PhD degree in Systems Medicine (curriculum in Medical Humanities)

European School of Molecular Medicine (SEMM) and University of Milan

Settore disciplinare: M-Fil/02

Clinical Ethics Committees in Oncological Care: assessing impact and exploring stakeholders' preferences on clinical ethics support services

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Academic Year 2019/2020

List of abbreviations

AIFA: Italian Medicine Agency (Agenzia Italiana del Farmaco)

CECs: Clinical Ethics Committees

CESS: Clinical Ethics Support Services

CNB: Italian Committee for Bioethics (Comitato Nazionale per la Bioetica)

DAT: advanced directives concerning treatment (Disposizioni Anticipate di Trattamento)

DGR: Regional Legislative Decree (Decreto Giunta Regionale)

EMA: European Medicines Agency

EU: European Union

IRBs: Institutional Review Boards

JCAHO: Joint Commission on the Accreditation of Healthcare Organizations

MCD: Moral Case Deliberation

PI: Principal Investigator

RECs: Research Ethics Committees

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Introduction

Technical developments and advances in scientific research and clinical medicine over the last decades have contributed to widen the horizon of therapeutic possibilities. New paths posed by modern medicine raise challenges for clinical practice and open up complicated scenarios in terms of decision-making, while also raising ethical dilemmas – namely: conflicts of evaluation and action, regarding situations at the crossroads between ethics and medicine, that could have not be solved only on a legal and/or deontological basis [1]–[3].

Ethics committees in the healthcare were born in this context and have been established over time in two different ways: on the one hand, committees dedicated to the evaluation of research protocols, or Research Ethics Committees (RECs), and on the other, committees dedicated to clinical practice, or Clinical Ethics Committees (CECs).

CECs were set up to support healthcare professionals in the management and resolution of these dilemmas [4] and were initially established in the 1980s in USA [5], [6]. CECs pursue this mission by performing three functions: ethics consultation, policy review and bioethics training [7]. In the last decades, their presence in hospitals and care centres has largely intensified and spread all over the world [8], also due to the increasing awareness of ethical issues in clinical practice [9].

In Italy, CECs have begun to arise only in recent years [10], the road to their diffusion throughout the country is still long but it is urgent to understand how CECs can fit into the national context. Until now, in fact, ethics committees in Italy have played the double role of REC and CEC, to the detriment of activities dedicated to clinical practice. In fact, it is unlikely that the Italian ethics committees have the time and resources to engage in the typical functions of the CECs, ending up focusing their activities on the evaluation of research protocols.

The state of play in the coming years will be further conditioned by the implementation of Regulation (EU) 536/20141, which imposes a reorganization of the ethics committees and a reduction in their number. As a consequence, ethical issues falling outside the scope of human trials will remain completely excluded.

The presence of a CEC becomes then essential to deal with those issues concerning the clinical dimension and to guarantee the humanization of care, whose importance has been underlined several times over the years also by the National Committee for Bioethics [10]–[12]. The lack of an ethics support service is particularly relevant in the most delicate clinical contexts, as in the case of oncology departments. The treatment of cancer pathologies, in fact, raises more and more

ethical questions and, to date, health professionals in the oncological area do not have any support in their management.

This lack was personally perceived by Professor Paolo Giovanni Casali, head of the Sarcoma Unit of the Fondazione IRCCS Istituto dei Tumori and supervisor of this PhD project. This project therefore stems from Professor Casali's desire to establish a CEC at the Institute and aims to understand the specific ethics support needs of an oncological context, bearing in mind the state of the art of CECs at an international level and the Italian regulatory context. A fundamental contribution has been provided by the bioethics expertise of Doc. Virginia Sanchini.

The project has the following structure. In Chapter I we presented an introduction to the history of ethics committees; we described the causes of their origin and how they have developed over the decades over the world; we described the functions that CECs perform within hospitals and healthcare centres. In line with the goals of the project, we gave particular attention to the Italian context, in order to better understand the current regulatory framework and the orientation of national institutions - the Italian Bioethics Committee above all - towards CECs.

In Chapter II we aimed to understand the role and impact that CECs have in the institutions where they carry out their activities. We then conducted a systematic review of the international literature on the evaluation of CEC's performance, with the aim of understanding their strengths and potential criticalities.

Finally, Chapter III contains the empirical contribution of this work. Chapter III describes a qualitative study that was conducted at the Fondazione IRCCS Istituto Tumori, involving the Institute's healthcare personnel and stakeholders. We carried out and analysed a series of semi-structured interviews with the aim of identifying the aspects and areas for which the staff and patients of the facility would need some form of ethics support. In addition to presenting the results of the study, we have included in the chapter some considerations on the ideal activities and methods for a CEC designed to operate at the Institute. These thoughts and considerations may be valid indications for the implementation of an ethics support service for any oncological context.

I. Chapter

The history and development of Ethics Committees

1. A new era for medical ethics: the onset of Ethics Committees

Ethics has entered the world of healthcare in an institutional form with the establishment of the first ethics committees, which developed as a result of a renewed awareness of the moral value of medical acts. Indeed, the early decades of the last century were the stage for numerous medical abusive acts, perpetrated at the expense of human subjects. In particular, the Nazi medical experiments are to be mentioned, the discovery of which raised doubts about the rightfulness and ethicality of certain medical and scientific conduct and led to an acknowledged need to protect human subjects of research. It was, however, some episodes occurred in the United States from the second half of the 20th century that led to the institutionalized use of ethical reasoning as a means of preventing abusive medical conduct, through the establishment of the first ethics committees [3]. Above all, three studies cast a shadow over medical conduct in clinical trials: the Jewish Chronic Disease Hospital study (Brooklyn, 1963), the Willowbrook Hepatitis Study (Staten Island, 1956-1970), and the Tuskegee Syphilis Experiment (1932-1972) [13]. As we will see in the next paragraph, these three studies remained in history because they were based on experimentation on fragile or disadvantaged human subjects

Alongside these events, the introduction of new equipment and instruments, products of technical-scientific progress, posed new scenarios in clinical practice and with them new and unprecedented challenges, raising issues of different nature, to which doctors were not prepared to respond [14]. The general interest in these issues was generated by highly contentious and paradigmatic cases, amongst which we will describe extensively below the cases of Ann Karen Quinlan and Baby Doe. The parties involved in these two stories became so conflicting that it proved impossible to find a solution within the clinical grounds and the cases had to be settled in court.

The origin of ethics committees therefore follows a double drive: on the one hand, the desire to guarantee ethical conduct in clinical trials; on the other, the need to develop a system that would enable healthcare professionals to face the new challenges in the clinical setting. The

establishment of the first ethics committees resulted from the acknowledgment of the importance of ethics in medicine, occurred consequently to the novelties in clinical practice combined with a rising awareness of patient's rights as subject of research.

Ethical issues in clinical trials: the origin of Research Ethics Committees

Historically, the wind of change affected first the field of research. Since the '60s, a number of experiments became known to the public, causing some scandal because of their misconduct in the management of clinical research involving human subjects [13], infringing the dignity and basic rights of the patients involved. Among misconducts in human-subject experimentation, three cases in particular are considered the paradigm of unethical research and are still cited today when referring to the origin of Ethics Committees [15].

The first case took place at the Jewish Chronic Disease Hospital in Brooklyn: in 1963, as part of a study on the connection between immune system and susceptibility to cancer, 22 elderly patients affected with comorbidities were injected with liver cancer cells without their consent. [16]. Custodio, Southam, and Mandel, the researchers who conducted the trial, stated that they had obtained oral consent to the injection, although no mention of the research study was made to the patients [17]. Several ethical objections were raised to the study. First of all, regarding the validity of the alleged informed consent: not only does the oral request for consent entail a lack of evidence, but – on a more substantial level – the issue of consent of elderly and disabled people is problematic in itself, since they may not be fully competent.

Injections on fragile subjects were also the causes of the scandal involving the Willowbrook experiment on hepatitis tracing, conducted by Doctor Krugman, which aimed at preventing and reducing the damage causes by the infection. To this end, several students living at Willowbrook State School, a school dedicated to mentally retarded children, were infected deliberately with hepatitis. The study lasted for fourteen years, from 1956 to 1970, and involved over 700 children [18]. As Krugman wrote, the aim of the study was to control the endemic spread of the virus that had affected the school through the immunization of children who were resident there [19]. Immunization was to be achieved through children's exposure to the virus, after being inoculated with gamma globulins, which had proved protective effects against severe damages caused by hepatitis. The assumption justifying the potential risk to the children was the inevitability for the residents to contract hepatitis at some point during their stay at the school.

The study was criticized for several reasons. Among them, a) the alleged incompleteness of the informed consent on the potential risks of the experiment; b) the use of doubly fragile subjects

(as children and as affected by mental retardation); c) a supposed conflict of interest in the admission of children to school (in 1964 it seems that, due to the overcrowding in the school buildings not dedicated to experimentation, only children whose parents had agreed to submit to the study could be admitted) [17].

The third one was a study named "Tuskegee Study of Untreated Syphilis in the Negro Male". The study was designed to observe the development of untreated syphilis in black population: more than 600 African American sharecroppers from Macon County (Alabama) were enrolled in the study. The sample included around 400 men affected with syphilis and around 200 non-affected men, as controls. None of them were informed about their condition nor signed any informed consent. Instead, the subjects of the study were told that they were treated for their "bad blood", a periphrasis that they associated with a generic state of malaise [17]. The experiment began in 1932 and lasted until 1972, despite the discovery of penicillin (in 1928) and its use as a standard treatment for syphilis since the late 1940s [16], [18], [20]. This study caused a scandal, since it featured strong criticalities: the racist exploitation of an uneducated and poor population; the experimentation on unconscious subjects, neglecting information about the study; the lack of therapeutic intervention, even though effective therapies were available, to the detriment of the benefit of the research subjects (about 100 people died during the study) [17].

These three cases, also reported by the press and local television at the time [21]–[23], were not the only cases of ethics misconducts in human-subject research. With an article published in '66, Henry K. Beecher denounced 22 unethical studies on human subjects as damaging to their health and conducted without consent [24]. The following year, a denunciation book written by the English physician Maurice H. Pappworth was released; in the book, he described at least 200 cases of unethical research [25], [26]. It seems that, at the time, the violation of research subjects' rights did not occur in sporadic cases, but was a rather common practice originating from a deep-rooted tendency to ignore patients' dignity and justify unethical means with (at least apparently) ethically legitimate ends [15].

These experiments had the effect of generating a suspicion towards clinical trial investigators and, with it, the awareness that their potential conflict of interest did not enable them to be the only judges of the ethical acceptability of a research protocol [27]. New regulations on the protection of human subjects involved in clinical trials were then introduced.

To this end, the *National Institution of Health* published a statement that only research protocols evaluated by independent commissions could be funded by the national public health service [13]. This directive was then converted into law in 1974 by the *National Research Act* [28], which

imposed the obligation for research protocols to be evaluated by independent commissions, labelled by the document as *Institutional Review Boards* (IRBs) [13]. These boards had the task of evaluating any program involving behavioural or biomedical research publicly funded, "in order to protect the rights of the human subjects of such research" [28].

The name Institutional Review Board is still in use in the American context, while in the rest of the world it has become increasingly popular the name *Research Ethics Committees* (RECs) [27]. The following year, in 1975, also the World Medical Association advocated the independent evaluation of biomedical research involving human subjects, stressing the importance of the experimental designs being examined by *super partes* organs. In the revision of the Helsinki Declaration of '75 it is written that the monitoring role should be entrusted to "*independent committees*" [29], which are precisely the research ethics committees just appointed one year before.

The *National Research Act* is also well known for having established of what is considered to be the first real bioethics committee, the *National Commission for the Protection of Human Subjects of Biomedical and Behavioral Sciences*, which had the task of identifying the moral principles that could guide new biomedical and behavioural research practices. The National Commission passed into history for the elaboration of the Belmont Report [30]. The report contained the fundamental ethical principles that were intended to be the basic guidelines for research on human subjects. (1) Respect for individuals: everyone must be granted their own autonomy in decision-making and opinion; in the case of people with reduced autonomy, they must be guaranteed maximum protection. This principle therefore requires that subjects participate freely and willingly in clinical trials and that they are adequately informed about their potential risks, with particular attention to the risk-benefit balance for people with limited autonomy. (2) Principle of beneficence: beneficence means the obligation on the part of the experimenter not to physically or morally harm the subject and therefore optimise the benefits by minimising as much as possible the damage that could occur. (3) Principle of justice: this principle is intended to be the criterion by which the benefits and burden of an experiment are distributed. With this principle, the Commission wanted to prevent researchers from systematically selecting disadvantaged subjects – economically disadvantaged individuals, ethnic minorities, or persons confined to institutions [30].

The *National Commission* also expressed the need for a federal law that would oblige all research on human subjects financially supported with public funds to be submitted to the evaluation of a review body, in order to ensure respect for the research subject's rights [31].

Today, RECs are present all over the world and are responsible for ensuring that research on human subjects respects fundamental ethical principles. Every centre where clinical trials are conducted has a reference REC and the trial is still subject to the approval of the study protocol by the REC itself.

Ethical Issues in clinical practice: the origin of Clinical Ethics Committees

As it happened for the origin of the RECs, even the committees dealing with ethical issues in clinical practice, or Clinical Ethics Committees (CECs), started to spread after some clinical cases led to the decision not to leave critical decisions to physicians alone [27].

Committees dealing with clinical ethics issues emerged, originally, in American Catholic hospitals in the 1960s, to debate ethical issues in medicine [4]. In the same years, American hospitals were required to approve, upon review, requests of abortion [32]. In those years, new equipment was also introduced in hospitals, which made it possible to perform kidney haemodialysis. Such therapy was very effective but could not be supplied to all those in need, due to the insufficient number of devices [3]. With the arrival of haemodialysis, it was necessary to decide who, among the potential beneficiaries (patients with renal failure), was more entitled to receive the new life-saving therapy. Ethics committees were then entrusted with this task and had to decide how to distribute these new resources and ethics committees [3], [33].

Besides the issue of resource allocation, ethical dilemmas arose about other sensitive areas of clinical practice and over the decades clinical ethics committees began to play a greater institutional role in deciding about end-of-life issues, abortion and infant care review [4]. The final endorsement to clinical ethics committees occurred in the ‘80s, following two cases that gained public notoriety and became paradigmatic.

The first was Karen Ann Quinlan’s case, instituted by the New Jersey Supreme Court in 1976 (In re Quinlan, 1976) and raised a major moral debate [34]. A year earlier, Karen (21 years old at the time) had entered a vegetative state after ingesting a mixture of alcohol and tranquilizers that caused her to stop breathing for at least 15 minutes and was on life support ever since. The case reached the courtroom because of a legal conflict between Karen's parents and her doctors. The trial concerned the authorization and validity of her parents’ decision to suspend Karen’s artificial ventilation, decision which the doctors opposed fearing potential legal repercussions [14], [32], [35]. Her father Joseph requested to be recognized as Karen’s guardian and consequently to authorize the interruption of all extraordinary procedures to support his daughter's life processes, by upholding her constitutional right to refuse treatment. The court

ruled that her ventilator could be removed without anyone being held criminally liable for removing the life-support systems, provided an ethics committee ("or like body") agreed on the prognosis of persistent vegetative state [32]. With this pronouncement, the court aimed also at discouraging physicians from seeking courtroom resolution for conflicts with patients and/or their relatives. However, Karen's case also posed other ethical issues, such as the decision-making on treatment of an unconscious subject and the qualification of artificial respiration, whether or not it can be considered as medical treatment.

The second case involved a baby known as "Baby Doe". He was born with Down syndrome and a birth defect that without surgery would have led to his death. Upon the paediatrician advice and due to his syndrome, his parents refused the surgery. Hospital administrators resorted to court to request the suspension of parental authority on the baby, in order to gain time to decide which therapeutic decision was in the baby's best interest. The court ruled in favour of the parents and the child died before the hospital could appeal to the Supreme Court [36]. However, the verdict raises several ethical concerns, above all whether refusing treatment to a child on the grounds of disability is appropriate and ethically justified.

Following these events, the *President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research* urged the establishment of hospital ethics committees that could address and contribute to solving the new ethical issues affecting clinical practice [27], [37].

As a result, the federal government issued recommendations for hospitals, especially those with neonatal intensive care units, to set up *ad hoc* committees to manage such conflicts [38].

CECs' role in hospitals entailed several tasks (see paragraph 1.4), but the ground-breaking goal was to provide recommendations and advice in individual cases raising ethically controversial issues [8], [39].

