forensic sciences

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Systematic Review

Biobanks: Archives or Resources? Their Secondary Use for Forensic Purposes—A Systematic Review

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Abstract: Since the biobanks' inception in 1980, millions of human biological samples have been stored worldwide for medical research or treatment purposes. Today the secondary use of biobanks plays an increasingly important role in research projects because it allows large-scale research starting from professional collections of biospecimens and related clinical data. It would be limiting, in the "-omics" era, to not consider the enormous potential value to law enforcement of these biospecimens, where the availability of high-performance techniques makes it possible to obtain a large amount of data, even within a single session. Therefore, the quality of the sample, in addition to the associated clinical information, becomes of crucial importance to derive scientifically valid information, including for forensic research purposes. Proposing the introduction of the concept of "solidarity", traditionally applied only to medical and research biobanks, led to public commitment to forensic medicine. Granting the forensic researcher this possibility certainly raises some questions regarding regulatory and ethical aspects of consent, privacy, confidentiality, transparency, and participant/donor trust. Since the debate has not stopped since the origin of biobanks, this review aims to explore the state of the art relating to the use of human biological material in medical biobanks for biomedical and forensic research.

Keywords: biobanks; secondary use; forensic research

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1. Introduction

In 2009 the famous USA magazine Time wrote about biobanks, as "one of the ten best ideas that can change the world" [1,2]. In fact, biobanks represent extraordinary tools that could be defined as long-term storehouses of thoroughly annotated biological materials [2,3] or, even better, organized biological sample collections with or without accompanying genetic or clinical information [4,5].

After fourteen years, the statement reported in the Time Journal is more truthful than ever. Nowadays, biobanks can considered a scientific infrastructure, established according to the logic and practices of scientific research by answering to scientific purposes in specific projects [6]. The development of biomedical research depends on the use of biobanks as fundamental research tools and, basically, by their appropriate management [7]. The need for well-annotated, carefully kept specimens has increased because of recent developments in molecular biology and genetics technologies. To testify to this technological need, in the last decade, biobanks have been established on several continents in response to that demand and their number is increasing [8].

The history of biobanks began much earlier than their importance being highlighted by the Times and can be divided into three phases: from 1980 to 1990, when attention was paid to the quantity of the samples; from 1990 to 2000, when the emphasis shifted to the quality

of the samples and their detailed description; and, finally, the era of modern biobanks, where the quantity, quality, and characteristics of the samples are central, together with the direct involvement of interested parties [2].

Biobanks can be both public and private; can be classified as cross-sectional, longitudinal, large-scale, disease-specific, population-based, or a combination of these; and offer platforms for hitherto unheard-of global partnerships [9]. Biobanks can be defined as healthcare biobanks, if they have research, therapeutic, or diagnostic purposes, or biobanks established for reasons of public security, better defined as forensic databases [3,10]. Health biobanks, one of the most promising tools for improving public health, can increase the understanding of diseases, the development of therapies and treatments for common multifactorial diseases, and the reasons for different responses to drugs by different patient groups [11], increasingly helping the development of personalized medicine as part of the protection of public and individual health. In fact, if the primary objective of personalized medicine is to identify the most effective therapies for the individual patient [12], today, its development is also possible thanks to biomedical research, which uses biobanks as a huge resource of genomic data that are linked to individual health and personal data (i.e., lifestyle, eating habits, physical activity, income, etc.) [12,13].

The open and dynamic nature of biobanks has significant ethical, legal, and social implications for individual and group autonomy regarding informed consent, privacy, confidentiality, secondary use of samples and data over time, benefits of the results, data, and advantages of sharing with different communities. Furthermore, a complication arises due to the expansion of international relations and divergent national perspectives as the scope and areas of concern vary depending on the legal, moral, and social systems of different nations, whether rich or developing [9,14]. Surely, a matter of great interest is represented by the secondary use of biological samples, which allows individuals to exploit already accessible resources and reduces the overall research costs [15–18]. In general, secondary use refers to the use of health and research data for purposes other than those originally established. Therefore, any use of samples or data for research purposes that goes beyond the parameters of the consent given should be considered a secondary use. Most regulations require the researcher to recontact research participants to obtain a new agreement when such secondary research is governed by a relatively complex legal and ethical framework in order to respect the privacy, confidentiality, and autonomy of the participants [7,19].

