milano, 2007.

[76] M. TOMASI, *Genetica e Costituzione*, cit., 32, 48. Genetic information are truly intertwining lives in S. RODOTÀ, *La vita e le regole*, Milano, 2006, 71.

[77] Due to the relational nature of genetic information, some ethicists argue that the concept of genetic privacy is a contradiction in terms, in R. ANDORNO, *op. cit.*, 437, referring to A. SOMMERVILLE, *English v. Genetic Privacy: orthodoxy or oxymoron?* in *Journal of Medical Ethics*, 25, 1999, 144-150.

[78] On reproductive issue in bioethical perspective, for example N. JUTH, *The Right Not to Know and the Duty to Tell: The Case of Relatives*, in *Journal of Law, Medicine and Ethics*, 1, 2014, *Special Issue*, 38-52, and references to R. RHODES, *Genetic Links, Family Ties and Social Bonds: Rights and Responsibilities in the Face of Genetic Knowledge*, in *Journal of Medicine and Philosophy*, 23, 1, 1998, 10-30; T. TAKALA, M. HÄYRY, *Genetic Ignorance, Moral Obligations and Social Duties*, in *Journal of Medicine and Philosophy*, 25, 1, 2000, 107-113.

harm to family members, because some form of prevention or treatment is available.[79] Similarly, Italian Constitutional Court case law, since the first judgement in 1956, admitted that any right under Italian Constitution is not absolute, all rights and interests need to strike a fair balance.[80]

U.S. *Guidelines*, since the original version of 2013, have always considered patients together with family members. Variants with a higher likelihood of causing the disease are treated as potentially involving family from the pre-test counselling to the return, interpretation and communication of results. IFs are contextualised regarding personal and family history, in the awareness that further screening on relatives might be necessary. So, the interests of family members are a fully-fledged part of IFs' discovery and communication strategies. Nevertheless, recommendations have not specified any formula to involve relatives, nor a way to balance the right to know of relatives with "the right not to know" of the patient.

Under French *Guidelines*, reporting to patients' relatives about genetic discovery of a primary or secondary variant in actionable genes is assumed not only as moral responsibility but also, in terms of French law, as legal duty for the proband.[81] Because the disclosure to relatives can be particularly painful for families, even deleterious in some cases, French *Guidelines* state that how this information is given to relatives should be included in the informed consent to allow the patient a better understanding and consideration of the implications of results. An envisage solution is that the medical genetic team, if the patient so authorises, disclose the results to the family, thereby protecting as much as possible the patient's anonymity.

The Italian Report of the Bioethics Committee seems to recommend the option of disclosure to relatives as well. The pre-test counselling should give information about the consequences of eventual IFs on biological relationships and suggest that results could, and in some circumstance should, with proper precaution, be reported to family members in case of severe disease needing immediate interventions.[82]

All the examined recommendations, obviously, do not analyse different sets of relations between the patient and his family, cooperative or conflicting. At a deep insight, it could be said that any problem

[79] R. ANDORNO, *op. cit.*, 438.

[80] ItCC no. 1 of 1956, on limits as integral parts of rights; more recently, ItCC no. 85 of 2013, par. 9 *Cons. dir.*, the ILVA case, concerning the conflict between safeguarding job conditions and pollution, on the lack of absoluteness of constitutional rights and the need for a fair balance between health, environmental protection, jobs, and private economic activity.

[81] The *SFMPP Recommendations*, cit., 1736, quoting M. TOURAINE, *Décret no. 2013–527 relatif aux conditions de mise en œuvre de l'information de la parentèle dans le cadre d'un examen des caractéristiques génétiques à finalité médicale*, in santéMdasedl (ed.), 20 June 2013. M. TOMASI, *Genetica e Costituzione*, cit., 120-121, 125, observes that only French legislation concerning genetic data, without mentioning specifically SFs, provides a duty of communication to relatives, and the patient may ask the clinician to disclose information to remain anonymous. Comparatively, in most legal systems, regulation of the issue is not provided by legislation, but by soft laws and in the circle of practitioners' autonomy.