2. Spreading of Clinical Ethics Committees

Clinical ethics support can be described as the provision of support and advice to healthcare professionals (or, in some cases, patients) on ethical issues arising in clinical practice [7]. As explained above, CECs were the first organs born with the precise purpose of providing clinical ethics support, but to date they are not the only service available for this purpose. Since its inception in the United States, the concept of clinical ethics support has spread rapidly throughout the world, and the services offering it, labelled Clinical Ethics Support Services (CESS), have

developed over the decades, albeit with significant differences depending on cultural and territorial contexts. [8]. To date, three standard ethics support services are primarily referred to in the literature: CECs, individual Ethics Consultant (EC) and Moral Case Deliberation (MCD). Ethics Consultants are individual or small groups of professionals from a range of backgrounds who are mainly engaged in clinical ethics activities (which we will describe shortly in section 4). In general, EC have either formal training in clinical ethics and/or related areas or they have become consultants over time, having acquired skills and expertise from practice, through direct experience in similar context. In the former case, EC may be healthcare and non-healthcare professionals with a formal training in clinical ethics, bioethics, or philosophical or theological ethics and experience in clinical settings. Otherwise, EC may be healthcare professionals with little – or even no – formal training in clinical ethics and whose main professional activities are elsewhere (i.e., in medicine, nursing, social work, or other) but who have a keen interest in clinical ethics and who have acquired training over the years in the field, through practical experience [40], [41].

A Moral Case Deliberation (MCD) is of a group meeting with a small number of participants who systematically and collaboratively reflect on moral questions within a concrete clinical case from their clinical practice [42]. MCD is conceived as a shared exploration: participants reflect on each other's assumptions and normative reasoning in a joint search for potential answers to a specific moral question or issue. and how participants reach a normative conclusion within the factual circumstances of the case. Hierarchical dynamics should be avoided in MCD, since all participants should have equal chances to reflect on the moral question and to propose what is morally good to do. These aspects of sharing and equality are vital to the formal structure of MCD, since it is conceived to be a dialogue and not a discussion or a debate, based on constructive disagreement. This process can also be implemented through the use of a structured conversation method and the presence of a trained facilitator, who must not guide the dialogue towards a given solution, nor morally validate it, but ensure that the assumptions described above are met in order to allow a constructive dialogue aimed at improving care in an ethical sense. [40], [43]

Although EC and MCD are rapidly growing, CECs remain in general the most widespread ethics support body, though they are not equally distributed everywhere and there are places where other forms of support have prevailed in terms of diffusion [44].

2.1 North America

United States

The birthplace of the first structured forms of ethical-clinical support, the CECs in the United States have become very popular, especially following the requests of the *President's Commission for the Study of Ethical Problems in Medicine and Behavioral Research* to establish clinical ethics committees [45]. In fact, while only 1% of US hospitals had a clinical practice committee in 1982, only 5 years later the percentage had risen to over 60% [37]. In the following years, the prevalence of CECs increased even further, reaching 93% of hospitals in the 1990s [46]. The most recent census figures show that there is an ethics support service in all hospitals with more than 400 beds, in all federal hospitals and Council of Teaching Hospitals member hospitals [47]. The provision of a CEC became a requirement for hospital accreditation in 1992, following the request of Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) [46], and it still is nowadays [8].

It is important to note, however, that the processes leading to the birth of CECs originated from a background of deep rupture with the past and a paradigm shift in the doctor-patient relationship, resulting from the crisis of medical authority combined with a parallel growth of the movement for patients' rights [27]. The discovery of practices that were disrespectful of people's basic rights as subjects of care had cast a shadow over the behaviour of health professionals and led to a new awareness on the part of patients themselves. As a result, CECs first and foremost emerged as bodies of the institution and served mainly as committees for risk management, i.e., as tools to defend the institution from the potential consequences of the rapid evolution in health care and the new issues that this evolution could bring [35], [48].

Canada

Although CECs appeared very soon in Canada, they were initially a sporadic presence and began to spread considerably in the early 1980s [49]. As it happened in the US, an association played an important part in the dissemination of CECs by suggesting that multidisciplinary ethics committees should deal with ethically relevant issues [50]. Data indicate that CECs' number in Canada has increased considerably in a five years span: if in 1984 only 18% of hospitals with more than 300 beds had a CEC [51], in 1989 the number rose to 54% [52], [53]. The most recent survey available reports the presence of a CEC in 85% of Canadian hospitals, but it dates back to 2010 [49].

2.2 Europe

In Europe, CECs began to spread in the late 1980s and early 1990s, but they developed with significant differences from the American model. While in North America CECs were conceived as committees of the institution, representative of the institution, in Europe they were intended as bodies within the institutions, but representative of a public health system [27]. Rather than defending the medical authority, which was still very strong in Europe, they played a democratic role, opening the debate on ethical-clinical issues to lay people [54].

CECs in Europe were born within a public perspective, as a place where health professionals can meet and discuss with non-health professionals, however affected by the new challenges in medical practice. This perspective stems from the deep-rooted belief that a group composed of a plurality of people with different skills and expertise – including but not limited to health care - is better suited to make good decisions on a complex issue such as clinical ethics than health professionals alone [27].

Another difference from the American context is the fact that CECs in Europe are generally poorly regulated, especially if compared with the committees dealing with clinical trials (RECs) [55].

Italy

In Italy, bodies for the regulation of experiments appeared spontaneously in the 1980s, when there was still no regulation on the subject [27]. In those years, there was a drive towards the formalization of the bodies responsible for monitoring clinical trials, based on international documents such as the *Helsinki's Declaration* and the *Proposed International Ethical Guidelines for Biomedical Research Involving Human Subjects*. The National Bioethics Committee, called "Comitato Nazionale per la Bioetica" (CNB), also gave a favourable opinion on this issue, supporting the urgency of regulating the ethics committees and the obligation to submit each research protocol to their opinion [56]. It should be noted that the CNB already suggested that ethics committees should be aimed at experimental medicine but also at medical care. According to the CNB's opinion, the ethics committees should therefore perform a dual function: not only should they evaluate research protocols, but also "*promote and defend the principles of medical ethics, with constant reference to the constitutional rights of the patient*"[56] (*translation mine*).

As a matter of fact, in 1992 the government issued the first official legislation on ethics committees [57], which transposed the European directive 91/507/CEE [58]. With the decree, the Ministry of Health made it mandatory for research protocols to be approved by an ethics

committee before proceeding with a clinical trial, thus institutionalizing ethics committees *de facto*.

The decree of '92 defined the rules for the documentation to be submitted for the approval of clinical trials and referred to the European directive guidance on the structure and organization of ethics committees, adding that they had to comply with the standards of good clinical practice (Annex 1 of the decree). However, the role assigned to the ethics committees only concerned experimental medicine, since the decree did not mention clinical ethics issues.

Subsequent legislation gradually clarified the EC's physiognomy, providing more detailed regulations on how they should be structured and what relationship should they have with the hosting institutions [Decree of 15 July 1997, Decree of 18 March 1998, Decree of 24 June 2003]. So far, the regulations on ethics committees still considered exclusively their role in regulating clinical trials. This also means that, according to the regulation, apparently the only ethical issues they have to deal with are those related to clinical research.

On the other hand, the CNB has spoken repeatedly about the issues related to clinical practice. Since 1997, the CNB has acknowledged the difference between the two functions of an ethics committee [11], and later it insisted on the appropriateness of establishing two different types of ethics committees in Italy, according to this dual function and following of the Anglo-Saxon trend [12]. In 2001, the CNB formally questioned the attribution of the dual role to a single body. A decade later, the legal framework changed, as a legislative decree establishing a new asset for ethics committees, including in their responsibilities issues «*on the use of medicines and medical devices, the use of surgical and clinical procedures*» [59] was enacted. This broadening of the tasks of the ethics committees towards the clinical area was reiterated and further expanded the following year, with a decree that explicitly refers to the advisory and training functions of ethics committees [60]:

> *(…) where not already assigned to specific bodies, Ethics Committees may also perform advisory functions in relation to ethical issues related to scientific and care activities, with the aim of protecting and promoting the values of the individual. The Ethics Committees may also propose training initiatives for healthcare workers on bioethics issues (*translation mine*).*

From 2013 onwards, in accordance with the decree, ethics committees were formally required to play a twofold role: evaluating and monitoring clinical trials on the one hand and dealing with ethical issues in clinical practice on the other, providing consultations and training. However, this last function been generally neglected. In fact, since the research-related activities fall under the obligation of law and require a large amount of resources (especially in terms of time), over

the years it has become almost consolidated practice that ECs dedicate most of their effort in dealing with clinical trials and seldom have the time and opportunity to address the ethically controversial cases occurring in clinical practice. All too often, ethical committees deal with issues of clinical practice only in theory, mainly due to a lack of resources:

> (…) as a matter of fact, the Ethics Committees set up by the regional deliberations mainly deal with clinical trials and, very often, they have a workload that would make it almost impossible to devote time to consultation on clinical cases [61] (*translation mine*).

Therefore, the question posed by the CNB in 2001 about the opportunity of introducing a dedicated institution dealing with the ethical questions that some aspects of clinical practice, arises again. To date, such committees are becoming a necessity [62], [63], since the upcoming entry into force of the Regulation EU 536, published by the European Commission in 2014. The new regulation provides for a reorganization of the ethics committees and a reduction in their number up to about 50%; this cut will naturally lead to a significant increase in the workload of the remaining ethics committees [64]. The ethics committees qualified to evaluate clinical trials will be overburdened, and they will hardly be able to deal with the studies that do not require clinical trials, let alone anything else. As a matter of fact, there will be no space left for ethical issues that go beyond the evaluation of trial protocols.

Yet, in recent decades, the importance of a moral reflection on the dynamics and challenges of clinical practice has been underlined repeatedly. Above all, the UNESCO conference *Universal Declaration on Bioethics and Human Rights* of October 2005 (UNESCO, 2005). In Italy, the CNB has drawn attention repeatedly to the need to establish bodies dedicated to ethical issues falling outside the scope of research:

> (…) the National Bioethics Committee (CNB) believes that particular attention should be paid to the role of Ethics Committees in the evaluation of all those aspects of clinical practice that do not directly concern diagnostic, therapeutic and rehabilitation trial protocols. In recent years, these aspects have acquired an increasingly important role as a result of the growing attention paid to the ethical profiles of health care, patients' increased awareness of their autonomy and also of those technological developments that foster new hopes and raise new questions [61] (*translation mine*).

According to the CNB, this need is even more pressing since the tasks of a clinical ethics committees "*require different care and skills than those required for the evaluation of pharmacological trial protocols*" [61] (*translation mine*).

In spite of the CNB's claims, nowadays only few hospitals have two separate committees [27] and the government has not issued any rigorous legal requirement for CECs yet. To date, there is no law nor decree that specify what their functions, composition and activities should be; the only national regulations or suggestions for CECs are the ones the CNB produced and called upon the legislator to provide on the matter [61]. So far, the Ministry of Health has not yet enacted laws specifically dedicated to clinical ethics committees; Regions and Autonomous Provinces could overcome the absence of national directives, since the Italian public healthcare is structured and regulated at a regional level, and they hold a certain degree of autonomy with regard to ethics committees. However, to date, only few Regions and Autonomous Provinces have adopted regulations on the subject. Veneto Region has regulated the CECs in 2004, with the resolution *Guidelines for the establishment and operation of Ethical Committees for clinical practice* (DGR 4049/2004), later ratified following the 2013 decree (DGR 983/2014).

With the resolution no. 73 of the 22 of January 2016, Friuli Venezia Giulia established the "ethical units for clinical practice", appointing them to deal with ethical issues arising from "clinical and care activities", especially those concerning reproductive issues and beginning of life, end-of-life and advanced directives.

The Autonomous Province of Bolzano instituted a provincial ethics committee by resolution no. 977 of the 31 of March 2003. It serves as an advisory body to the provincial council and is responsible for organizing and providing ethics consultation activities in the province, in support of decision-making processes in critical cases.

3. The scope of Clinical Ethics Committees

The pathways leading to the emergence of CECs are complex and multifaceted: there is no single cause, but rather a combination of interconnected motivations of different nature. A first crucial role was played by technical-scientific innovations, which have brought into hospital wards equipment that enabled hitherto ground-breaking medical interventions and therapies. Health professionals were not prepared to face the questions those new scenarios brought with them [12]. At the same time, there was a growing awareness that ethical issues in medicine, as they affect human dignity, are of interest to everyone, whether they concern the end of life or new-borns with serious pathologies or disabilities, and not only primarily involved stakeholders. Ethics committees, whether they deal with research or clinical practice, therefore arose from the desire that crucial issues in medicine should not be decided solely by doctors. Although clinical

ethics education is now available in most medical schools and post-graduate training programs, healthcare professionals are seldom sensitive towards ethical issues [65].

Since these issues have not only medical but also ethical, legal and social significance, it seemed that the best way to deal with them was at a collegiate level, involving professionals with expertise in these subjects. It was therefore necessary to have a multidisciplinary body to support the management of these dilemmas. If, on the one hand, the suspicion towards health professionals was raised and the medical authority began to enter crisis, on the other hand the CECs were in principle a tool to support clinicians and professional ethics.

Since their first appearance, the CECs have had the aim of contributing to the humanization of care, understood as the guarantee of consideration of the patient as a whole and from different points of view, to serve as a tool against the depersonalisation and dehumanization of medicine [27], [35].

4. Functions, activities and composition of CECs

4.1 Functions

As previously explained, in most cases, there are no strict legal requirements to regulate the structure or purpose of the CECs as is the case for RECs [32]. As a result, the existing CECs are not entirely superimposable and can carry out their activities in very different ways. However, CECs tend to perform three functions, already identified in the early years of CECs development [66] and which the literature over time has categorized and standardized as follows. a) Ethics consultation: advising healthcare professionals in the therapeutic decision-making process when they face cases with complex ethical aspects. b) bioethics training: providing education to CEC's members or clinical staff on relevant bioethics issues. c) Policy revision and/or drafting: supporting the management of common ethical issues by outlining and/or reviewing institutional guidelines [44].

In the following paragraphs, these functions will be described in detail.

a) Ethics consultation

Ethics consultation is defined as the function of providing guidance or advice on clinical cases raising ethical dilemmas. This practice has many labels, such as *case discussion* or *case analysis* (see paragraph xxx, Chapter II) and can be carried out in a number of different ways [9]. Furthermore, it is not an exclusive of CECs: other forms of ethical support services exist and

perform ethics consultation [40], [43], [67]. However, for the purposes of this work, we will only consider the practice of ethics consultation as performed by CECs.

There is a plurality of methods to provide ethics consultation [68], as well as some common characteristics. Health professionals are the main requestors of consultations – generally, but not exclusively, doctors; in literature, CECs accepting or open to consultations requests from patients or their families are the exception rather than the rule [ref]. Multidisciplinarity is an essential factor in case discussion, to ensure that every aspect of the ethical issue is taken into account in order to elaborate the most suitable treatment path for the individual patient.

Differently from RECs' pronunciations on research protocols, in the case of CECs, the applicant is not required to follow the recommendations received. The reasons why CEC's consults are not mandatory are easily explainable. First, as described in Paragraph xxx, CECs are hardly legally regulated. For this formal reason, CECs' judgments on individual cases have no legal value and therefore cannot be binding. Secondly, from a substantive point of view, doctors have legal responsibility for therapeutic decisions and cannot delegate it to third parties. However, even though healthcare professionals do not have any obligation in following the outcomes of CECs' consultations, they may have nonetheless a judicial value on some level. In the event that a doctor has to legally justify their professional conduct, the fact that they have requested the assistance from the CEC may be favourable to them. Weather they accepted and followed the CEC's recommendation or not, having consulted a CEC demonstrates at least the professional's willingness to share the decisional process and to be helped examining all the ethical concerns of the case [69].

Furthermore, it should be noted that CECs do not necessarily provide a single or unambiguous advice. CECS may provide a definite opinion as well as a set of suitable options. Alternatively, a CEC may not give any option at all, whether because its members did not find an internal agreement or because they meant to offer only a space for debate in the first place, with no intention or goal to achieve a definitive solution [68].

CEC's members generally consider ethics consultation as the main function, for two main reasons. First, CECs were initially created and established to discuss ethical concerns related to medical decision making, thus ethics consultation represents their very first scope from an historic perspective [44] and it largely contributed to the diffusion of CECs. As a matter of fact, it was endorsed by courts already in 1976 – as a consequence of the Quinlan case [70]– even if the label of ethics consultation was elaborated in the early 80s a few years later [71], [72]. This practice spread rapidly in healthcare centres, partly due to acts of associations that made the

presence of a body for the consideration of ethical problems a fundamental requirement for accreditation (Patient Self-Determination Act, 1991, Joint Commission's Accreditation of Healthcare Organizations, 1993) [44]. The diffusion of ethics consultation services raised concerns about how this practice was carried out and efforts were made to regulate it. The bioethics organizations The American Society for Bioethics and Humanities set up task force to define which core competencies CECs members and consultants should have [41], [73].

The second reason for the value given to ethics consultation as their main task lies in CECs qualification: their members perceive them as clinical-oriented bodies, promoters of professional ethics and patients' rights, and therefore as a support for clinicians in making the best possible decisions.

Despite the importance attached to this function, ethics consultation is the least practiced among CECs' activities today [74], both in Europe [75], [76] and in the United States [77]. However, they seem to have a positive impact on the institutions in which they work [7], [78]–[80], even if the evaluation of their work and effectiveness raises many problems (on this topic, see Chapter II).