Moreover, it is well known, in anticipation of being a guarantee for the provision of data, modern biobanks function as complex infrastructures in which doctors, biologists, nurses, technicians, and bioethicists work together with the aim of ensuring the right to use human biological materials [20].

Considering what has been said, the establishment of a biobank certainly represents a fundamental pillar on which to build an effective, efficient, and modern research system. In fact, sporadic collections of waste/residual material from biological samples taken for diagnostic and/or therapeutic purposes, over time, have slowly begun to transform into biobanks through a process of harmonization and common governance. The universe of biobanks itself (including research biobanks) has evolved over the last twenty years through progress based on governance, harmonization, the standardization of sample collection and preservation, and above all through social involvement [21]. The end result of this evolution is the role of biobanks as a valuable source of high-quality human samples and extracted data [3,22,23], which can vary based on sample size, study focus, type of biological samples, the collecting method, and data storage and processing procedures [7]. It is also important to remember that the data acquired includes information on the health, environment, and lifestyle of population groups often monitored for long or very long periods of time [9].

Biobanking is an expensive endeavor that requires dedicated staff to acquire patient consent and collect samples so its outcomes depend on the amount of funding available

since then. The costs of establishing and maintaining a biobank or biobanking system are often unclear at the outset of a project [8].

The acquisition and storage of human biological material for medical studies always require a purpose adequately determined on an individual basis from the perspective of a potential donor. It is therefore important to specify, as precisely as possible, the reason for the collection, storage, and intended use of the data. The use of human biological material and associated data, including cross-border exchange, must be widely enabled by biobanks to address future medical research goals and public health challenges [24].

Alongside these health biobanks, we find those designed for forensic purposes, the "Forensic DNA Databases" in which the rights of the person are intertwined with the interests of justice. Forensic databases are genetic databases used by police forces as a valid tool for the prevention and resolution of national and international crimes through the identification of the suspects and the comparison between these profiles and those derived from crime scene samples. The development of these banks has certainly been aided by the growing number of terrorist incidents [3,10,11,25].

Next to these are the population databases created specifically for forensic purposes, such as the reference database of the STR haplotype of the Y chromosome (YHRD), the EDNAP Forensic mtDNA Population Database (EMPOP), and the STRs for Identity ENFSI Reference Database (STRidER), useful for defining the informativity of a genetic profile typed in a case of forensic interest. Although the potential of biobanks dedicated to forensic research can be truly relevant to respond to issues of medical legal interest, such as the study of injury models, the estimation of post-mortem interval, the development of new analysis methods, and instrumental techniques in the field of forensic genetics and toxicology, the infrastructures dedicated or open to this type of study are still poorly represented [23].

The question arises of whether biobanking, which allows the long-term preservation of biological material, including genetic material, can be used for forensic research purposes, not necessarily conceived at the time of sample donation and consent [26,27]. Our narrative review of the literature tries to answer this question by assessing potential, risks, and ethical issues.

2. Materials and Methods

This narrative review was prepared according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [16].

Articles reported in this review have been identified and selected through the single or combined use of the following keywords: ("biobank" OR "biospeciment" OR "stored biological sample" OR "residual material") AND ("forensic research" OR "forensic use" OR "secondary use" OR "research use") from the Pubmed and Scopus databases.

Two reviewers (G.F. and G.S.) individually carried out the initial research of the papers and discussed the results obtained. By using the search protocol described above, the search was performed by analyzing and synthesizing the information collected and selecting the articles showing greater relevance, specificity, and scientific evidence. However, in the case of disagreements, research supervisor consensus (S.G.) was sought. The researchers' analysis continued in the following order: titles were screened first and, then, abstracts and full papers. The full text of all papers included on the basis of title and abstract were then evaluated.