[82] Report *Gestione degli "incidental findings"*, cit., 18: "Le persone che si sottopongono al test devono, inoltre, essere informate che i risultati dell'analisi possono avere importanti implicazioni per i loro familiari e che, in questo caso, è opportuno, in certe circostanze doveroso, consentire a questi ultimi, con le dovute cautele e modalità, di venirne a conoscenza" and note no. 38, about a duty of communication: "Ad esempio nel caso di informazioni di malattie gravi per le quali è necessario mettere in atto subito misure preventive o terapeutiche".

concerning "the right not to know" does not arise when relatives could be autonomously involved in testing. In this situation, each adult individual will decide, independent of the others, about the opportunity to be tested and will eventually exercise "the right not to know". The main issue concerns situations where the patient has to discover genetic information because, if information is not made available, relatives unable to be personally investigated would suffer serious harm. In this case, a first way to facilitate communication goes with information and persuasion of the patient himself. It means explanation of the family nature of genomic information and encouragement of family involvement and discussion. This informal approach depends on counselling and consent, as we will see in the next paragraph.[83] If this approach is not useful, or not possible in the circumstances of the case, we argue that a mandatory *involvement* of family members is required, and that family members should be contacted, whenever possible, even against the will of the patient. As we said, family members should have the same opportunity for pre-test evaluation and information, and they are entitled to the same opt-in opt-out option. If their personal testing is not viable, certainly their need for protection may affect and endanger "the right not to know" of the patient.[84] This seems to be the main limit to the exercise of this right. In our opinion, this conclusion complies with the constitutional pattern described above, where self-determination goes with solidarity and responsibility.

11. The positive side of the right not to know: Consent

Positive obligation as a side of "the right not to know" relies essentially on consent. It is already well acquired that consent is not a single act, but a procedure. Its centrality being assumed, in recent years' literature specified its limits. Attempts are made to avoid consent as a mere ritual, a form to fill out to defend practitioners, rather than protect patients.[85] All the examined guidelines insist on the need and centrality of pre-test and post-test extensive counselling by the clinician who knows the

[83] This is a "responsibility-generating factor" approach for M. TOMASI, *Genetica e Costituzione*, cit., 119.

[84] This is in fact the solution provided for in the Italian DPA general authorisation. Compared to the first version in 2007, since 2011 the authorisation has been revised in the light of ongoing experience and experts' opinions to allow the processing and communication of genetic data indispensable to family members for health protection purposes without the consent of the data subject. The current text of the authorisation no. 146 of 2019, cit., provides that the results of a genetic test may be communicated to members of the same genetic line at their request when the data subject consented or when it is essential to avoid harm to their health, including reproductive risk, and the data subject's consent is not given or cannot be given due to unavailability (par. 4.6). Furthermore, par. 4.7 is expressly dedicated to the protection of the health of third parties and provides that if the consent of the data subject is not given or cannot be given due to physical impossibility, incapacity or unavailability, the processing of genetic data and their communication may be carried out when it is indispensable to enable the third party to make an informed reproductive choice or is justified by the need for preventive or therapeutic measures.

[85] G. CALABRESI, *Reflections on medical experimentation in humans*, in *Dedalus*, *Journal of the American Academy of Arts and Science*, 98, 1969, 405, considering that, as an academic, informed consent seemed to strike the best balance between different interests, while as a judge it was completely insufficient, because beyond the sheets of paper, people face showed they did not know what happened at all. [My apology if this quotation is incorrect; it was written in my notebook, and I was unable to check it anymore].

patient's physical conditions, history and expectations, with the help of geneticists or other consultants.[86]

The U.S. and Italian *Recommendations* do not set a specific procedure for the exercise of "the right not to know" SFs. In contrast, French *Guidelines* adopt a new scheme, the so-called double consent, which seems an interesting solution related to secondary findings.[87] The major point of this procedure is to respect the patient's desire to know or ignore results.