Lastly, ethics consultation can also have an educational value: in the long term, healthcare professionals who request consultations and participate in the CEC's discussions, can in fact learn the methodologies of ethical analysis, as a sort of bottom-up and field-training [81].

b) Policy/guidelines development and/or revision

This function is intended to draft or revise recommendations and operational guidelines of an ethical nature. These serve to assist health care professionals in the management of cases with recurring problems and can be translated into guidelines or policies (of a stronger regulatory nature than guidelines) [14]. Typical topics mainly depend on the type of healthcare institution in which the CEC operates and may concern issues such as non-resuscitation orders, withholding/withdrawing of therapies, informed consent in case of minors or patients with cognitive impairment, Jehovah's Witnesses management (these are just some examples).

The drafting of guidelines or policies has a close link with the ethics consultation function: in fact, if an ethics committee is often faced with cases involving the same problem, it may be appropriate to work on a document to guide health care professionals in this regard. Similarly, the new guidelines developed by the ethics committee have the potential to influence the work of healthcare professionals in the long term [27].

Since the formulation of policies or guidelines requires an initial common reflection on the ethical principles at stake in the various issues and their interpretation, it can be an opportunity for CEC's members both to get further training on these issues and to start working as a team (especially for newly formed CECs). Moreover, it is - like ethics consultation - an activity that requires the intervention of healthcare professionals from within the institution, both to investigate what the common problems are and to have an insight into how they are addressed. This process allows the CEC to make itself known to the staff and the staff to feel a sense of "ownership" towards the application of moral principles inside the institution [82].

As observed in the case of ethics consultations, policies and guidelines are not binding either, although they may also enjoy a similar legal value [69].

c) Bioethics education and training

Bioethics education is often considered the most important function among the three mentioned [80], even if it is neglected in many institutions [83]. The relevance ascribed to this function depends on the extent that training activities can have within an institution. By raising awareness and sensitivity among health care staff in recognizing bioethics issues that are relevant to their daily clinical life and educating them to manage them, the impact of CEC can be very significant [80]. Education can thereby have an irreplaceable preventative function, nurturing the awareness of health care professionals and encouraging them to use the ethical counselling service appropriately [84], thus helping to avoid the onset of conflicts in ethical matters [85].

In addition, with bioethics education interventions a CEC can address simultaneously a larger number of health professionals than the other two functions. Ethics consultation, although it might play an educational role, can in fact sensitize a limited number of professionals because it involves only those who require the intervention - and therefore a small percentage of hospital staff members (especially considering the above data on its actual use in practice). The processes of guidelines' development theoretically involve a higher share (if not all) of health care professionals, but new policies take a long time before becoming practice within an institution; hence, the educational value of this function has to be considered only in the long term.

Naturally, the first form of training in order of priority and principle should be that directed to the very members of a CEC. In-house training is a precondition for the proper accomplishment of all other functions [86], thus, in order to be able to perform effectively and provide training themselves, it is essential for CEC's members to be trained on relevant bioethics issues.

4.2 Composition

As previously observed, CECs generally are not as highly disciplined as RECs [55]. However, guidelines published by bioethics organizations over the years provide minimum guidance for the implementation of new CECs, and supply some indication on the issue of their composition [87]–[91].

These documents recommend what kind of competence members need in order to contribute successfully to the CEC's activities. The ideal competences include – but are not limited to – the ability to identify, understand and analyse ethical issues at stake in individual cases, to facilitate case discussion and mediate in conflicts [88]. Such abilities naturally require technical skills, such as knowledge of the basic concepts of moral theories and the faculty of moral reasoning; interpersonal skills, including the talent of communicate and active listening and clarity of exposition; and individual skills and values, such as patience and propensity for reflection [87].

As for RECs, multidisciplinarity is recognized in literature as a key and basic feature for CECs. The inclusion of professionals with different and complementary skills and expertise is believed to be a prerequisite for the efficiency of a CEC [92]. It has become common practice that a CEC shall comprise a maximum of twenty experts, including a number of physicians of mixed specialization (including a paediatrician), representatives from other health professions, such as nurses and clinical psychologists, an expert in medical ethics, an attorney at law (or an expert in legal disciplines), a social worker and a representative of Patient Advocacy associations [27].

Clearly, in order for all these players to be properly represented and to compensate for any absences in committee meetings, the number of members cannot be too small; on the other hand, too large a committee would make it impossible to give the proper space to each member to actively participate in sessions and case discussions.

5. Conclusions

Ethics committees were born with the aim of bringing ethical reflection into the world of medicine and healthcare, both in the context of research on human subjects and in clinical practice, among the hospital wards. Over the course of half a century, both types of ethics committees that we have described in this chapter – RECs and CECs – have spread in all countries, albeit to different degrees. While RECs have been institutionally established everywhere for decades and are nowadays strictly regulated, CECs have only been spreading out of North America in more recent times. In Italy, there is still no clear distinction between the two types of committees at an institutional level and CECs are only appearing in recent years.

As a tool to support healthcare professionals in the management of clinical ethics issues, CECs have great potential to have a major impact on healthcare and patients' wellbeing.
The next chapter will precisely address the issue of CECs' impact on clinical practice, with the purpose of determining whether and how their activities may impact and hopefully benefit healthcare professionals and patients.

Chapter II

Evaluating the effectiveness of clinical ethics committees: a systematic review

1. Background

As we have described in Chapter I, Clinical Ethics Committees are bodies originally established with the aim of supporting healthcare professionals in managing controversial ethical issues affecting clinical practice [37] that cannot be settled simply in terms of medical competence [93]. The same aim is pursued by all those services commonly labelled as Clinical Ethics Support Services (CESS), i.e., services aiming at supporting health-care professionals and/or patients and their relatives in dealing with health-related clinical ethics issues. Clinical Ethics Committees represent one of the most common explicit forms of CESS, together with facilitation of Moral Case Deliberation (MCD) and individual ethics consultants [40].

CECs deliver ethics support in many ways, by undertaking a variety of tasks and functions (extensive description in Chapter I, § 4.1): ethics consultation, policies formation and/or revision, and bioethics education [80]. Although CECs developed in parallel with Research Ethics Committees (RECs), CECs are much less enforced, and their tasks are much less harmonized.

Since their first appearance in the late 1970, CECs and the other forms of ethical support services have grown up widely in the United States [4]. Although the number of publications concerning CECs is high, their actual effectiveness in clinical practice has yet to be clarified. As a matter of fact, CECs are generally the most common model of CESS in many countries [40], but the latest literature investigating performance evaluation focus more on other forms of CESS [94], [95] or CESS in general, including some recent literature reviews [96], [97]. Indeed, most of the scientific literature on CECs either reports the history of their development [4], [5], or describes their activities and functions [9], or provides theoretical contributions about their role in hospitals and care centres [37], [98]. Therefore, despite having been established in order to address the need for an ethics discussion on controversial and morally sensitive clinical cases, it is still unclear whether and to what extent they managed to accomplish this task.

Contrary to what one may expect, this is not a recent question, as the need for a thorough evaluation of CECs' performance was recognized early in the formation of these committees [99], [100]. After more than 40 years since their beginnings, the matter is still unclear and studies

investigating how CECs actually affect healthcare are still limited. As a consequence of the dearth of evidence available about their effectiveness [101], some authors challenged the need to establish CECs [6], [102], [103], especially from a cost-benefit perspective.

Nowadays, the question around CECs' effectiveness is even more relevant, since many countries – Italy included – have only recently started to implement CESS in its different forms [8]. In particular, in those countries where no specific founds are appointed for this function, ethics support services are delivered either by RECs or by CECs, developed following RECs' institutional framings [104].

Drawing from these premises, the overarching aim of this systematic review is to gain a comprehensive overview on the *assessed effectiveness of CECs*, both interpreted as *subjective* outcome, namely the index of how the stakeholders who benefited from CECs experienced it, and as *objective* outcome, that is, the tangible consequence of CECs' activities, measurable in daily clinical practice (e.g., as a change in the management of patient care path).

By collecting and clarifying evaluation tools used to assess the effectiveness of CECs in healthcare, we also try to answer the question whether CECs are useful resources.

2. Methods

2.1 Search strategy

Many studies refer to ethics committees as broadly conceived, thus including both CECs and RECs. Therefore, the search string had to be narrowed down in order to include only ethics committees devoted to clinical practice. The search focus was represented by CECs. Furthermore, all the possible definitions of CECs had to be taken into account: *clinical ethics committees*, *hospital ethics committees*, *institutional ethics committees*. Therefore, as terms and/or keywords (e.g., mesh terms) all the expressions referring to – or containing under their trees – the aforementioned terms were included.

On these premises, the string was built in relation to two semantic groups: group A included all possible definitions and mesh terms related to CECs; group B contained all terms pertaining to assessment, impact, and/or evaluation. In particular, group A contained the following terms: Clinical ethics committee*, hospital ethics committee*; while group B contained: impact, effectiveness, evaluation*, assessment*.

The two groups were then gathered according to the properties and Boolean operators of each database (see Table 1). The choice of the terms as well as the search strings were developed by

the first author (Chiara Crico) in consultation with the second author (Virginia Sanchini). In order to cover both the fields of healthcare science, clinical/medical ethics and bioethics, we searched seven electronic databases: PubMed, Ovid MEDLINE, Scopus, Philosopher's Index, Embase and Web of Science. The database search was performed in November 2019 and included all relevant literature published up to that date (see Table 1). Language restriction was applied to the results, thus excluding studies not available in English. A total number of 3,267 records was retrieved through the queries.

The screening process was then carried out by the first (CC) and the second author (VS) according to the PRISMA guidelines [105] and managing citations and available texts with Mendeley software (version 1.19.4).

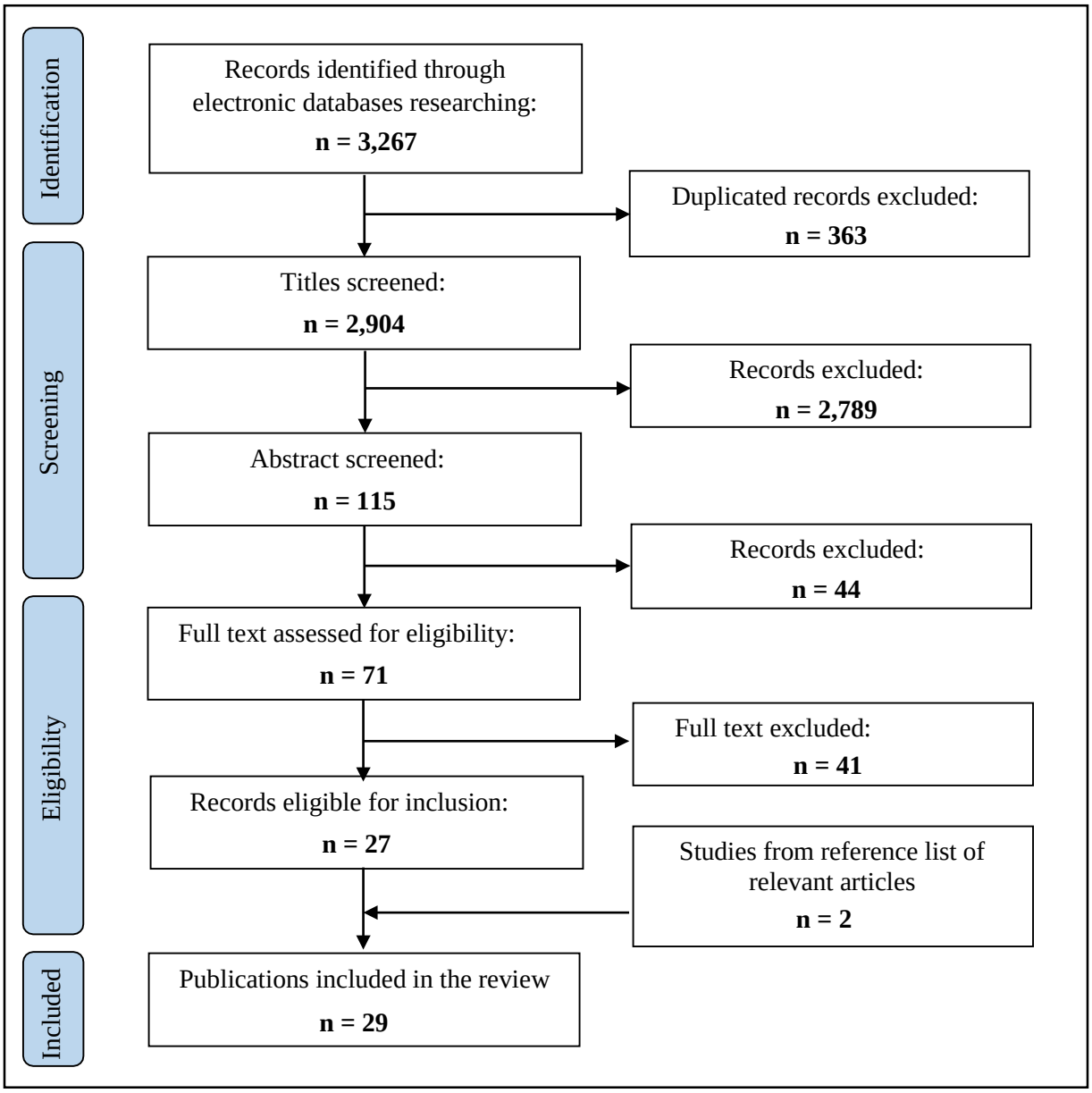
First, duplicates (363) were excluded. The first author (CC) screened the remaining titles, according to pre-set inclusion and exclusion criteria (see below). The abstract screening (115) was then performed by the first author (CC) and the second author (VS) independently, to ensure scientific and methodological rigorousness of the abstract selection. In 91,5% of the abstracts there was agreement between the two authors, but consensus was reached after discussing doubtful candidate abstracts. A screening of the full text of the remaining records (71) was then performed by first author (CC) and the second author (VS) independently. After this step, a total of 27 articles were included in the review process.

Bibliographies of relevant articles were examined and two additional articles that met the inclusion criteria were retrieved through reference manual searching and included.

Finally, a total of 29 studies were included in the review. All the articles included were considered of a sufficient quality, based on the peer review process and on the academic reputation of the journals.

The full process of selection is reported in the flow chart in Figure 1.

Figure 1 *Flow Chart showing the electronic databases search and articles selection procedure.*



2.2 Inclusion and exclusion criteria

Inclusion criteria

Publications included in the review were compiled with both the following conditions: (a) address CECs as a specific topic and (b) provide an evaluation, assessment, impact of one or more aspects of CECs' performance, whether *theoretically* – such as the description of an assessment model – or *empirically*, through quantitative and/or qualitative measures.

Exclusion criteria

The following publications were excluded from the review: (a) studies addressing topics other than CECs as their main focus; (b) studies concerning CECs but not providing any form of evaluation, assessment, impact (e.g., describing CECs' functions, without providing any assessment); articles (c) with no full text available and (d) not published in English, (e) editorials, books, and book chapters; (f) articles meeting the inclusion criteria but of insufficient quality, both in terms of research methodology and level of relevance, were also excluded.

Table 1 *Number of records for each database*

Database	Date of search	Number of results
Philosopher's index	29/11/2019	71
Embase	29/11/2019	230
PubMed	29/11/2019	132
Ovid Medline	29/11/2019	660
Web of Science	29/11/2019	2,127
Scopus	29/11/2019	47
	Total	*3,267*

3. Results

***Table 2**: General description of the included studies*

N°	Authors	Title	Country	Year of publication
1	Sullivan & Egan	A measure of growth	USA	1993
2	J. C. White, Dunn, & Homer	A practical instrument to evaluate ethics consultation	USA	1997
3	Smith, Day, Collins, & Erenberg	A survey of awareness and effectiveness of bioethics resources	USA	1992
4	B.D. White, Zaner, Bliton, Hickson, & Sergent	An account of the usefulness of a Pilot Clinical Ethics Programme at a Community Hospital	USA	1993
5	Day, Smith, Erenberg, & Collins	An Assessment of a Formal Ethics Committee Consultation Process	USA	1994
6	Førde, Pedersen, & Akre	Clinicians' evaluation of clinical ethics consultations in Norway: a qualitative study.	Norway	2007
7	Scheirton	Determinants of hospital ethics committee success	USA	1992
8	Shetach	Dilemmas of ethics committee's effectiveness	Israel	2012
9	Bahus & Førde	Discussing End-of-Life Decisions in a Clinical Ethics Committee: An Interview Study of Norwegian Doctors' Experience.	Norway	2016
10	Hern	Ethics and human values committee survey: (AMI Denver Hospitals: Saint Luke's, Presbyterian Denver, Presbyterian Aurora: Summer 1989). A study of physician attitudes and perceptions of a hospital ethics committee.	USA	1990
11	Storch, Griener, Marshall, & Olineck	Ethics Committees in Canadian Hospitals: Report of the 1989 Survey	Canada	1990
12	Storch & Griener	Ethics Committees in Canadian Hospitals: Report of the 1990 Pilot Study	Canada	1992
13	Povar	Evaluating Ethics Committees: What do we Mean by Success?	USA	1991
14	Jansen et al.	Evaluation of a paediatric clinical ethics service.	Australia	2018

15	Førde & Pedersen	Evaluation of case consultations in clinical ethics committees	Norway	2012
16	Hernando Robles	Evaluation of healthcare ethics committees: the experience of an HEC in Spain	Spain	1999
17	Gaudine, Thorne, LeFort, & Lamb	Evolution of hospital clinical ethics committees in Canada	Canada	2010
18	Moeller et al.	Functions and Outcomes of a Clinical Medical Ethics Committee: A Review of 100 Consults	USA	2012
19	Wilson, Neff-Smith, Phillips, & Fletcher	HECs: are They Evaluating their Performance?	USA, Canada, Puerto Rico, Columbia,	1993
20	Perkins & Saathoff	Impact of Medical Ethics Consultations on Physicians: an Exploratory Study	USA	1988
21	Magelssen, Pedersen, & Førde	Importance of systematic deliberation and stakeholder presence: a national study of clinical ethics committees	Norway	2019
22	Cohen	Interdisciplinary consultation on the care of the critically ill and dying: the role of one hospital ethics committee	USA	1982
23	Scheirton	Measuring Hospital Ethics Committee Success	USA	1993
24	Frolic et al.	Opening the black box of Ethics Policy Work: Evaluating a Covert Practice	USA	2014
25	Schochow, Rubeis, & Steger	The Application of Standards and Recommendations to Clinical Ethics Consultation in Practice: An Evaluation at German Hospitals.	Germany	2017
26	Hauschildt et al.	The Use of an Online Comment System in Clinical Ethics Consultation	USA	2017
27	Pedersen, Akre, & Førde	What is happening during case deliberations in clinical ethics committees? A pilot study	Norway	2009
28	Ramsauer & Frewer	Clinical Ethics Committees and Paediatrics: an Evaluation of Case Consultation	Germany	2009
29	Orr, Morton, deLeon, & Fals	Evaluation of an Ethics Consultation Service: Patient and Family Perspective	USA	1996

3.1 General description of results

Twenty-seven articles from the research queries and two more papers identified through the snowball method met our inclusion criteria and became part of this systematic review (see Figure 1).