The selection procedure has provided the inclusion of articles published in the last 23 years, from 2000 to today. Both articles and reviews have been considered; they are written in English or Italian and with the free full text available. A total of 294 works were identified on the PubMed and Scopus databases. Duplicates were removed and a total of 189 articles were screened first by title. Then, a total of 104 works were screened by abstract; after that, 63 articles were investigated in their full-text form for eligibility. The number of articles excluded or included was reported in a PRISMA flowchart (Figure 1).

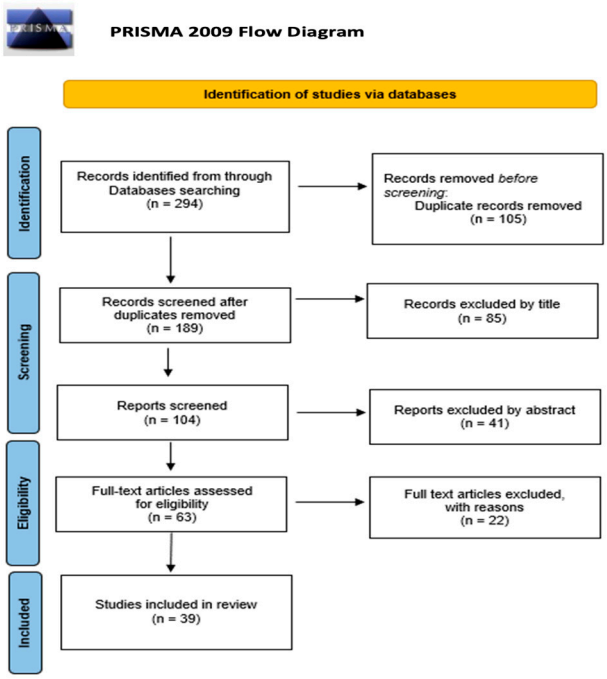

Figure 1. Flow chart of the selection process for the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2009.

3. Results

In order to make the results obtained in this review easier to understand for the reader, they have been summarized in the following categories: (a) Forensic Biobanks; (b) Potential Use of Biobanks for Forensic and Research Purposes; (c) Risks and Problems Related to Forensic Biobanks. The risks and limitations related to the use of biobanks for forensic purposes are summarized in Table 1.

3.1. Forensic Biobanks

Biobanks have been described in a plethora of ways and this represents a serious difficulty in defining the inclusion and exclusion parameters for the texts to be analyzed. Therefore, we choose to use, for this review, the concept of forensic biobanks referring to forensic DNA databases and genetic databases used in the criminal justice system [11]. This definition is quite different from the idea of medical biobanks, except for forensic DNA databases where biological samples, along with personal information, are stored together with DNA profiles. In these circumstances, forensic DNA databases are comparable to the common concept of biobanks [11].

Before addressing the topic of forensic biobanks, it is important to distinguish the different existing types on the basis of sample gathering and, partly related to this, the kind of control donors have over their samples. Tamburrini suggests at least three different kinds of forensic biobanks could be outlined [10]:

1. Forensic databases, totally separated from medical biobanks, where the biological material is gathered from suspects, convicted felons, victims, and other persons involved in the criminal investigation [10,11]. In the work of Machado and Silva in 2015, European countries are distinguished based on the criteria of inclusion of profiles in databases. The authors indicate countries with legislation having expansive effects (Austria, Denmark, Estonia, Finland, Latvia, Lithuania, Scotland, Slovakia, and England and Wales) and countries with legislation having restrictive effects (Belgium, France, Germany, Hungary, Ireland, Italy, Luxemburg, The Netherlands, Poland, Portugal, Romania, Spain, and Sweden). In the first group, the inclusion criteria allow samples to be taken from individuals suspected of any crime. In the second group,

however, the condition generally imposed for the inclusion of profiles in databases is that an individual is suspected or convicted of a crime that involves a prison sentence or the crimes committed are considered serious [11];

2. Forensic databases created by enlarging the area of application of existing medical biobanks. In this case, the biobank population is represented by all those who voluntarily agree to contribute to a sample [10];
3. Forensic databases, as (2) previously stated, but containing also all the genetic information from newborns collected at birth for medical research purposes, with or without any explicit statement precluding forensic uses. Also, in this case, sample collection is voluntary, subject to the consent of parents or legal representatives [10].