Briefly, double consent means that a first informed consent about the possibility of SFs is given during the initial medical procedure, motivating the primary genetic analysis. A second informed consent form is offered after the announcement of the primary findings, so that the patient could, with more autonomy, differentiate the issues and confirm or refuse access to this information. Information and informed consent must mention the medical impact of SFs on relatives. The clinical utility (regarding screening and prevention), for personal and family reasons, of a secondary discovery of a pathogenic variant within an actionable gene must be explained to the patient and counterbalanced by the arguments against this information. Because of the possibility to reconsider the given decision, SFs should be reported in a second report independent of the primary findings.

Two features characterise this formula. First, the dissociation of consent, and independence of the reports, concerning the primary investigation and secondary results. The need to dissociate the announcement of the primary findings from that of SFs was supported by patient associations to limit the psychological impact generated. Second, the role of time. Time is given, between the first and the second, confirmatory consent, to better understand and reflect. The main idea is a period of reflection, leaving the opportunity for patients to express their opinion again.[88]

Recent Italian Law no. 219 of 2017 on free and informed consent also emphasises the importance of time. Art. 8 states that the time of communication between the clinician and the patient represents the time of medical care ["Il tempo della comunicazione tra medico e paziente costituisce tempo di cura"]. And precisely in giving effectiveness to "time" comprises, in our opinion, the positive obligation, the active side of "the right not to know". Previous references to positive and negative

[86] The Italian Bioethics Committee's Report, for example, suggests the support of a psychologist in the pre-test counselling. Communication of IFs is for the clinician ordering the examination, due to the trust relation with the patient, but participation of other consultants is envisaged to better explain the results and their implications and to help plan next clinical steps. Outside the doctor-patient relationship, the Italian Committee insists properly on the need for extension of practitioners' competences in genetic counselling, including communication's abilities, and, more generally, for the implementation of school programmes and educational initiative on genetic issues, to improve knowledge of basic concepts of genetics, increase consciousness and the ability to form personal opinions. The U.S. *Guidelines* too mainly entrust the doctor-patient relationship with great flexibility.

[87] M. TOMASI, *Genetica e Costituzione*, cit., 254-287, analyses different models of consent, occurred over time to overcome the conditions of specificity and actuality required in traditional consent, like blanket consent, sectoral consent, multi-layered or dynamic consent, this latter suitable to communicate IFs.

[88] See in detail the diagram in Figure no. 3, *Recommended steps for reporting secondary findings to the patient*, in *SFMPP Recommendations*, cit., 1737. The second SFs consent, proposed during the reporting of primary findings, should also be offered again to patients who have stated in the first consent that they did not want to know the SFs. Thus, as for all patients, these patients will have the right to return to the decision after a period of reflection. Even if no formal pilot experiment of such a double consent was performed by the group, this agrees with the dynamic consent approach recently proposed to provide adaptive consent for research.

aspects of freedom are useful to argue, at the end, that the fulfilment of the right to know or not to know requires a specific, positive intervention to implement appropriate organisational measures. Literature on consent fosters dialogue and relational dimensions to overcome patients' constitutive asymmetry, scientific incompetence, and vulnerability. Reference is made to a dynamic process, scientifically comprehensive, devoid of technicalities, suited to the sociocultural conditions of the patient, and humanly sensitive.[89] Educational, financial and organisational investments are necessary to achieve those objectives. It has been specified that, under Italian Law on consent, the representation of time for information as part of the medical process remains a mere statement, because any budget has been allocated to implement it. Actually, there could not be time if structures and staff are not reinforced to perform ordinary tasks dealing with other duties.[90] Once again, "the right not to know" demonstrates that negative liberty is empty if it is not surrounded by measures and resources that make the opportunity of choice available, regarding understanding and affordability.

12. Conclusions: Double consent as a nudge

The paper overviewed the IFs issue from the clinicians' perspective, about actionability, and the patients' perspective, on "the right not to know", discussing two main theoretical rationales, autonomy and privacy, and moving from the US debate on positive and negative liberty to the French and Italian experiences. Concerning the pretension to refuse knowledge, the position of family members was analysed as the main limit to the individual right of choice. Furthermore, we argued that, to collect all interest, the negative exercise of the right not to know should rely on positive measures, shaping the procedure of consent.