Publication dates range from 1982 to 2019, with six articles published in the last five years (9, 14, 21, 25, and 26). Of the twenty-nine articles included in the review, twenty-three made an evaluation based on data collected through empirical research and/or on the documents drafted by CECs' members, such as the reports of meetings and discussions (1, 3-7, 9-12, 14, 15, 17, 18, 20-23, 25-29). The remaining six articles describe theoretical models for CECs' evaluation (2, 8, 13, 16, 19, and 24). Amongst the latter, two articles also provide empirical data in support of (2) and/or to test (19) such model. It should be noted that two articles included in the review refer to the same study (7, 23). However, since they report different aspects of the same study, respectively the theoretical (7) and empirical (23) part of an assessment model for CECs' effectiveness, we decided to include both publications.

The tools used for CECs' evaluation were the followings: surveys only (2, 3, 4, 5, 7, 11, 14, 17, 19, 21, 23, and 25), interviews only (6, 9, 10, 12, 20, and 27), survey plus interviews (1, 29), survey plus anecdotal evidence (22). In addition, the authors of three studies made qualitative analyses on reports from case consultation (15, 18, and 26), or used medical charts to compare data from surveys and interviews (18, 20). The assessment tools are outlined in detail in Table 3.

The enrolled participants are physicians in 12 studies (41,4%) (2-6, 9, 10, 14, 20-22, and 24), CECs' members in eight studies (26,6%) (1, 7, 17, 19, 21, 23, 27, 28), and the category of those who requested CEC' intervention or were somewhat involved in the CEC' processes, mainly as part of the attending healthcare team, in nine studies (30%) (2, 5, 6, 9, 12, 14, 20, 21, and 23). Patients and their families who took part in ethics consultation were invited to participate only in 10% of studies, in which they were asked to provide comments about the ethics services offered by the CEC (2, 5, and 29). In two studies, the composition of the sample is not clear, as the identity of respondents is not specified (11, 25). There was no sample in the three studies analysing reports from case consultation (15, 18, and 26) and in the four theoretical studies (8, 13, 16, and 24).

3.2 Function subjected to evaluation

Of the three functions that are typically attributed to CECs – ethics consultation, bioethics training, and revision and/or development of clinical policies – the mostly evaluated is ethics consultation, being the only subject assessed in sixteen studies (55,2%) (2, 4-6, 9, 10, 14, 15, 18, 20,21, 25-29). This function may be performed in different ways, often in relation to the context in which the CEC is located [68], [130], [131]. The predominant expression, according to our review, is "*ethics/clinical ethics consultation"* (2, 4, 9, 14, 17, 18, 20, 21, 25-29). The same can also be labelled as "*case consultation"* (3, 5, 6, 10, 12, 13, 15, 16, 18, 23, and 24), prospective and retrospective "*case review"* (7, 11), "*discussion forum"* (19), and "*case discussion"* (22).

We found that different conversation methodologies were used to carry out consultations [131]. This is in line with the fact that there is no unique mandatory procedure to perform them, though some countries proposed standards for ethics consultation [73]. Among the methods described in this review, two are explicitly mentioned: the six-step model (15), a conversation methodology used to facilitate the research of possible solutions for an ethical issue, by outlining its elements and context (medical facts, involved parties, values at stake); the Nijmegen method (25), which applies relevant concepts from different normative ethical theories (such as hermeneutics and pragmatism) to case discussion [132], [133]. In study 18, it is stated that the CEC choose which methodology to adopt depending on circumstances. With respect to remaining articles (2, 4-6, 9, 10, 14, 20, 21, 26-29), despite providing some insights on how CECs conducted ethics consultation, they do not specify which conversation methodology they were using, making it difficult to define whether they were following a specific methodology or adapting the consultation to the single case.

Of the other articles dealing with CECs' functions, seven perform a general assessment of all three standard functions (1, 3, 7, 11, 12, 17, and 23) and one outlines a model to perform assessments (16).

Two studies propose a framework for measuring (13) and/or reaching (18) CEC's success in all the three above-mentioned functions. Among the other theoretical papers, one deals with the function of preparation and/or revision of clinical policies and provides a model for their successful development (24). The function of policy preparation and/or revision is also assessed, together with ethics consultation, in study 22.

The selection process did not identify studies focusing only on education and training in bioethics, though this is considered a core function of CECs (1, 11), with a positive impact for the healthcare staff (17).

Finally, study 19 investigates whether CECs carry out some kind of self-evaluation.
No selected article provides a comprehensive evaluation of CECs, looking at CECs' functions separately.

3.3 General findings

Terminological premises and review scope

The aim of the present work is to review the results of CECs' assessments in order to clarify their effectiveness. To reach this aim, we systematically looked into the included articles in order to identify the exact expressions that refer to CECs' evaluation. We found a variety of terms referring to CEC's evaluation: effectiveness (1, 3, 5, 7, 8, 10-12, 17, 19, 23, 24), which is the most recurrent expression, efficacy (8, 14, 24), impact (6, 11, 13, 17, 18, 20, 23-27), success (2, 3, 7, 8, 13, 16-19, 23, 24), performance (1, 2, 19-21, 26), usefulness (1, 4, 6, 9, 16, 21, 23, 24, 28), helpfulness (2, 3, 5, 9, 12, 14, 21, 24, 29) (see Table 3). Note that, in many cases, even within the same article, these terms and expressions are used in an interchangeable manner, as synonyms, although they may have different connotations. In fact, the literature on the evaluation of CECs is heterogeneous and not only the *expressions* used to indicate CECs' performance, but also the *meaning* of these expressions, as well as the *outcomes* considered as index of effectiveness, differ. In general, all the above-mentioned terms may refer either to more objective outcomes, namely the tangible consequence of CECs' activities on clinical practice (e.g., as a change in the management of patient care path), or to a more subjective outcome, namely, the experiences of the stakeholders – healthcare professionals, patients, and their families – who benefited from CECs' services (e.g., satisfaction or perceived usefulness of the services). In this second meaning, CEC's impact was measured mainly through questionnaires and/or semi-structured interviews.

The variety of both the expressions used in relation to CECs' evaluation and their interpretation resulted in a variety of assessment tools employed as well as outcome observed in the selected articles: although we collected a reasonable number of articles about CECs' evaluation, we were not able to find a standardized and unique measure for evaluating CECs' efficacy. In those reported cases in which the same assessment criterion is used (e.g., satisfaction), neither there is a unique way for measuring it, nor it may be found a validated instrument justifying its use.

***Table 3**: Details on evaluation and terminology*

N°	EVALUATED FUNCTION	MEASURED ASPECTS	EVALUATION TOOL/S	TERMS INDICATING EFFECTIVENESS (recurrence)
1	CEC in general	Perceived helpfulness; Satisfaction	Survey + Interviews	Effectiveness (1); Performance (2); Usefulness (1).
2	Ethics consultation	Satisfaction, change in knowledge, in patient care, in length of stay and in intensity of treatment	Survey	Helpfulness (1); Performance (9); Success (1).
3	Ethics consultation	Perceived helpfulness	Survey	Effectiveness (5); Helpfulness (1).
4	CEC in general	Perceived effectiveness; Satisfaction	Survey	Effectiveness (5); Impact (2); Usefulness (2).
5	Ethics consultation	Perceived effectiveness	Survey	Effectiveness (19); Helpfulness (1).
6	Ethics consultation	Perceived usefulness	Semi-structured interviews	Impact (1); Success (1); Usefulness (3).
7	CEC in general	Satisfaction	Survey	Effectiveness (1); Success (46).
8	CEC in general	Mission clarification; CEC Authority; Composition; Appropriate set of regulations and procedures; Efficient follow-up procedures	(not applicable)	Effectiveness (19); Efficiency (5); Performance (2); Success (3).
9	Ethics consultation	Satisfaction	Semi-structured interviews	Helpfulness (2); Usefulness (2).
10	Ethics consultation	Perceived effectiveness; Satisfaction	Semi-structured interviews	Effectiveness (3).
11	CEC in general	Perceived effectiveness	Survey	Effectiveness (7); Impact (1); Usefulness (1).
12	CEC in general	Perceived effectiveness	Interviews	Effectiveness (4); Helpfulness (4).
13	CEC in general	Institutional acceptance; Consensus within CEC's members	(not applicable)	Impact (1); Success (38); Usefulness (1).
14	Ethics consultation	Perceived helpfulness	Survey	Efficacy (7); Helpfulness (6); Usefulness (1).
15	Ethics consultation	Adoption of systematic approach	Qualitative report analysis	Usefulness (1).

16	CEC in general	Method of case deliberation; Members' participation in discussions; N. of recommendations followed; Compliance with accreditation rules	(not applicable)	Effectiveness (2); Helpfulness (1); Success (4); Usefulness (2).
17	CEC in general	Perceived effectiveness; Satisfaction	Survey	Effectiveness (16); Impact (13); Success (1).
18	Ethics consultation	N° days required to complete consult; Percentage of recommendations followed; Patient outcome	Descriptive statistics on data + qualitative analysis on case reports	Efficacy (1); impact (2); Success (1); Usefulness (1).
19	CEC in general	Extent of CECs self-evaluation	Survey	Effectiveness (9); Efficacy (1); Efficiency (1); Performance (4); Success (4).
20	Ethics consultation	Perceived impact; Change in patient management	Semi-structured interview + Revision of medical charts	Impact (14); Success (1); Usefulness (1).
21	Ethics consultation	Satisfaction	Survey	Helpfulness (9); Success (2); Usefulness (10).
22	Ethics consultation Policy development	Perceived impact	Survey + anecdotal evidence	Effectiveness (1); Impact (1);
23	CEC in general	N° of developed guidelines; N° of requests for educational programs; N° of requests for case consultation; Change in patient management	Survey	Effectiveness (11); Impact (5); Success (49); Usefulness (2).
24	Policy development	Perceived impact	Anecdotal evidence	Effectiveness (2); Efficiency (1); Helpfulness (9); Impact (3); Success (16).
25	Ethics consultation	Adherence to international standards	Survey	Impact (1).
26	Ethics consultation	Efficacy of the adoption of an online system for case discussion	Analysis of reports	Impact (2); Performance (1); Success (1).
27	Ethics consultation	Method of deliberation	Observation + Semi-structured interviews	Impact (1).
28	Ethics consultation	Usefulness; Satisfaction; Time spent on discussion	Qualitative analysis on reports	Performance (1); Usefulness (2).
29	CEC in general	Perceived helpfulness; Change in patient management	Survey	Helpfulness (48); Efficacy (1).

Subjective measures: users' perception of CEC effectiveness

Most findings concern users' perceptions. In particular, most studies investigate whether users and providers consider CEC's activities, especially ethics consultation, to be helpful (1-6, 9, 10-12, 14, 20, 21, 22, and 29). Users are represented by physicians, staff members, residents or trainees (4, 6, 9, 10, 12, 20), nurses (4, 12), members of the healthcare team in general (2, 3, 5, 14, 21, 22), or professionals working within the hospital, such as social workers and pastoral care staff (3). Patients and their families are also included as users of the consultancy service, but only in a minority of studies (2, 5, and 29).

Despite potentially raising conflicts of interests, in some cases the evaluation of CEC's performance is provided by hospital administrators (11, 12) and CEC's own members, who are asked to assess how they perceive the impact of their own consultation activities (1, 4, 7, 17, 19, 21, and 23).

Satisfaction and positive overall judgment towards ethics consultation prevail over dissatisfaction not only in all the studies involving CEC's members, as expected (1, 4, 7, 17, 19, 21, 23), but also when they involve users, with only one study reporting a higher percentage (66,6%) of physicians' negative impression (10). Although data reported by the studies and tools used to collect them are too diverse to enable real comparisons, there seems to be a difference in users' reported satisfaction levels. For instance, patients' families or surrogates (i.e., layers, guardians, or friends) express appreciably lower average scores in satisfaction than the other groups of respondents. In fact, they rate ethics consultation helpful in 57% of the cases, according to study 29, and two out of six participants (33,3%) of study 5 claim they were very dissatisfied with the consultancy. On the other hand, according to the studies reporting percentages, perceived helpfulness ranges from 65% (4) to 96% (3) for healthcare professionals and from 81% (1) to 88% (4) for CEC's members.

Among healthcare professionals, physicians seem the least satisfied category. In general, physicians are usually more critical towards different aspects of consultation services, even when they declare an overall satisfaction. They complain about the long response timelines to receive recommendations about cases submitted (9, 21), the lack of any systematic structure, improper analyses (9), and biases in case discussions (21). Physicians also express concerns about the composition of CECs, by which the presence of specialized professionals, or key figures whose presence during consultation sessions is essential for the completeness of the case discussion, should be increased (5, 6). In this view, including an acceptable number of clinicians would also prevent CEC discussions from being too theoretical and far from the daily routine of clinical

practice (10). Other physicians raise doubts over CEC members' expertise on matters discussed (9, 10) as well as on consultations' real usefulness, questioning their need (12) and their effectiveness (10).

Differently, in all the studies in which they were enrolled, nurses appear as more satisfied than physicians do, especially in relation to ethics consultation: although they seem to have less awareness and access to the ethics consultation services, 83% of nurses rate it as effective, in comparison to 65% of physicians (4, 12).

Although a unique and standardized tool for measuring CECs' effectiveness was not found, articles selected provide relevant data on the impact of CECs' activities, which may help in shedding some light on this topic. In more than one article, ethics consultation is considered to strengthen the decisions regarding patient management and to support physicians in their treatment intentions (4, 9, 10, and 20). Many physicians also report they learnt how to fruitfully discuss ethically sensitive issues from case consultations (6, 20, and 21). Other studies find the process of ethics consultation useful to improve quality of care (3) and to promote care values, even, in some cases, by helping hospitals to preserve their (religious) identity (12).

Other authors report a positive correlation between the degree of clinicians (2, 20) and/or patients' families (29) satisfaction with respect to ethics service and the change in patient's treatment, perceived as a positive result of the ethics consultation process. Remarkably, some changes in treatment plan occurred in thirty-one out of fifty-nine patients in study 20 and in 33% of patients in study 29.

Meetings devoted to ethics consultation are also considered as helpful opportunities to discuss ethically relevant issues (6, 9, 11, and 20), insofar as they are also able to provide healthcare professionals and patients' families with emotional and social support (4). This evidence is also supported by studies showing a correlation between ethics consultation and a decrease in the level of distress among hospital staff members (14), and among patients and their surrogates (29). In study 14, twenty-eight of the thirty-five healthcare professionals involved in the study reported a decrease in moral distress due to consulting ethics services, while in study 29, patients and their surrogates declare that ethics consultation was "reassuring", "supportive" and "took the weight off" their shoulders (29, p. 137). In general, ethics consultation may give a voice to all the individuals facing – albeit differently – ethical issues in clinical practice, thus making physicians, patients and their families feel that their concerns and perspectives matter (6, 39).

Objective measures of CEC effectiveness

More objective evaluation measures include qualitative analyses of ethics consultation reports, with the aim of evaluating how CECs work during case deliberation and/or how case discussion is conducted (15, 18, 26-28). These studies also report, when available, the number of cases in which CECs' suggestions have been then actually followed by relevant players (18), as well as the following information: the reason for requesting the consultation (18), whether ethical issues have been correctly identified and analysed, by what method (15, 26), if the discussion takes place following a specific structure or set of steps (15), how much time is dedicated to the meeting (27, 29), and how much time is needed to provide requesters with a response (18, 29).