Bexeliu et al., in 2007, recalled that, in the early 1990s, several states introduced forensic biobanks containing samples from crime scenes and suspects. The most famous of these biobanks was the Combined DNA Index System (CODIS), established in 1994, which, after 15 years, included more than one million samples of criminal profiles from all 50 states of the United States, the US Army, and the FBI. Following the American example, since the 2000s, most European countries have introduced national bio-forensic banks, including Sweden, Denmark, Finland, and Norway [28]. The authors report that the United Kingdom had a national biobank consisting of over 2.8 million samples collected by suspected criminals, representing the largest biobank in the world in 2007 [28,29].

In Italy, Law n.85/2009 regulates the establishment of the forensic DNA database and introduces articles amending the Criminal Procedure Code. The law, through its 33 articles, regulates the collection of the DNA profiles of criminals, data on biological evidence found at crime scenes, missing persons and their relatives, unidentified bodies, and comparison of DNA profiles for personal identification purposes. Furthermore, according to Law n.85, DNA samples are stored for 20 years and genetic data for 40 years. In 2010, Tozzo et al. [4] underlined that thanks to the amendments to the Criminal Procedure Code, during routine police investigations, samples can be acquired by the judicial authority without the need for consent, where the interests of justice prevail over the individual right to provide informed consent [4].

3.2. Potential Use of Biobanks for Forensic and Research Purposes

DNA profiles can be obtained from samples stored in biobanks and, in turn, can be used in criminal investigations by comparing them with DNA profiles obtained from a crime scene [30]. In the article published in 2020 by de Groot et al. [31], the authors point out that over the years, the forensic use of medical biobanks has occurred several times, especially in high-profile cases. From the most famous arrest in 2018, after 40 years of the "Golden State Killer" [31]**,** to other cases cited by Bexelius et al. [29]. For example, authors reported how in 2003, the identity of the killer of Swedish Foreign Minister Anna Lindh was ascertained thanks to a medical biobank containing biological samples from all newborns dating back to 1975. It is also true that after this episode, and despite the positive conclusion, the Swedish law prohibited such forensic use of medical biobanks, with the support of national public opinion [29]. On the other hand, Tamburrini [10] poses the question in terms of choice between the promise of a very effective instrument to fight criminality and the threat of granting access to confidential genetic information. Although, in particular situations, the decision to sacrifice confidentiality for the resolution of a crime should not be considered, superficially, a violation of privacy because, as the author claims, "we would act to protect the physical and psychological integrity of actual and future victims" [10,31,32].

We must also consider that medical biobanks are not set up to be fully scanned to compare a DNA profile from a crime scene (unlike forensic genetic databases); therefore, the police will already have a suspect. Additionally, de Groot et al. [31] point out that, when the suspect is known, there are often multiple alternatives for obtaining a DNA sample (toothbrush, a discarded coffee cup, or through familial testing). In contrast, Hartman et al. [33] reported in an article published in 2011 that Guthrie cards and medical specimens (tissue

biopsies) are a good source of direct reference specimens; meanwhile, objects such as toothbrushes, razors, and hair brushes can also be a source of contamination as they are potentially shared by more than one individual, leading to misidentifications [33].

When no information about the identity of a suspect is available, the authors explore the potential secondary role of biobanks in other practical forensic applications. In the scientific literature, it is reported that biological samples collected for scientific research, medical diagnostics and screening, and other non-physical purposes are often used, in different countries, for a variety of forensic purposes, from criminal identification to the identification of disaster victims or family relationship analysis [30]. Examples of this practice are those reported by Hartman et al. [33] and Bexelius et al. [29]. In the first case, following the 2009 Victorian Bushfires Disaster, Guthrie cards, collected and stored in Australia from the mid-1970s onwards as part of the national PKU screening programme, provided an excellent source of DNA useful in the process of disaster victim identification (DVI) through direct comparison [33]. Even in 2004, following the catastrophic tsunami, medical samples had to be used to identify the victims. In this context, Bexelius points out that the Swedish Parliament granted a special permit for the first time with general media support [28,29].