As we said before, there is a certain degree of paternalism either in avoiding knowledge, assuming that patient cannot understand the choice or cannot bear the pain, or in the duty to inform and the obligation to know, as the only way to make choices and control circumstances of life. The double consent formula suggested by the French *Guidelines* in 2018 seems a good procedural attempt to strike a balance. During the works of the SFMMP, a short animation movie was promoted to explain to the public the issue of secondary findings and to disseminate recommendations.[91] The movie is centred on the patient, a little puppet, and accompanies him in a cosy atmosphere through hospital laboratories and counselling rooms to finally make the choice to have information or not. In a loyal and transparent way, it tends to suggest that knowledge of pathogenic variations could be useful to health. Can we consider this formula as a nudge, a small push, in the meaning of Thaler and

[89] See L. PALAZZANI, *Informed Consent, Experimentation and Emerging Ethical Problems*, in this *Review*, *Special Issue*, 1, 2019, *I-Consent. Improving the Guidelines for Informed Consent, Including Vulnerable Population, Under a Gender Perspective*, 11-22, spec. 16-18, where "time to reflect" is part of the suggested ethical requirements. I-Consent focuses on research, but many recommendations are suitable for clinical settings.

[90] See A. CARMINATI, *Libertà di cura e autonomia del medico. Profili costituzionali*, cit., 171.

[91] The animation movie, in French and English, is very useful to disseminate the issue, https://www.youtube.com/watch?v=Z1k3xN5rKvU. It is offered to patient and focuses on the opt-in opt-out chance.

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Sunstein?[92] A nudge is any aspect of the choice architecture that alters people's behaviour predictably without forbidding any options.[93] Nudges are everywhere, and push every minimal decision, but unthinkingly, as in advertisement. The authors explained that every day, we make decisions on topics ranging from school, education, meals and health, and we are susceptible to various biases. People make good choices in contexts in which they have experience, good information, and prompt feedback. They do less well in contexts in which they are inexperienced and poorly informed, and in which feedback is slow or infrequent. Choice architecture, both good and bad, is pervasive and unavoidable, and it greatly affects personal decisions. Therefore, the authors argued that public and private actors can design choice environments that make it easier for people to choose what is best for themselves, their families and society, without restricting freedom of decision. "Good nudges" could be "built" to drive people to appropriate decisions for themselves and their families. Particularly, people need nudges for decisions that are *difficult and rare*, for which they do not get prompt feedback, and when they have trouble translating aspects of the situation into terms that they can easily understand. Health is liable to be a choice environment. Doctors are presented as crucial choice architects, and with an understanding of how humans think, they could do far more to improve people's health. The authors' principal claim is that patients and doctors should be free to make their own agreements and that doctors' task is to help patients to map opportunities and to understand which option fits better with his personal wellbeing.[94] Thaler and Sunstein called themselves libertarian paternalists, suggesting that not only government, but employers, management boards, universities, clubs and single families could adopt measures to nudge members towards choices that will increase their wellbeing. They claimed that libertarian paternalism is not an oxymoron, because choice architects can preserve freedom of choice while also nudging people in directions that will improve their lives.[95]

This theory has been criticised exactly because of paternalism, and it is worth recalling that it moves from an economic framework, denying that consumer and client are rational agents. In fact, French *Guidelines* seem to be a real nudge in the sense of Thaler and Sunstein because they try to strike actionability, so high possibility of health measures, with the more intimate desire of patients about themselves, leaving them the final decision. Actually, concerning secondary findings, it is hard to find a settlement that is not, in some way, paternalistic, being constant the risk of applying one personal idea of rationality or wellbeing. In the end, a procedure divided into steps, bringing out different shades, based on time, allowing reflection, and preserving freedom, seems, in this complex pattern, a good solution to consider.

[92] R. THALER, C.R. SUNSTEIN, *Nudge, Improving Decisions about Health, Wealth and Happiness*, Yale University Press, 2008, *La spinta gentile. La nuova strategia per migliorare le nostre decisioni su denaro, salute, felicità*, trad. it. A. Oliveri, Milano, 2009 [VIII ed. 2018].
[93] *Ibid.*, 9.
[94] *Ibid.*, 102.
[95] *Ivi.*