Considerations resulting from the theoretical articles are in line with the aforementioned empirical data. More than one article underlines the importance of multidisciplinarity, encouraging CEC to be composed in such a way so as to incorporate all relevant expertise and disciplines (8, 13, 16). They also highlight the importance of having systematic discussions during CEC's meetings (8, 16). Another point is the concept of *meaningful consensus* as a criterion for successfully delivering ethics consultations (13). With respect to the latter, the idea was raised that consensus among CEC's members in case discussion is not necessarily a value *per se*, as it could be due to a lack of divergent views or the dominance of a single committee member.

4. Discussion

This review shows that CECs seem to exert a positive impact both on the healthcare personnel and the institutions in which they work, but many aspects of their functioning are still left to dissect. It is apparent that there is a great diversity in the procedures they adopt, mostly in relation to their cultural and geographical contexts. This also makes it difficult to get to shared criteria for their evaluation.

Heterogeneity in assessments raises methodological difficulties to make straightforward comparisons and to identify the key factors for a positive impact. Criteria by which CECs' activity is considered successful, and the definition of success itself, varies considerably from study to study, and from context to context. This makes it difficult to evaluate CECs' performance. Therefore, the adoption of clear (and, as much as possible, common) standards would be useful. However, cultural diversities should be also respected. CECs are meant to be so close to clinical practice that a globally harmonized metric of their success may be

unconceivable and possibly not desirable. Nonetheless, as a matter of fact, CECs – particularly in regard to their function of ethics consultation– were largely reported as beneficial by both users and providers in many studies.

Clearly, ethical consultation is perceived as the main core business of CECs. Unfortunately, assessing its efficacy is problematic [134], [135]. There is no consensus about which tools to use [128]. Most studies adopted satisfaction as a measure of effectiveness. However, satisfaction and/or perceived helpfulness are obviously subjective criteria and, as such, depend on multiple variables that are not always quantifiable or reliable. In any case, it is more than reasonable that users' satisfaction may be a tool, if properly thematized. Delany and Hall provide a broad view of satisfaction, which combines empowerment, enhanced understanding and the feeling of being more prepared to face some conditions [136]. Following this concept, satisfaction would be determined by an increased understanding of ethical issues and moral values at stake, thanks to multidisciplinary discussions and ethical analyses during case discussions, with a willingness to follow insights and recommendations as a result. In the end, with regard to the primary objective of CECs – namely, to provide support to healthcare professionals on clinical cases – satisfaction may well be a reasonable performance indicator. The decreased level of distress, reported as a result of ethics consultations, also seems to indicate successful support of healthcare professionals, at least at an emotional level. Although not widely reported, it is important to underline that some studies mention changes in patient management and therapeutic plans as a consequence of ethical consultancy.

Albeit few studies have investigated this aspect and more research is needed, this finding could indicate how a broadening of perspectives as allowed by the ethical multidisciplinary review can affect the decision-making process and impact on clinical decisions, thus improving the quality of patient care [137], [138]. To ensure that this is the case, the composition of committees should include as much expertise as possible in the relevant areas of ethical-clinical issues that are addressed, including experts in ethics and bioethics [139], to maximize multidisciplinarity [140].

In regard to the educational function, the lack of studies thereon is worth mentioning. In our review, although several authors stress its importance [52], [106], bioethics training would seem to be underestimated or underreported. Indeed, amongst the three functions of CECs, this should be the easiest to assess. In addition, its impact should almost be a given: by being properly trained, healthcare professionals will inevitably become more sensitive to ethical issues, and potential ethical threats may be prevented. The possible lack of resources allocated to bioethical training, as compared to those devoted to ethics consultation, would suggest that CECs see ethics

consultation as their main task [128]. This is not surprising assuming that CECs were originally established to support healthcare professionals in facing and managing ethical issues involved in clinical practice. This function is therefore perceived as the main one, and the most tangible, the other functions, albeit considered helpful and worthy [108], being perceived as less important, or at least less urgent or less rewarding in the short run. On the other hand, one may observe that the most effective way to train physicians about bioethical issues is likely through real clinical case discussions [81], [111], [120]. Thus, the function of ethics consultation could actually imply an educational added value as a kind of "by-product", in a way which could be less theoretical and more palatable to clinicians than more conventional training strategies. Of course, it should be noted that this "field training" would be less accessible than "class training" and limited to those who require the support of CECs, namely those who in some ways are already prone to recognize the ethically problematic aspects of a clinical case and are willing to discuss it.

Regarding the function of working out and reviewing institutional policies, any attempt to evaluate its impact is difficult. Indeed, whatever the processes of drafting these institutional guidelines, how much they actually affect clinical practice is an open issue. Investigating this item is challenging, in the end as much as it has always been challenging in clinical medicine to assess the impact of clinical practice guidelines. Probably, however, an outstanding added value of guidelines in general is the process of their preparation, as long as it involves many clinicians and leads them to be aware of, and discuss, issues which may often be underappreciated or ignored. In this sense, it is more than likely that CECs may expose clinicians and health administrators to a multidisciplinary array of skills and perspectives which otherwise could be missed.

One last observation based on publication dates and the geographical distribution of the studies we reviewed seems to indicate a decrease over the last years in the number of articles about CECs' functions and activities in the United States, where nowadays they are viewed as being routinely a component of healthcare institutions. In the US, CECs' presence in hospitals and healthcare institutions may be so deeply rooted that investigating their effectiveness may not seem an interesting matter anymore. On the other hand, the interest in CECs is on the rise in Europe, where CECs are still developing [81], [114], [125]

4.1 Proposed quality evaluation of selected studies

All the 29 selected articles were considered of sufficient quality for inclusion in the present review. However, quality varies from article to article, depending on how studies were designed

and carried out, as well as on the comprehensiveness of data. Therefore, while for the theoretical articles providing models of evaluation we considered sufficient the quality criteria listed in *Methods* (reliability of peer-review processes and academic reputation of the journals), we proposed a quality assessment (from sufficient to high) for the ones reporting empirical data, according to shared standard in literature [141]. Data considered for quality assessment were the followings: the type of evaluation tool, whether the complete dataset was reported, the number and description of enrolled subjects or the number of documents analysed, and the response rate. We excluded potentially interesting papers (i.e., papers that could have met our inclusion criteria) if they showed an insufficient quality, according to our exclusion criteria. A few articles are rated as qualitatively barely sufficient: that is because they provide a mere interpretation of the data rather than a comprehensive presentation, as they neither display the instruments used to collect them nor give a precise description of them. We instead rated as medium or high quality those articles that contained at least a description of the evaluation instrument (content of the questions asked, number of questions, duration of the interviews, etc.) or of the data collected or both (high quality) and a sample number congruent with the objectives of the study.

Table 4: Quality of the studies included in the systematic review

N°	Measure of evaluation	Attached evaluation tool	Comprehensive response dataset	Sample size	Sample description	Response rate	Overall quality rating		
							Sufficient	Medium	High
1	Review of minutes of CECs' meetings, Survey, Semi-structured interviews			21 (survey) 14 (interviews)	CEC's members (current and former)	81% (survey) 66% (oral evaluation)	X		
2	Survey	X	X	45	Consultation requestor (healthcare professionals, patients and families)	60%			X
3	Survey	X	X	1957	Staff and resident physicians, nurses, social workers, pastoral care staff	41%			X
4	3 surveys (pre-test, post-test + follow up)		X	157 (Pre-test) 168 (Post-test)	Nurses/physicians of critical and special care units (pre-test and post-test) Ethicists/nurses/physicians (follow-up)	29/10% (pre-test) 18/19% (post-test); 98/54/52% (follow-up)		X	
5	Survey (2 versions: for healthcare staff and patient's family members	X	X	46	Healthcare staff (40) and patient's family members (6) involved in one of the 16 HEC consultations object of the evaluation	54% (staff members) 30% (family members)			X
6	Semi-structured interviews		X	8 (for 10 consultations)	Physicians (from 6 different hospitals)	50%		X	
7	Survey		X	137	HEC chairpersons of hospitals with >100 medical residents	83%		X	
9	Semi-structured interviews	X	X	15	Physicians who requested CEC consultation	/			X
10	Semi-structured interviews	X		10	Physicians who admitted at least 25 patients at local hospital in the previous 12 months	25% (met inclusion criteria)		X	
11	Survey			72	Respondents from English language hospitals with >300 beds	84,5%	X		
12	Survey, Semi-structured interviews			?	Staff from 5 hospitals with a CEC physicians, nurses and administrators	/	X		

14	Web-based survey	X	X	35 (11 cases surveyed)	Staff involved in a consultation: consultant physicians (16), nurses (10), allied healthcare professionals (4), trainee physicians (3), social workers (2)	36%		X	
15	Case discussion reports	X	X	17	(not applicable)	46%			X
17	Survey	X	X	107	Chairpersons of French and English-language hospitals with a CEC and >100 beds	51%			X
18	Case discussion reports		X	100 (for 98 patients)	(not applicable)	(not applicable)		X	
19	Survey	X	X	236	CEC members of active and functioning CECs				X
20	Telephone semi-structured interview, Revision of medical charts (to be compared with interviews)		X	34 physicians	Physicians requesting CEC consultations	94%		X	
21	Survey (2 versions: CEC members, clinicians), each to be replied in relation to a single consultation	X	X	64	CECs' members and clinicians who took part in CEC meetings	52,7% (participating CECs) 63% (reported consultations)			X
22	Informal survey, Anecdotal evidence			(Not available)	Local hospital staff	(Not available)	X		
23	Survey		X	127	Chairperson of CECs from hospitals with >100 beds and a major affiliation with a medical school	83%		X	
24	(not applicable)			(not applicable)	(not applicable)	(not applicable)			
25	Survey		X	545	Not available	29,3%		X	
26	Case discussion reports		X	159	CEC members	(not applicable)		X	
27	Observations of committees deliberating a paper case (25 minutes) Semi-structured group interviews	X	X	9 CECS	CEC members				X
28	Case discussion reports			16	CEC ethicists	(not applicable)	X		
29	Survey, Semi-structured interviews		X	56	Patients or surrogates	90,3%		X	

Legend: x = yes

4.2 How assessing CECs' effectiveness? Possible suggestions for CECs' evaluation

Our comprehensive analysis may suggest some proposals to improve the way we can assess CECs' effectiveness in regard to their three main functions.

With regard to the most widely evaluated function – *ethics consultation* – as many suggest, it is essential to assess whether and how ethical advice impacts on clinical decisions and their stakeholders. This means investigating whether and to what extent health professionals think that ethics consultations improve patient care, and specularly, whether and to what extent patients and their families think that it resulted in a better and more comprehensive care process. We propose that the best way to maximize the amount of collected data and their exhaustiveness is to use both quantitative and qualitative methods. Indeed, questionnaires are the preferred methods to collect large amounts of data, for they facilitate researchers in reaching many people rapidly. On the other hand, qualitative methods, such as semi-structured interviews or focus groups, provide more extensive data, as they allow to deepen topics of interest and follow experiential flows. We also propose that consultation services should be monitored in the long run: given the specificity of ethical consultation and the low number of consultations per year [75]–[77], data on a service collected longitudinally would be highly informative and would make it easier to intercept any potential impact of ethics consultation, for instance greater therapy compliance by patients, or less conflicts with families.

With respect to the *bioethics training* function, a comprehensive assessment should consider a twofold aspect. First, it should evaluate the acquisition of theoretical notions by using simple tests. As an example, to evaluate the effectiveness of a training session on the informed consent process, it should be assessed whether the trainee has learned the ethical pillars of a valid informed consent form and process (e.g., information, comprehension, voluntariness).

When training also aims to transfer operational skills (as stated by the American Society for Bioethics and Humanities), any assessment on the application of such skills should take into account that this is an ongoing and iterative process. The evaluation methods should also be modelled accordingly to the specific skill/s conveyed, and on the audience, it is addressed – namely, the hospital staff or the internal members of the CEC itself. As an example, in the first case, if the skills conveyed regard performing ethics consultation, the training sessions should teach the healthcare professionals first to recognize whether a case is ethically sensitive and then the key elements of ethics consultation (e.g. learning how to analyse, from an ethics standpoint, a

clinical case, at least in a preliminary way); in this case, the assessment should require the trainee to apply the acquired skills, for instance by asking trainees to discuss an *ad hoc* clinical ethics case, recognizing the moral dilemma and analysing the underlying ethical problem. Depending on the resources available, such an assessment can be made either through an oral test, or a focus group, or through a written examination.

Concerning the in-house training for CEC's members, as this is on-going training, the assessment should also be on-going. In this case, the members' skills to provide ethics consultation can be tested either through a test at the end of each course (e.g., by giving a case and verifying that they are able to analyse it); or through a training day in which this skill is updated and reinforced, for example by collecting particularly relevant cases and using them to practice moral case analysis. Again, the evaluation can be either oral or written.

With regard to the third function – *policy preparation and/or policy revision* – a key element to evaluate CECs' performance is to verify if policies have been approved and enforced. Moreover, as it is always fundamental that healthcare professionals of a given institution develop an "ownership feeling" with respect to policies affecting their practice, satisfaction questionnaires may be useful. However, it should be noted that this function is the most complicated to assess, because the implementation of any new or modified policy depends on many factors, such as, for example, administrative and organizational ones.

5. Limitations

A limitation of our systematic research concerns the publication dates of studies included. Although we included five papers published within the last five years, more than half of the articles (16 studies) were written and published before the year 2000. Data reported by those studies would need an update. Only in one case, we noticed an update of data concerning the same CEC through the use of the same questionnaire [49], [52].

6. Conclusions

The aim of this systematic review was to provide an answer to the question whether CECs may be useful, by collecting all evaluation tools used by researchers to assess their impact in clinical practice. Although a definitive answer cannot be given, our work systematically collected available

information. By doing it, this study provides a comprehensive overview of CECs' impact, highlighting some key elements of their performance. Amongst the three most typical functions of CECs, i.e., clinical ethics consultation, ethical education and the development of institutional clinical policies, ethics consultation is largely overwhelming.

Despite the lack of standardized assessment tools, CECs appear to be beneficial at the very least in terms of healthcare professionals' satisfaction. Indeed, the presence of CECs correlates with a lower moral distress among staff members.

However, this systematic review stresses the importance of developing standardized tools for evaluating ethics consultation. More work is needed to collect more data with respect to what patients and/or their surrogates perceive. Definitely, in view of an increasingly demand of personalized medicine, patient perspective cannot be left aside.

Chapter III

Stakeholders' experiences and expectations regarding how to manage ethical issues in clinical oncological practice: a qualitative study

1. Introduction

As explained in the previous chapters, the emergence of Clinical Ethics Support Services (CESS) was due to a combination of factors. A greater awareness about ethical implications of clinical decision-making, together with the advances in biomedical research and technology, led to radical changes in the world of health care and health professionals have found themselves facing an ever-increasing outbreak of ethical dilemmas related to clinical practice [9]. As described in Chapter I, it soon became clear that these new problems needed to be tackled at a multidisciplinary level, as their resolution requires multi-faceted expertise. CESS – and Clinical Ethics Committees in particular – were first conceived and developed precisely for this purpose, as a structured tool for providing support in addressing ethically sensitive issues in clinical practice, as guidance in the clinical decision-making process and safeguard of patient rights [40], [41]. While CESS have become widespread in North America as early as the 1980s, they began to develop in Europe at a slow pace a decade later, and not equally in all countries. With the exception of the northern countries, CESS have just started to extensively develop in Europe and healthcare facilities started to provide clinical ethics support only in later years [8], [142], [143].

As we explained in Chapter I, in Italy structured forms of CESS have not yet been developed. However, Ethics Committees are meant ideally to deal with both research and clinical practice [27]. Since their first diffusion within hospitals, they have in fact formally held two distinct roles: on the one hand the humanization of medicine, through the promotion of the dignity of the subjects of the care processes, on the other hand the evaluation of experimental protocols and the

monitoring of clinical trials, as defined and reiterated several times by the Italian National Committee for Bioethics [10], [56]. The evaluation of clinical trials, required by ministerial obligation [57] is such an onerous activity in terms of time and resources that it hardly leaves time for ethical issues beyond the scope of research. Hence, in Italy the presence of a body dedicated solely to ethical questions that clinical practice inevitably raises is increasingly perceived as a necessity [62], [63] and in recent years the first Italian committees dedicated solely to clinical practice have begun to appear in hospitals and healthcare institutes [27].

Clinical Ethics Committees and CESS in general are becoming increasingly widespread and seem to receive the appreciation of users [7], [78]–[80], [126], as we underlined in Chapter II. However, ethics support services still endure many weaknesses and limitations and operators – especially physician – complain that committees do not always meet their support needs [144].

In the perspective of an increase in the number of ethics support services in Italian hospitals, and to ensure their effectiveness, it seems useful to clarify what are the actual needs and desires for ethics support of potential users of such services. Researching and analysing the needs and expectations towards clinical ethics support is a necessary preliminary operation to outline a service tailored to the specific demands of real health care institutes, healthcare professionals and patients.