Back in 2007, Levitt [32] proposed an initiative to exchange information between forensic databases across Europe with the aim of fighting crime and terrorism. The author also recognized the possibility of a stealth mission of the forensic database, a database originally intended to help capture serious offenders that becomes usable for different purposes, including search and family matching [32]. In the forensic field, when it comes to research, the issue still appears controversial. Although, the literature has extensively discussed the potential significance of the proposed forensic database mission. More recently, since biobanks dedicated to research are still limited to collections established in different local facilities, Tozzo et al. highlight the urgent need to develop an international network among forensic institutes [23,34]. The proposal of Tozzo et al. [23] considers the expansion of biobanks, physically located in different places but connected in a single network, thus improving research in the forensic field: from forensic toxicology to pathology and forensic genetics and to all those areas in which it is necessary to obtain results that are reproducible [23].

Wiskott et al. [34] report that in 2022 in Switzerland, at the University Center of Legal Medicine (Lausanne–Geneva), many biological samples are routinely collected during autopsies. Most of these are used in forensic investigations (histopathology, toxicology, microbiology, clinical chemistry, and genetics) in the medical–legal context and destroyed after three years. The authors underline the complex and confused ethical and legal framework that prevents the use of those samples for research purposes. As already widely discussed, medical samples can be a resource for forensic research, as well as forensic samples being valuable for research, in clinical studies (where they may be used as a negative control in an oncologic cohort, for example), epidemiologic studies, and public health studies. These kinds of samples are a precious resource because they come partly from young and healthy people, poorly represented in institutional biobanks; often, it is possible to collect valuable tissues and organs that are not easily available from healthy patients, such as the brain or the heart. Given the precious resource that these samples represent for forensic research, Wiskott and colleagues decided, at the beginning of 2019, to establish a research biobank [34]. In this Forensic Pathology Biobank are samples collected during all the medico-legal autopsies that are performed every year in the center (tissues, biological fluids as well as histological samples included in paraffin, slides, post-mortem images, and ante-mortem medical samples). After 3 years from collection, samples and clinical data are anonymized and made available to researchers, thus opening up the door to a wide range of new possibilities in forensic and clinical research as well as in the genomics, proteomics, or metabolomics fields [34].

Lately, van Deventer has taken into account forensic molecular pathology, not only as a useful tool to define the causes and manner of death but rather as an emerging field

with significant clinical impact on the diagnosis of both preventable and hereditary causes of death [35].

Over the years, different population-based biobanks have also been established. The Balanovska research group [2] believes that these possess a more lasting value, storing information on genetic diversity in the era of globalism, when the gene pools of many small populations disappear or they lose their ancient gene pool. Moreover, because allelic frequencies vary within different populations, these biobanks could play an increasing role in identifying ethnic origin from DNA, providing fundamental investigative information to forensic experts under the condition that the reference databases are as representative as possible [2].

Also, the authors of this review explore, with their works, potential applications in the forensic research of residual materials stored in biobanks. Some applications may concern the study of injury patterns; postmortem interval estimation; new methodologies for DNA analysis, ranging from the introduction of new markers to appearance and ancestry inference and microbiome analysis; and even new instrumental and analysis techniques in the forensic genetics fields [23].

Since human identification is, by nature, comparative, the application of these new methodologies could be especially useful in investigative cases where there are no potential suspects and there is no correspondence between the DNA sample collected and the genetic profiles entered in the criminal database. The recent technological advance has included the analysis of the microbiome for identification purposes among the new investigative tools available to the researcher [13,36,37]. This is motivated by the fact that, through microbiome prediction starting from biological samples found at the crime scene, probabilistic information may be acquired as to the same characteristics of the donor, such as past exposures; visits to other countries; predisposition to certain medical conditions; sexual practices; diet; and consumption of tobacco, alcohol, and other drugs [13,38]. The combination of these elements, therefore, narrows the circle of possible perpetrators and promotes investigations, integrating information into the other evidence.

About this, Caenazzo and Tozzo [13] stressed the need to create population microbiome biobanks specifically dedicated to forensic human identification. Since the establishment and development of microbiome research biobanks for clinical applications are already very structured, the expansion of studies based on their applicability for forensic purposes is still in its infancy [13].