In the context of facilities dedicated to the treatment of extremely delicate diseases, such as cancer hospitals, investigating what we may define as “ethical needs” of stakeholders becomes even more important. Indeed, there are some peculiarities of this specific disease that need to be properly considered: even if the life expectancy of oncological patients in general has increased significantly in recent decades, there is no doubt that the diagnosis of cancer is still strongly associated with death [145] and that it has a comprehensive significant impact on people's lives [146]: oncological therapies can be very invasive and debilitating for patients and the therapeutic process may last for many years and, in some cases, even a lifetime. Consequently, the ethics support needs of people working in this context – and their patients – are pathology-specific and should be investigated as such.

Based on these premises, we carried out a qualitative study aimed at collecting the clinical ethics experiences of the stakeholders of an oncological institution, the Fondazione IRCCS Istituto Nazionale dei Tumori, through the collection of semi-structured interviews. Since the purpose of the study was to investigate the aspects and dynamics of clinical practice for which a clinical ethics

support would be desirable and/or advisable, the subjects of the interviews were key professional figures working within the Institute, such as healthcare professionals (e.g., physicians and nurses), Ethics Committee' members and Patient Advocacy Group' members. Participants were interviewed about their professional experience with ethical clinical issues, their perspective on ethics support, expectations and desires. In the present work, we show the result from the thematic analysis performed on the transcribed texts of the interviews, with the aim of highlighting the participants' needs and wishes regarding ethical support.

2. Methods

2.1 Study design and recruitment

A devoted research protocol for the qualitative study was designed by the first and second author (CC and VS), revised and approved by the third author (PGC), Principal Investigator (PI) of the Study. It was submitted in February 2019 to the Research Ethics Committee of the Fondazione IRCCS Istituto Nazionale dei Tumori, in Milan (Research Protocol Title: "Investigation of ethical-clinical expectations within an oncological institution"; Code "INT 65/19") and approved in March 2019. The enrolment phase lasted from June to December 2019. In June, an email was sent by the third author and PI of the Study (PGC) to a selected group of one hundred stakeholders of the Fondazione IRCCS Istituto Nazionale dei Tumori. The choice of potential participants was mainly based on two criteria: a) interest towards ethical dimensions of care practice, based on familiarity with ethical issues encountered in daily activity; b) in-depth knowledge of the internal Institute's dynamics. Upon these criteria, stakeholders invited to participate in the study belonged to one or more of the following categories: directors of all the operative units; members of the institutional research ethics committee; members of the main patients' Advocacy Groups working within the Institute; head nurses; young physicians (<40 years old) with some experience in the conduction of clinical research. Doctors in the latter category were included also on the basis of the following assumptions, based on our knowledge about the modality doctors are trained over the last few decades: a) they should have some (even very basic) knowledge of clinical ethics, as they graduated after the introduction of mandatory bioethics courses at university. b) Anticipating the development of a new ethics support service, it is expected that such a service will take a few years to become fully operational; doctors in this age group will be the ones who, with highest probability, may have the opportunity to relate to the service in the near future. c) In general,

medical culture has evolved greatly in recent decades; compared to their senior colleagues, newly educated doctors have been trained after the shift in the doctor-patient relationship that marked the transition from paternalism to a patient-centred approach, in the context of personalized medicine. The order of the interviewees visible in the first table (Table 1) followed the chronological order of sampling. Following the logic of "theoretical sampling" [147], we progressively recruited research participants according to the first emerging results. Along the way, for example, it seemed necessary to include a number of members of the institute's ethics committee, on the assumption that they were more used to conceptualizing ethical dilemmas.

The email sent to prospective interviewees contained a brief explanation of the study primary and secondary objectives, along with the invitation to express suggestions related to the study, as well as the request for availability to undergo the interview. Those who responded positively to the invitation were then contacted by the first author (CC) via email or telephone to arrange a meeting for the interview.

2.2 Interview scope and questions

The in-depth interviews followed a semi-structured outline based on ten questions (the complete set of questions is present in Appendix 1) on the following issues: common ethical problems in oncology, both from the point of view of clinicians and patients; individual and institutional strategies currently implemented to address them; wishes and expectations for a potential ethics support service.

The topics have been selected and the questions designed considering both the context of the oncological institution where the study was carried out, and the data available in the literature, referring to qualitative studies with similar purposes and characteristics [111], [126].

Given the nature of the study, focused on bioethical issues in clinical oncology, the interview script was developed by the first author (CC), with the support and review of the second author (VS), senior bioethicist, and the third author (PGC), medical oncologist. In addition, the cloth was checked by a micro-sample of other subjects asked to verify the comprehensibility of the questions. The interview script was also attached to the trial protocol submitted to the ethics committee.

Despite the guided structure, the in-depth interviews followed the flow of the conversation and the questions were adapted from time to time to the interviewee's sensitivities and interests, without constraining the conversation on specific topics [148], [149]. In general, the questions aimed at eliciting stakeholders' personal *experiences* with ethically challenging situations encountered in

their clinical daily practice: whether they faced some ethically sensitive issues, in what clinical domains, their content; whether they asked for some support and to whom, and whether they were satisfied with the support received. In addition to the experiences, our questions aimed also at investigating stakeholders' *expectations* towards the potential implementation a clinical ethics support service in their Institution: whether they would consider it valuable, which kind of ethical issues should be addressed first, how the service should be structured, etc.

In order for the answers to be as spontaneous and unbiased as possible, participants were given in advance the minimum information about the topics of the interview to allow a free and informed participation in the study. The interviews took place at the Fondazione IRCCS Istituto Nazionale dei Tumori in most cases. Interviews were then recorded, and the audio files transcribed verbatim by the first author (CC), then translated in English for further analysis.

2.3 Analysis

Transcripts were read by the first and the second author (CC and VS), who analysed the transcriptions following the criteria of Grounded Theory [147], [149]–[151]. In the first phase (*open coding*), the first and second author coded the transcripts line-by-line, assigning a code to each emerging theme that was faithful and descriptive of the subjects' experience, attempting to bring out as many concepts as possible. In the second phase of analysis (*axial coding*), always the same authors (CC and VS) gradually identified the common aspects among the subjects' transcript responses and built broader categories accordingly. In this phase, it was often necessary to analyse and clarify the terms used by the participants (different participants often used different and rarely standard terms). In the last phase of analysis (*selective coding*), the relationships between the conceptual categories were outlined, thus leading to greater abstraction from the empirical data and the identification of the core categories, on which our interpretative model is based.

The first author (CC) used the software Nvivo 12 to conduct the analysis, while the second author (VS) performed coding by hand. To increase reliability, the two authors performed the analysis individually and then presented each other the codes for comparison and mutual evaluation [152]. Codes and categories that were not agreed upon were debated and discussed between the two authors (CC and VS) until consensus was reached.

3. Results

3.1 Description of study participants

Table 1 Demographic characteristics and professional information of the study sample

Interviewee No.	Age	Profession	Institute Department (if applicable)	Research Ethics Committee Member	Professional Experience (years)
1	45-60	Medical Oncologist	Genitourinary Medical Oncology	No	>10
2	45-60	Anaesthesiologist	Intensive care Unit	No	>10
3	45-60	Medical Oncologist	Paediatric Oncology	No	>10
4	45-60	Medical Oncologist	Paediatric Oncology	No	>10
5	45-60	Clinical Psychologist	Senology	No	>10
6	over 60	Radiation Therapist	Prostate Cancer Unit	No	>10
7	30-45	Geriatrician	Patient support care	No	>5, <10
8	30-45	Medical Oncologist	Soft Tissue Sarcomas	No	>5, <10
9	30-45	Medical Oncologist	Hemato-oncology	No	>10
10	45-60	Surgeon	Soft Tissue Sarcomas	No	>10
11	45-60	Patient Advocacy Group member	/	No	>10
12	over 60	Medical Oncologist and Nuclear Physician	/	Yes	>10
13	45-60	Medical Oncologist and Palliative Care	/	Yes	>10
14	over 60	Attorney at law	/	Yes	>10
15	45-60	Case manager	Soft Tissue Sarcomas	No	>10
16	over 60	Paediatrician Hemato-oncologist	/	Yes	>10
17	over 60	Medical Oncologist	/	Yes	>10
18	over 60	Patient Advocacy Group member	/	Yes	>10
19	45-60	Head nurse	Hospice	Yes	>10
20	30-45	Research Nurse	Head and neck oncology	No	>5, <10
21	45-60	Chaplain	/	Yes	>10

Of the hundred people invited to participate in the study, 41 people expressed their wish to attend the semi-structured interviews, 50 did not give explicit availability to the interviews but they appreciated and welcomed the study proposal, 9 never replied.

Among the subjects available for the semi-structured interviews, 21 subjects were actually enrolled in the study; the remaining 20 eventually declined the participation, mainly due to a lack of time. The 21 participants included belonged to one or more of the following categories: eight Ethics Committee's members[1], six head of departments, three physicians under forty years of age, two members of Patient Advocacy Groups, two nurses, one medical director, one case manager. For the demographic details of the study participants, see Table 1. The interviews were conducted by the first author (CC) and lasted between 15 and 76 minutes, with an average of 42 minutes. Healthcare professionals (physicians, surgeons or nurses) members of the Institute staff who participated in the study belong to one of the following units: Mesenchymal Soft Tissue Tumours (sarcomas) Oncology (3), Clinical Psychology (1), Genitourinary Oncology (1), Intensive Care (1), Paediatric Oncology (2), Patient Support Treatment (1), Haematology (1), Oncological paediatrics (2), Radiotherapy (1), Palliative Care, Pain Therapy and CPR (1). Members of the institutional Research Ethics Committee (EC) enrolled in the study had clinical experience in Palliative Care (3), Diagnostic Imaging and Radiotherapy (1), Paediatrics Oncology (1). The remaining participants among the EC members are a Patient Advocate, an attorney, the Institute chaplain. Two of the interviewed members of the EC were also part of the hospital staff. All interviews' transcripts, translated in English, are attached in Appendix 2.

3.2 *Emerging clinical ethics themes*

About half (6/10) of the guiding questions in the semi-structured interview (see Appendix 1) aimed at investigating the experiences of healthcare staff and other relevant stakeholders working within an Italian cancer institute – the Fondazione IRCCS Istituto Nazionale dei Tumori – in addressing ethical issues occurring in clinical practice. Such questions were firstly purposed to understand whether interviewed subjects were able to *recognize* the clinical ethics problems encountered in their daily practice. In case this happened, questions were also intended to understand whether there are some clinical ethics issues which are more frequent that others, and also whether they were able to address and/or resolve them, and by which means.

[1] Of the Ethics Committee's members, one belongs also to a Patient Advocacy group, while another is also a nurse.

Based on the collected answers, we first observed that the majority of interviewees (11/21) struggled to clearly identify the clinical ethics issues encountered in their practice, often being unable to distinguish them from purely clinical or psychological issues. Therefore, this finding seems to point to the fact that stakeholders interested in the bioethical discourse – though lacking education or professional training in bioethics – may be unable to recognize merely what an ethical issue is. However, this struggle to identify ethical issues seems to be due to a failure to focus on and articulate the numerous problems they experience, rather than an inability to recognize that there are problems. As a matter of fact, although not always qualified as ethical problems, in all the interviews critical issues emerge, therefore enabling us to identify general ethical themes. On these grounds, after a necessary preliminary screening of the answers, we were able to prepare a list presenting the most frequent clinical ethics issues, as reported by interviewed participants. Through thematic analysis, we were then able to identify the underlying topics and group the issues by themes.

A first distinction can be made between issues that emerged from the direct and personal experience of clinicians and issues reported to interviewed clinicians by patients or directly expressed by interviewed patient advocates.

Table 2 reports the ethical themes as inferred and thematized by the first (CC) and the second author (VS) on the basis of what emerged from the responses. The themes have been categorized as follows, from the most to the less recurrent ones: communication issues, end-of-life issues, medical-decision-making, genetic testing and counselling, resources allocation, informed consent, privacy issues, issues related to the "medical culture", and practical problems. In order to determine the frequency of the themes, we assigned a numerical value to the recurrences with which they were mentioned by the participants. Although not in all cases the frequency of recurrence reflects the importance assigned to the single theme – it may be that an issue (and related theme) was mentioned briefly by an interviewee and thoroughly elaborated by another one – since we wanted to a have a preliminary view on the topic, we focused on the number of mentions.

Table 2: Description of emerging themes and their sub-categories

THEMES	DESCRIPTION	EXAMPLES OF POTENTIAL ISSUES
Communication issues	It includes all the issues related to the *content* of communication as well as to the *process* of communication.	Communicate the worsening of the prognosis Lack of empathy Transparency and completeness of information Unreliable or non-filtered information Incomprehension among colleagues Presence of potential barriers [language, low health literacy]
End of life	It includes all those controversial issues related to treatment in the terminal phase of oncological disease, mainly from a moral but also legal and regulatory standpoint.	Assisted suicide Advanced Directives Palliative deep sedation Withholding/withdrawing treatment Transition from active therapies to palliative care Feeling of abandonment of terminally ills
Resource allocation	It refers to obstacles to a fair distribution of healthcare resources; in this study, resources are intended primarily as clinical and surgical time, availability of drugs and treatments, and accessibility to updated therapies, both in terms of cost and availability.	Economic discrimination [high cost of branded drugs, new drugs available only for purchase] Territorial differences in therapies availability Age-based restriction of therapeutic proposals (*Ageism*)
Genetic mutations: testing and counselling	It refers to innovative genetic testing techniques open up a wide range of scenarios, all of which raise ethical issues. This category is at the crossroads between the issues of decision-making, informed consent, privacy and patient autonomy.	Communication of the result of the genetic test to relatives Understanding the meaning of genetic testing Awareness on therapeutic choices Prognosis reliability
Informed consent	It refers to problems related to the principle of self-determination and the right to information, such as patients failing to understand clinical information, due to the lack of health literacy, awareness of treatment options, due to their diminished autonomy.	Informed Consent in paediatrics Auto-determination in non-competent patients Right to information Patient manipulation towards selected therapeutic choices
Medical Culture	It refers to cultural aspects of medical practice with potential ethically relevant impacts on the former. It includes the contemporary tendency to conceive the medical act as a procedural activity and physicians as mere technicians.	*Acting* medicine vs *thinking* medicine Struggle in dealing with death and mortality Terminal illness perceived as medical failure Cancer as taboo word
Medical Decision Making	It includes all borderline cases in which standard therapeutic guidelines and protocols cannot simply be top down applied, or conflict with the patient's values (i.e., in the absence of sufficient scientific evidence to support a specific therapeutic choice or in cases of uncertain prognosis).	Uncertainty of prognosis in rare cancers Newly diagnosed cancer in the elderly Cancer during pregnancy Jehovah witnesses and surgery
Practical problems	It includes issues that are neither purely clinical nor purely ethical, but which are perceived as ethically worthy since they affect the quality of care, albeit indirectly.	Obsolescence of office supplies Limited medical time

Communication issues

In the next sections, we will explain in greater details some of the issues and problems listed in Table 2, which will be then further addressed in the Discussion section.

With respect to the first theme, "Communication", we report here the difficulty that many clinicians encounter when treatment does not bring the desired results and they have to communicate this news to patients and/or family members. According to the responses collected from members belonging to certain categories – nurses and patient representatives, but also physicians from critical clinical areas (n. 2, 5, 11, 19, 20) – it is not uncommon for doctors to fail to clearly explain what is going on, expressing in vague terms concepts such as the worsening prognosis and the implications arising from it. As our interviewees have shown us, in most cases, this happens not only because of the difficulties resulting from a vehicle of very bad news, but also because doctors find it hard to admit they are losing a patient:

> But the oncologist has, even rightly, the goal of treating the patient, so after 3 years in here I somehow realize that for them it's almost like a defeat to let the patient go [*Interviewee n. 7*].

> (…) the doctor himself, as well as the nurse, never gives up in the face of illness [*Interviewee n. 20*]

Other problems relate to transparency and/or completeness of communication, with information being conveyed in such a way as to direct the patient towards some treatment choices rather than others. This seems to be the case of prostate cancer patients: they do not always receive adequate information about their treatment options and are guided to one or the other by means of poor information:

> I experience, let's say, ethical issues for example in patients I receive with prostate cancer, who have been informed by a fellow surgeon, who did not fully inform them of their treatment options, or worse, who denigrate for instance an equally effective therapy or, let's say, who put other personal interests at the centre, instead of patients. In other words, they use patients as means and not as ends. [Interviewee n. 6].

The processes of communication are also important in the clinical context and related issues have been reported. How physicians communicate information may not be substantial in the care path, but it acquires different values depending both on the individual patient's experience and on his/her prognosis. Many interviewees, belonging to the healthcare staff and patient representatives, report a lack of empathy among physicians as a significant issue (n. 1, 5, 6, 10, 11, 18). If the lack of empathy may be accepted in conditions of full recovery, when facing

situations of poor prognosis, these (seemingly secondary) aspects start acquiring greater importance, thus making a difference to the patients' quality of life:

> Obviously in a context in which, in fact, your healing power is relative - and it's not zero, far from it, meaning that anyway tumours heal, it's not that they don't heal, but anyway they don't heal all - all the other aspects of the relationship become relevant too. They would be relevant anyway, but even more so where you are not able to guarantee everyone the success of what you are doing, in short. Because it is undeniable: one goes to hospital to get treatment, certainly not to be pampered in the first place. If he gets better, even if they kicked his ass, it's okay if you want. The point is, when this does not happen and in any case the aspect of listening is equally important, the aspect of finding a comfortable environment, of being listened to and being put... [*Interviewee n. 10*]

End-of-life

A second thematic category concerns end-of-life issues, within which we included different aspects reported by the interviewees that are particularly relevant and worth mentioning.
The first aspect concerns the advanced directives, i.e., the statement patients can sign in anticipation of a clinical deterioration by advancing their preferences regarding treatment options (such as the request not to be resuscitated under certain conditions). Some interviewees (n. 2, 7, 12, 14) reported that these arrangements are not enforced or that patients are not explicitly asked for prior authorization to undergo or refuse certain medical treatments:

> There is often no awareness of what the patient wanted in terms of critical area and perspectives of a life that is not completely autonomous. [*Interviewee n. 2*]

As a result, doctors are forced to adopt a conservative approach, performing clinical acts that are not always in patient's best interests.

> And we, I mean us doctors who are on call in the wards, we find ourselves in this dilemma especially on call nights (…). And it happens that you're suddenly called at night because a patient has been sick... We are called if a patient is sick. But, of course, we don't know all the patients of the Institute. So, before starting the shift, in some department doctors leave the instruction if, for instance, there is a patient who has given instructions not to be resuscitated or if the doctor himself, after talking to the patient, said that the situation is so advanced that it is not appropriate to subject the patient to procedures that would not be advantageous for them. This happens in very few if not in a single ward, this passing on of information. (…) I found myself there, that you

> have the emergency - life or death of the patient - and you don't have the chance to understand or know what the patient would want. [Interviewee n. 7]

Some operators report (emotional) difficulties to cope with the demands of family members, especially in the paediatric area, in implementing disproportionate therapies or in continuing therapies that are more burdensome than beneficial to patients (n. 2-4, 7, 15, 16, 19). Alternatively, they complain about finding themselves alone in handling second opinion requests from relatives of patients hospitalized elsewhere (n. 1, 13, 15).

Resource allocation

Another theme that emerged in many interviews is that of resource allocation (n. 1, 8-10, 13, 15). This issue is particularly relevant where resources are limited – e.g., in terms of medical time or availability of drugs, in the case of experimental therapies – and clinicians often have to decide on their own how to allocate them among patients (n. 8-10). In clinical areas with frequent cases of patients with uncertain prognosis, this decision becomes even more difficult, as it cannot always be based on the evidence of the data. How to decide in case a patient could theoretically be treated, even if with highly uncertain outcomes and with considerable use of resources perhaps to the detriment of other patients?

> (*About patients with uncertain prognosis*) What to propose, what to do, towards complicated situations, where there is a great level of uncertainty concerning the effectiveness of a treatment? A great level of uncertainty especially about the benefit that one choice or another can give to the patient, also considering the expense, the social expense, the physical expense for the patient, the cost... In short, in terms of a cost-benefit rationale to all intents and purposes, I mean. In other words, on the one hand, we have a doubtful benefit that we can give to a human life. On the other hand, we have all the other things: the risk of damaging the patient, the risk of worsening one' s quality of life, one' s survival, the economic damage that can be done to the National Healthcare System, or the social damage, or... [*Interviewee n. 8*]

Other interviewees also point to an unequal distribution of resources across the territory, with highly specialized centres located in some areas more than in others, and uneven criteria for drug reimbursement across the country, leading to potential economic disadvantages for patients (n. 1, 13, 15). Although these issues may appear far from the ambulatory reality, they actually pose questions also at the level of daily clinical practice:

> This rather grey area is not ethically irrelevant. Because it poses the clinician the problem: I have in front of me a patient who could benefit from this drug, but he has to pay for it. Can he pay for it? [*Interviewee n. 13*]

3.3 Interviewees' preferences about clinical ethics support services

Another set of questions (7-9) aimed at exploring participants' preferences on the topic of clinical ethics support services, with the aim of understanding how they would like to be supported both individually and as units in the management of controversial clinical ethics issues.

Also, in this case we observed that, except for a few research ethics committee members (2 out of the 8), most interviewees were unaware of the bioethics literature on clinical ethics support services, therefore ignoring that institutional forms of clinical ethics support already exist, as well as the functions attributed to them. In answering questions about the characteristics of an ideal clinical ethics support services – in particular about its composition and main functions – almost all the respondents (1, 5-17, 19, 20) mentioned some of the activities traditionally ascribed to the standard functions of the Clinical Ethics Committees, namely, ethics consultation, bioethics training, and drafting and/or revising policy and guidelines.

In the next sections, we will report findings related to specific aspects of clinical ethics support services emerged during the interview. Even though most interviewees were not familiar with the standard definition of bioethics literature and talked in lay terms, we will employ such definitions in reporting their answers, assuming the terms they used refer to the semantic cluster pertaining to those definitions.

How do healthcare professionals manage clinical ethics issues?

Stakeholders' responses reveal that apparently there is no shared approach valid at institutional level, dedicated to the management of ethical issues. There seem to be no *ad hoc* protocols devoted to ethics support and the responsibility for the resolution for conflict resolution falls entirely on the clinicians (n. 2, 3, 4, 14). As a result, healthcare professionals – physicians in particular – deal with ethical issues in the same way as they do with clinically complex cases: they resort to discussion among colleagues of their own medical equip (n. 2-5, 8, 10, 13, 19). Some are used also to contact other specialists when needed, such as physicians from other wards or other health professionals, especially psychologists (55.5%):

> We are very used to sharing, meaning that in my opinion the worst thing that can happen when faced with a difficult decision is to make it alone. So, we see each other every day and the goal of the daily meeting is to meet to discuss difficult cases. We see each other once a week in a

> multidisciplinary context and in this context, we discuss multidisciplinary difficult cases. So, I would say that sharing is our (...) best weapon. [*Interviewee n. 8*]

However, entertaining a dialogue with colleagues does not always entail a decisive resolution of an ethical issue. Interviewees report that, in the most complex cases and if a solution cannot be shared between doctor and patient, it may be necessary to resort to the court (n. 3, 14). Or again, physicians may be forced to choose a downward compromise, which does not necessarily correspond to the patient's best interests (n. 2, 7).

In any case, in the absence of shared strategies operating at institutional level, the criterion by which clinicians handle ethical issues is the "common sense":

> (*Such complex issues*) basically are handled with much good will, with much good will, meaning that it is the human factor that makes things go in the right direction at the right time. However, this is not always possible: there are wards, there are working groups where this is lacking, for different reasons. (…) I mean, the solution is surely to have more resources. Surely to also have the possibility of, how to say, to have networks of collaboration. [*Interviewee n. 15*]

What kind of clinical ethics support service would satisfy stakeholders' preferences? Preferred functions/activities

The questions concerning the broader issue of clinical ethics support services (questions 7-10 in Appendix 1) were aimed at identifying the thematic issues and purposes for which the interviewees would make use of a clinical ethics support service, if available. Based on these findings, it seems also possible to define, in the first place, what characteristics such service should have and what functions it should perform in order to meet the needs of the stakeholders working within the Fondazione IRCCS Istituto Nazionale Tumori. Secondly, it can be assumed that these needs are common – or at least similar - to many (if not the majority) oncological centres or departments and therefore that these characteristics can be applied to any service intended to operate in such a context.

Despite some differences in its ideal characteristics, clinical ethics consultation, interpreted in its simpler meaning of case discussion, emerged as the most desired activity. In particular, some interviewees expressed the desire to have a body to which report clinical ethical issues and ask for support and advice (interviewees n. 1, 5, 7-10 12, 14-16, 19).

> So sometimes, especially for those of us who sometimes get somewhat involved to face delicate choices and then ... Sometimes you, so to speak, you need an additional interlocutor, besides

> your professionalism, someone to discuss with... A moment of reflection, that's it, because that's what's missing. [*Interviewee n. 5*]

> (…) there are situations in which, as I told you at the beginning, it is only through sharing, discussion, confrontation... Here, however, we need the humility that us doctors very often do not have. It seems to us that our experience is everything; it's not like that, you know? And so, having also... I always believe in external help. [*Interviewee n. 16*]

Others wished to have a space to discuss general problems affecting clinical practice, such as access to innovative treatments for patients at a very advanced stage or hospital policy on second opinion requests (n. 13, 17). Some also pictured the support service as a body for supervising how healthcare professionals handle ethical issues in clinical practice; in this scenario, the committee's members would have to do a sort of "ethical performance review", analysing the staff's management of complex cases (n. 16, 19).

> I haven't had clinical activity for 15 years now, but that is a context in which what we were saying, supervision, would be vital, wouldn't it? A support, a sharing. Also, because in those situations you are so involved that it is absolutely necessary to have a context that allows you to be understood and, from a certain point of view, I would also say evaluated. [*Interviewee n. 6*]

For a few interviewees, the presence of a clinical ethics support service where problematic cases can be discussed represents an opportunity to be aware of what is the institutional viewpoint and to share the responsibility for the choice, considered either as legal liability (n. 13, 14) or as moral burden (n. 5, 8, 21), or both (n. 3, 4).

Five interviewees stress that a clinical ethics support service, implemented in the form of CEC, should not only provide answers to specific clinical ethics criticalities, but also play a more proactive role (n. 17). It should discuss and analyse the most common and relevant clinical ethics issues recurrent in the Institution, and consequently develop proper (or reviewing already existent) guidelines (n. 5, 12, 13) and operational protocols (n. 14) to advise and inform operators. Similarly, some operators reported that they would find it useful to have some guidance on how to address the most frequent clinical ethical issues arising in clinical practice (n. 9) or even the less common but nonetheless relevant ones, e.g., the treatment of minors from Jehovah's Witnesses families (n. 3, 4).

Some interviewees mentioned the importance of outlining and reviewing guidelines and protocols, looking at these activities as endowed with an educational dimension, as valuable tools to create an ethical culture in the long term. The effort to examine the most relevant and recurrent

clinical ethics issues in the Institution in an attempt to rethink their management promotes ethical reflection (n. 5) and can lead, over time, to the development of shared strategies among operators (n. 7). According to others, rethinking operative protocols through the help of a devoted clinical ethics support service could be an opportunity to improve patient's management (n. 14, 15, 20).

Another activity that participants indicated as important for clinical ethics support service to perform is training (n. 1, 6, 7, 14, 16, 17 and 19). Educating health care professionals on ethically sensitive issues occurring in clinical practice means, for the interviewed, raising professionals' awareness and improving their ethical sensitivity (n. 1, 6, 16), thus making them potentially better prepared in the management of complex cases, preventing further complications and reduce cases of litigation with patients (n. 14) or between colleagues (n. 7). In this respect, communication is the area in which there is the greatest perceived training need: educating operators to improve their communication with patients is a key element both to ensure a better therapeutic process and prevent conflicts (n. 1, 7, 11, 14).

In the interviews, also other support activities are mentioned as potentially beneficial. Some stakeholders consider it useful to have a *super partes* body acting as mediator among colleagues (n. 8) or with patients and relatives (n. 3, 4, 15) in case of conflict. Some others think the clinical ethics support service should guarantee that the Institute takes (active) care of patients, providing them better support both in the management of their treatment (n. 9) and in some particularly difficult moments of their disease, such as the communication of the diagnosis to the patient and any worsening of the prognosis (n. 11, 18).

What kind of clinical ethics support service would satisfy stakeholders' preferences?

Preferences over institutional arrangement of a clinical ethics support service

Question n. 9 belonged to the broader issue of clinical ethics support services and aimed at exploring participants' preferences over the institutional arrangement of an ideal clinical ethics support service to be implemented in the Institution. Not all participants expressed well-defined preferences on this topic: some interviewees only declared themselves in favour of the entire committee (n. 9) or individual ethics consultant (n. 3, 4, 11, 18) arrangement. Two participants did not express any opinion on this matter (n. 15, 20). In general, most stakeholders believe that a clinical ethics support service organized in the form of a proper committee may better respond to their support needs; moreover, they reported that this should have a multidisciplinary composition which may help promoting discussion among members (n. 2, 6-9, 12, 14, 19, 21):

> If the culture of multidisciplinarity were to develop, a culture in which in which everyone really listens and is listened to (…) I think that, if in all these areas we talked about there was the space and time to confront each other, the issues would already be well managed and all. [*Interviewee n. 5]*

Drawing from the opinion that a clinical ethics support service should not advocate to a single moral perspective (n. 7, 9, 12), a plurality of perspectives may guarantee less subjective and/or partisan considerations (n. 7, 12, 21). According to participants, the unavoidable moral pluralism characterizing our societies should be represented within the committee and guaranteed by the presence of a plurality of members (n. 6, 13). For some interviewees, an ideal service should have a flexible structure in order to adapt to the different support needs and circumstances that may arise. According to this latter set of opinions, the ideal structure would be a more complex one, constituted of an entire committee, devoted to policy development and/or revision and discussion of non-urgent cases, and ethics/bioethics consultants or a small group of consultants, who can offer support in cases requiring immediate intervention (n. 1, 5, 8). Alternatively, clinical ethics support may be provided by individual consultants – especially in relation to the function of clinical ethics consultation – provided that they are members of the committee and report to this after each intervention (n. 13, 16, 17).

Who should provide clinical ethics support? Ideal composition of the clinical ethics support service

Few participants expressed explicit preferences about the ideal composition of a potential clinical ethics support service. As already reported, multidisciplinarity represents the characteristic that most consider essential for a fair decision-making process, which requires, according to the interviewed, the participation of professionals belonging to different fields and with complementary skills and different experiences (n. 1-6, 12-14, 16). Only four interviewees explicitly indicate specific professional profiles to be necessarily included as members of such a committee (n. 1-4, 13): besides physicians, the most mentioned profile is the clinical ethics expert or bioethicist (n. 1-4, 13), followed by the psychologist (n. 1, 2), the expert in communication, the patient advocate, and the forensic doctor (n. 13).

4. Discussion

4.1 Preliminary considerations: difficulties in identifying ethical issues

The first important aspect that emerges from the interviews is a marked difficulty for health personnel to identify what an ethical problem is. When asked to report a clinical ethics issue (or, in a simpler manner, a clinical issue presenting also an ethical/moral trait/layer), in most cases the answers highlight the lack of clear understanding on it. In the best-case scenario, participants reported issues that were at the cross-roads of ethical, psychological and spiritual domains, but they often also report problems of a completely different nature. This preliminary finding shows that health care personnel are not generally used to reflecting on the ethical aspects of medicine, either because they are not trained to do so or because it is not even something that they usually learn in their daily practice, being uncommon in their work environment.

In most of the cases, however, ethical issues are interpreted, by stakeholders interviewed, as problems related to "communication", as they themselves define them. In this macro-area, doctors and nurses include a very multifaceted set of problems and themes that are not actually limited to the sole communication. Although it is undisputable that some communication problems also present an ethics connotation (patient-physician communication, for instance), and that it is not always straightforward to draw a line between purely ethical and purely communicative problems, our findings seem to show that the very first purpose of any clinical ethics support service should be that of helping professionals to learn what an ethical problem is, and to distinguish it from other kind of problems.

Notwithstanding these considerations, as already said, in analysing the texts of the interviews some clinical ethical issues have emerged, as shown in Table 2. Amongst them, in what follows we focus on three main topics, which were most recurrently reported by participants and considered as mostly urgent and relevant. In this regard, it is useful to emphasise that the ethically relevant issues emerged in our study, in particular end-of-life issues and issues concerning communication, are similar to those found in the literature [153]–[155]. This comparison validates on the one hand our results, on the other hand confirms that the observations we will make in the next paragraphs can easily be applied to other care contexts. However, resource allocation issues seem to be more context-specific, as they are not so clearly reflected in the literature: it would be useful to investigate whether this peculiarity is due to the oncological context of our study or to the Italian healthcare organisation and management.

4.2 Communication and informed consent process

As anticipated, the theme of communication was pointed out as one of the mostly relevant and problematic by the side of interviewees. Within this broad theme, however, it is necessary to make a distinction – which was not made by interviewees themselves – between issues related to the *content* and the *process* of communication.

Regarding the former, we may observe that operators struggle in communicating the deterioration of the medical condition to the patient and its potential implications [156]. The notice of a prognostic worsening is not always straightforward [157]. Such communication flaw may even lead to very serious consequences [158], such as in the case of patients transferred in hospice while being unaware of their real state medical condition. The lack of transparent information may also be detrimental to their right of self-determination, thus affecting patient's decision-making and his/her autonomy [159]. This reality, far from being a novelty in oncology literature, may be interpreted as a manifestation of physicians tendency to avoid talking about of death [160]–[163].