3.3. Risks and Problems Related to Forensic Biobanks

In order to summarize the risks and problems related to forensic biobanks, we decided to enrich the categorization proposed by Tamburrini [10] in Table 1. The main objections described by Tamburrini concern: (a) the discrimination against certain social groups, in particular, when the data are kept even after the suspect has been destitute or acquitted in trial; (b) the abuse of control and violation of privacy; (c) the post-mortem use of biomaterial; and (d) the informed consent open to the biomaterials' secondary uses. Finally, the author argued that all these problematic aspects can be conducive to the discredit of genetic biobanks in general, thus weakening people's willingness to contribute their samples to the repositories [10,31].

Table 1. Risks and limitations of biobank use for forensic purposes.

Risks and Problems Related to Forensic Biobanks	
Discrimination against certain social groups	
Tozzo and Caenazzo, 2020 [6] Dhai and Mahomed, 2013 [9] Tamburrini, 2011 [10] Machado and Silva, 2015 [11] Bak et al., 2020 [39] Bathe and McGuire, 2009 [40] Cambon-Thomsen et al., 2007 [41]	Social risks include stigmatization and discrimination. Data might be associated with individual or group characteristics, criminal behavior, or medical conditions. Stored information turns into a registry of a particular social group since criminals often come from certain social categories. After all, when in a biobank, the percentage of patients is over-represented compared to that of healthy individuals, the access of the police to it can be targeted at patients.

Table 1. *Cont.*

Risks and Problems Related to Forensic Biobanks	
Abuse of control and violation of privacy	
Paris, 2022 [3] Tozzo and Caenazzo, 2020 [6] Wiskott et al., 2022 [34] Norlin et al., 2012 [42] Tamburrini, 2011 [10] Machado and Silva, 2015 [11] Caenazzo and Tozzo, 2021 [13] Dranseika et al., 2016 [30] De Groot et al., 2021 [31] Bathe and McGuire, 2009 [40] Cambon-Thomsen et al., 2007 [41] Virani and Longstaff, 2015 [43] Kurihara et al., 2020 [44]	Nowadays, the concept of confidentiality extends to data privacy, data sharing and secondary use of samples, informed consent, sample ownership, and the benefit of sharing. This includes both the physical and psychological integrity of a person. Anonymization is proposed as a solution to privacy issues; although, this is never entirely possible. Plus, anonymization techniques significantly hinder the progress of scientific research.
Post-mortem use of biomaterial	
Moraia et al., 2014 [7] Dhai and Mahomed, 2013 [9] Tassé, 2011 [19] Wiskott et al., 2022 [34] De Groot et al., 2021 [31] Bak et al., 2020 [39] Hanold et al., 2017 [45] Tassé et al., 2010 [46]	The ethical question that governs biomedical research is addressed, also, when it involves participants' deaths. Even if samples and data have been collected prior to the death of the participant with valid consent, this raises ethical and legal issues since genetic research has an impact, also, on family members. The authors questioned whether the post-mortem use and sharing of identifiable research data were ethically permissible at all. When consent from a deceased persons is missing, guidelines are not always clear for the research activity and do not consider the impact of a secondary use on the biological family of the deceased.
Informed consent open to biomaterials' secondary uses	
Paris, 2022 [3] Tozzo et al., 2010 [4] Moraia et al., 2014 [7] Dhaia and Mohamed, 2013 [9] Tassé, 2010 [19] Jahns et al., 2019 [24] Machado and Silva, 2015 [11] De Groot et al., 2021 [31] Cambon-Thomsen et al., 2007 [41] Virani et al., 2015 [43] Kurihara et al., 2020 [44] Hanold et al., 2017 [45] Tassé et al., 2010 [46] Warner et al., 2018 [47] Caufield et al., Mungwira et al., 2015 [48] Chen et al., 2005 [49] Kondylakis et al., 2017 [50] Gefenas et al., 2022 [51] Moodley et al., 2014 [52] Staunton et al., 2013 [53]	Informed consent allows individuals to exercise their fundamental right to decide whether and how their body, body parts, and associated data will be used in research. Analyzing the various types of informed consent available to date, it is evident that well-drafted consent must consider: (a) the possibility of contacting the child upon reaching a legal mutual; (b) the death of the donor; and (c) the secondary use of samples and data. Since a study could be carried out several years after sample collection and it might use research topics and techniques that were unimaginable at the time, it should be determined in what way these can be considered in the consent given at the time of the first data collection. Also, restrictions to certain secondary uses should be shown and permitted to be chosen by the person involved.