Among the problems related to the *process* of communication, participants reported two main concerns raised by their patients: first, the lack of empathy in the physician-patient interaction; second, the fact of being always exposed to different doctors during their therapeutic path. Although patients have shown to experience the latter as a lack of continuity of care, this is actually simply due to the rotation of the members of the medical team, as the idea is that the Institution itself – and not individual doctors – takes charge of patient's care. In any case, this gives us a lot of information about what is considered as relevant in the patient's view.

4.3 End-of-life

The second theme is the end of life. End of life is linked to any medical context, but, in a more robust manner, to the oncology context, inevitably affecting different aspects related to the treatment of cancer.

As already said, one of the issues raised by participants concerned the lack of advanced directives' implementation within the institution. Although in Italy there is a law that provides for this possibility (n.219 of December 22, 2017, "Norme in materia di consenso informato e di disposizioni anticipate di trattamento"), this instrument is not yet used as a practice at the IRCCS Istituto Nazionale Tumori, and, we hypothesize, also in many other hospitals. It may then happen that patients in an advanced stage of illness become unconscious or in need of resuscitation, but they have not signed any disposition nor left their will in oral form, thus leaving the intensive care or on call doctors with no guidance on their therapeutic preferences. Problems arise when

these patients have not had the opportunity to express their wishes, due to lack of adequate information about their prognosis, treatment options and/or their rights to refuse unwanted medical interventions and are forced to undergo possibly unwanted treatment. The occurrence of such problems should be limited, given that there is a tool that, although recent, could be applied in anticipation of a worsening clinical condition.

Linked to this issue is the matter of assisted suicide. Although it may not concern a large percentage of patients, this topic is particularly relevant today as a result of the sentence 242/19 of the Italian Constitutional Court [165]. In the absence of an *ad hoc* law on assisted suicide, the Constitutional Court decriminalizes the aid to suicide under certain conditions and entrusts Ethics Committees with the responsibility of protecting situations of particular vulnerability. Of course, the issue itself does not only concern Ethics Committees operating in oncological institutions, but all Italian Ethics Committees in general, which therefore find themselves having to decide on a matter that would formally fall within their competence but which they rarely deal with in daily practice. Furthermore, this issue is particularly relevant in oncology, since several studies have found a much higher suicide rate among cancer patients than the general population [166]–[168].

In conclusion, the issues related to therapies withdrawing or withholding in the terminal stages of the disease seem particularly relevant for stakeholders working with cancer pathologies [169]–[172]. In addition to the patient's clinical status, such as the severity of the physical condition and the prognosis, many different aspects are involved in this area, such as the religion and culture of the individual patient, but also the doctor's attitude towards end-of-life and the regulatory framework in which he or she operates [173]. Complex concepts of great ethical importance, such as respect for the patient's autonomy and values, quality of life, and the concept of proportionality of treatment, also play an important role. In conclusion, it is hard to imagine that doctors with little knowledge of ethics literature and a poor ability to analyse ethical problems would be comfortable dealing with such issues on their own.

4.4 Resource allocation

The last theme that we discuss is the allocation of (scarce medical) resources. This was an issue frequently reported by the sample of subjects' interviewed, while being also a very traditional and historical issue within bioethics literature: it was, in fact, a problem of allocation of scarce resources that contributed to the birth and diffusion of clinical ethical committees (see the case related to God's Committee and kidney patients: [3], [84], [174]. Deciding how to deliver a

limited resource represents a paradigmatic problem of multidisciplinary expertise, since it not only involves taking into account the clinical conditions of potential beneficiaries, but also many ethical, social, legal and economic factors.

If we consider the specific (national) context of this investigation, in Italy there are, to date, territorial differences in the distribution of certain healthcare resources; this may represent a source of potential discrimination between patients. Despite the national networks established over the decades, designed to guarantee the same quality of care to patients throughout the country (i.e. the Rare Cancer Network), there are still important differences in the availability of healthcare resources, such as differences in equipment or diagnostic tools quality available in the hospitals, in the access to experimental treatments and to specialized centres, since clinical research and excellence centres are not fairly distributed across the country. On top of these obstacles, there is the time to define the potential redeemability and price of drugs approved by the European Medicines Agency (EMA): the Italian Medicine Agency (AIFA) statistically takes on average up to one year (352 days) to complete the negotiation procedure for a drug [175]. Thus, there may be the case of a drug recognized as effective and hence purchasable, but not yet reimbursable by the Italian health system. Furthermore, once AIFA decides upon a drug redeemability, each Region can establish further restrictions on the reimbursement handbook, resulting in the same drug being reimbursable in one Region and not in another. Traveling for health reasons is of course possible, but it represents a cost and can therefore be a significant economic strain for some segments of the population [176].

4.5 Strategies to address clinical ethics issues

We found that the hospital lacks a shared strategy for the management of clinical ethics problems. When possible, they rely on multidisciplinary meetings, where different specialists discuss the most complex cases encountered in their practice [177]–[180]. For some interviewees, such multidisciplinary meetings also represent the opportunity to share their decisional responsibility, benefiting from other professionally expert perspectives.

Meetings among medical professionals seem to be the only available institutional strategy to deal with the most complex cases. However, it should be noted that such meetings do not really present an inclusive multidisciplinary approach. In fact, they generally involve only physicians, though from different medical areas: oncologists, surgeons, radiotherapists, radiologists, anatomopathologist. Other important categories of health professionals, such as nurses and psychologists, are mostly excluded or only occasionally consulted. Moreover, even including nurses and psychologists we would not comply with the requirement of real multidisciplinarity.

In the context of ethical committees, this implies, for instance, the involvement of professionals belonging to different fields, not exclusively medical [181].

From what emerged from the interviews, it seems that the management of the most ethically complex issues is left to the common sense and good will of single individuals, that would be the only guiding criteria in the absence of specific dedicated guidelines or other institutional support [135], [144]. This means that a key part of care, and one that is set to become increasingly important, is left to be handled by individual clinicians on the basis of their own personal characteristics or skills.

Although medical culture is moving increasingly in the direction of personalized medicine [130], [182]–[184], treatment paths seem to be still organized considering only the *clinical* needs of patients. Little attention is paid to support for health care professionals when dealing with clinical ethics cases [185].

As a result, health care professionals are left alone to decide on these issues and bear full responsibility for them. Thus, the proper management of ethically relevant issues is delegated to individual and subjective criteria of physicians who, according to our results, have inadequate training in ethics and are still mostly unready to deal with ethical issues.

As reported above, multidisciplinary confrontation is experienced as an aid in the management of the decision burden and therefore as a sharing of responsibility. However, this may not be enough, and the possibility to rely on an ethics support service seems desirable for all the participants in the study, with no exception.

However, they express different – and sometimes conflicting – wishes about the ideal functioning of such a service. If some interviewees imagine a service that acts primarily on need, and thus on individual cases, in a way comparable to what the literature refers to as the activity of clinical ethics consultation, the first step to raise awareness on ethical issues is training, in line with most interviewees' opinion.

In any case, from all participants interviewed emerges the desire, if not the need, to have a space dedicated to reflection, where healthcare professionals and operators can report the problems they face in clinical practice and have feedback and/or guidance from experts on the subject.

5. Conclusions

As previously observed, At the Fondazione IRCCS Istituto Nazionale Tumori there are currently no specific strategies designed by the Institute for the resolution of clinical ethical issues, nor

devoted discussion forums. As a result, the Institute's healthcare staff is mostly illiterate with respect to bioethics issues related to oncological contexts, and is left alone in dealing with them, with no other tool then their medical education and personal conscience.

However, the positive and encouraging feedback we received with respect to the purpose of our study clearly indicates a general increasing interest with respect to these issues. Likewise, the replies of the enrolled participants confirm the desire of healthcare professionals to have a benchmark for the management of clinical ethics issues and able to provide support when needed. If referred to the Italian context, data collected confirm the tendency, characterising the majority of ethics committees, to deal solely with clinical research [63], and it is reasonable that the situation within the Fondazione IRCCS Istituto Nazionale Tumori is comparable, in this respect, to that of any oncology institute/department operating in a facility with no clinical ethics support service. In the light of these results, it seems therefore fundamental to rethink ethics committees in light of a systematic recognition of the ethical aspect of care, in order to guarantee a re-humanization of medicine, as suggested by the National Italian Committee [10], and in line with the bioethical literature [186]–[188].

If we consider the specificity of the oncological context, an increased sensitivity for the ethical dimension of clinical care and its humanization becomes even more relevant. In particular some of our findings, in particular the issues related to the need of a clear and transparent communication, in particular with respect to the worsening of their prognosis, as well as end-of-life issues, are crucial for patients suffering from a life-threatening and high-impact disease such as cancer.

6. Limitations

Despite carefulness in the study design, this study presents the same shortcomings of other qualitative works.

First, the findings reported and discussed come from a limited number of participants.

Moreover, since participation in the study was on a voluntary basis and required a minimum time of 30 minutes, a selection bias in our sample cannot be excluded: it is likely that only or mainly professionals who are already sensitive to ethical-clinical issues have made themselves available. Moreover, the third author (PGC) of the paper, oncologist and director of his unit, also acts as secretary of the Research Ethics Committee. His involvement in this study may have encouraged fellow members of the research ethics committee to participate in the project.

Another possible limitation concerns the fact that some interviewees are members of the Institute's ethics committee. Their membership may impact both positively and negatively our results. Indeed, on the one hand, ethics committee's members have undeniable expertise in ethics and are used to reasoning over bioethical issues. At the same time, however, the issues they deal with concern mainly research, therefore finding it hard to go beyond issues and categories pertaining to research ethics.

Conclusions

Throughout this work, an attempt has been made to give a detailed picture of the current situation of some specific fundamental features characterizing Clinical Ethical Committees, namely their assessments and stakeholders' expectations with respect to their roles and functioning both on a national and international scale.

Chapter I was aimed at providing a descriptive introduction on the origin and birth of CECs. In particular, it reported that CECs were born in the context of great changes occurred in medicine and clinical practice and, consequently, observing that they were designed as a means of addressing unprecedented challenges, with the aim of providing ethical support in medical decision-making and safeguard patient's dignity and rights [3], [4].

Over the decades of CECs' activity, many have critically asked themselves whether their role within healthcare institutions really enabled those asking for their advice to achieve such goals and purposes [53], [100]. We attempted to answer this complex question both in Chapter II, by collecting data from studies that assessed their effectiveness, and, in Chapter III, on the basis of stakeholders' experiences, in particular healthcare professionals and, occasionally, patients or their families.

Although it is difficult to provide a systematic response to this question and despite the many limitations that CECs still present today [8], their impact in clinical practice seems to be overall positive [144]. Drawing from our twofold analysis, it seems that CEC's activities really do contribute to a humanization of care, at least in its simple meaning of promoting a reflection on care processes that holds together all the aspects and dimensions involved, with a particularly close eye on the ethical sphere.

The effort to adopt a therapeutic approach that considers the individual comprehensively targets, first and foremost, the improvement of the experience of care processes, both from the patient's and the clinician's point of view but is not limited to this. The results we have shown in Chapter II seem to confirm that the first objective is at least partially successful: not only do they indicate that health professionals are generally satisfied with the service offered by CECs, but also - more importantly - there is a widespread opinion that CECs have a positive impact on the quality of care. Furthermore, the results also show a link between the use of the services offered by a CEC and a decrease in moral distress among hospital staff members, although the data available is not sufficient to uniquely associate this effect with the impact of CECs.

The psychological impact that ethics support has on health professionals is still under-investigated. However, it represents an interesting topic that needs to be further investigated, especially considering the risk of burnout that health professionals run, especially in oncology departments [189]–[192].

As shown by the results of the qualitative study, at Fondazione IRCCS Istituto Nazionale Tumori, no institutional strategy for the resolution of clinical ethics problems has been already in place. Reflection on ethical issues does not find common ground in the hospital and is delegated to individual initiatives. The health professionals we interviewed tend to use the same strategies for the resolution of ethical problems that they use for complex clinical cases - the use of a multidisciplinary team on all – which, though its importance, does not appear enough for this purpose.

Despite the aforementioned threats, our findings seem to support some considerations. Firstly, it should be noted that the study was welcomed by the majority of the professionals we approached. The same occurred with the consequent proposal to introduce an ethics support service within the Institute. The positive – and in many cases encouraging – feedback we received indicates a widespread interest towards bioethics issues, although there is a general lack of training on the subject. In fact, from the answers collected, it emerged on the one hand the confirmation of the desire to have a support tool for the management of clinical ethics problems, and on the other hand the evidence that health care personnel are mostly untrained on bioethics issues that are relevant in an oncological context and do not know the literature on the subject. And this consideration is all the more significant considering that our sample may have been potentially affected by a selection bias. In fact, as it has been reported in the section about the limitation of the study in Chapter III, it is reasonable to think that the participants interviewed were, at least in part, professionals already interested in moral dilemmas affecting clinical practice, both for professional reasons (e.g., in the case of stakeholders working in very sensitive areas, such as rare cancers) and for personal inclination. However, the lack of adequate training affects also younger health professionals, despite having been trained as physicians in a time when all medical schools teach bioethics classes. In this regard, it might be considered that, although medical education has opened up towards clinical ethics, it is still apparently oriented to train practitioners as mere *technicians*, with little or no room left for reflection on the meaning and the ethics of medical practice.

The risk for medicine of falling into technicality, which also emerged from the qualitative study that we conducted, denounced by the same health professionals, seems to stem also from a lack

of spaces and occasions for a devoted meta-level reflection, and increases with the seriousness of the pathology and its impact on people's expectations and quality of life. Indeed, while the consideration of the patient first and foremost as a person, exceeding the sum of his/her symptoms, is always relevant and applied to any field of medicine, in the case of potentially life-threatening diseases, such as cancer, this becomes vital: in this context, it is ever more important to offer a course of treatment that is as respectful of the person's comprehensiveness as possible. This is confirmed by the experiences reported by the professionals we interviewed: according to the results of our study, carried out in an oncological context, the topics related to end-of-life and communication processes in the terminal phase of the illness are amongst the most frequently mentioned and emphasized. The clinical daily reality of an oncological hospital is intrinsically connected to the dimensions of prognosis worsening and end of life. Besides its specificity, the latter is also a concept that is somehow transversal to all the other issues we examined in Chapter III, insofar as it lies in the background of all themes identified, as a constant reference.

Drawing from our research findings and on the basis of the trajectory developed within this PhD project, briefly summarized in what afore, we would like to make some final considerations on the possible future directions of this project.

This PhD project originated from the desire of Prof. Paolo Giovanni Casali, head of Sarcoma Unit, of developing a new Clinical Ethics Committee within the Fondazione IRCCS Istituto Nazionale Tumori, to be added to the one already in place within the Institution (fully devoted to the discussion and review of scientific research protocol), and from the bioethics expertise of Doc. Virginia Sanchini, who played a fundamental role in identifying literature gaps and relevant clinical ethics issues on which to build this research project, worthy of national and international consideration.

In spite of the limitations highlighted in Chapter II, ethics support services in general and CECs in particular proved to play an essential role in the promotion of devoted reflection on the ethics of clinical practice. For a CEC to be effective, it seems crucial to begin with training function, in order to make health professionals aware of the ethical issues specific to their clinical context. Bioethics education can help them gain a more comprehensive view of the patient, based on a greater understanding of the non-clinical dimensions of the patient's therapeutic pathway, including the ethical and value-based perspective. The multidisciplinary approach plays a key role: as in the processes of decision-making over the most complex cases health professionals consider every medical aspect of the patient's pathology and therapy, through a multidisciplinary discussion with the relevant clinical, surgical and radiological specialists, in the same way, when

faced with a case raising ethical issues, it is important that the other constituent aspects of the case, whether ethical, legal, psychological or social, are also considered, by consulting professionals with expertise in these fields. To be truly ethical, the composition of a CEC must therefore take these aspects into account.

Rethinking care processes incorporating the ethical aspect of clinical practice, despite being important at all levels of care and in all clinical contexts, seems crucial in oncology. The results we have described in Chapter III were aimed at providing a picture of the specific situation of the Fondazione IRCCS Istituto Nazionale Tumori, but at least some of the considerations we have drawn from this study can be easily extended to other oncology institutes with similar characteristics, and that have the intention to develop a clinical ethics support service. The introduction of an ethical body, built on the basis of the specific needs of each individual context, can be a valid tool to achieve the aim of a more humanized health care, as suggested by the National Bioethics Committee's recommendations [61] and in line with the international trend [8], [193], [194].

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Appendix 1

1. In your activity as a doctor/nurse, did you face any clinical case with raising ethical issues? Which ones? Can you give me a few examples?
2. In your experience, which are the most common ethical issues, and which would require immediate action?
3. Do you feel that patients are experiencing the same issues? Or do you think that patients point out other issues?
4. What was the most difficult ethical experience you had to deal with, from an ethics perspective? Why? How did you manage it?
5. Did you need external support? Yes/No, from whom?
6. Do you occasionally discuss ethical issues with other staff members?
7. What kind of ethical support service do health professionals need?
8. In your opinion, does a doctor need the same kind of support as other health professionals? If yes, why? If not, why?
9. In your opinion, what kind of body would be best suited to provide ethics support in this Institute? A single expert/a committee?
10. What should this body deal with, in order of priority?