3.3.1. Discrimination against Certain Social Groups

Some authors recognize that forensic databases can be socially discriminatory, claiming they risk being influenced by those who are regularly arrested, affecting investigators accordingly [6,9–11,39–41]. Since criminals often come from certain social categories, almost being stigmatized, the stored data turn into a registry of that particular social group beyond comparison. This discriminatory effect is particularly annoying when the collected data are not destroyed once the suspect is dismissed from the investigation or even acquitted in court. However, Tamburrini places particular emphasis on forensic databases aimed at solving and preventing criminality and here is how: once again, the question manifests as a difficult trade-off [10].

In terms of the forensic use of biobanks, De Groot et al. [31] argue that the issue of discrimination also concerns the fact that, in many medical biobanks, the percentage of

patients is over-represented compared to that of healthy individuals. Therefore, police access to these biobanks will be disproportionately targeted at patients [31].

Despite the complicated legal and ethical framework, Machado and Silva [11] admit the use of biological samples stored in criminal DNA databases in scientific and medical research. Undeniably, when it comes to DNA databases, genetic discrimination is much feared. By the way, social risks include stigmatization and discrimination, involving both research participants and non-participants [9]. Machado and Silva [11] report the case of genetic databases in which the data might be associated with individual or group characteristics, criminal behavior, or medical conditions; this may be seen as a restriction of individual privacy and lead to discrimination and stigmatization [11,41]. Dhai and Mahomed [9], more specifically, remember that stigma and discrimination may arise when research results indicate that members of some subpopulations are more likely to have a genotype that confers an increased risk of disease or other traits. Bathe and McGuire [40] discuss how much this risk can extended in different areas: discrimination from governments based on ethnicity or susceptibility to mental illness, discrimination in health coverage by insurance companies based on disease susceptibility, or discrimination by employers because of behavioral predispositions [9,40].

Considering that these risks must be recognized and taking measures to avoid or minimize their occurrence, Cambon-Thomsen et al. [41] do not neglect the importance of informing participants. However, the authors believe that informing participants of the risks of stigmatization by providing too much detail on this remote possibility could have a negative impact on recruitment, alarming them and leading them to question the legitimacy and true nature of the proposed research. Truthfully, discriminatory events cannot be easily foreseen and the lack of transparency leads to imprecision and may even generate skepticism [6,41]. De Groot et al., in 2020 [31], argued that public confidence in genetic research depends on research participants and patients who know that third-party access to their sensitive information is strictly prohibited. That is why the forensic use of biobanks could negatively affect confidence in health professionals and medical institutions but also in medical research in general [31].

As the problem exists and cannot be ignored, from a more pragmatic perspective, several works propose possible remedies. Bathe and McGuire, as other authors, have sustained genetic anti-discrimination laws instead of genetic privacy laws. These laws would protect against the misuse of genetic information to avoid potential harm [40]. The law governs that genetic information cannot be used for decisions on health coverage, rates, or pre-existing circumstances and it prohibits most employers from using it in hiring and/or dismissal decisions. Despite this, Bathe et al. [40], also mention different situations that are potentially stigmatizing, such as research on small defined populations with a propensity to certain disease states. This research requires special consideration because of the magnitude of the potential risks on employment, insurance, health care, or social interactions [40].

As we have seen before, stigmatization involves not only research but, above all, DNA forensic databases. In this regard, if we want to avoid the risk of discrimination, the solution proposed by Tamburrini in 2011 [10] is to allow the forensic uses of medical biobanks, instead of creating special forensic databases. In order to easily neutralize discrimination, the practice should be extended to the entire population. Tamburrini claims that if everyone is registered, there is no discrimination. Therefore, the most promising alternative is the collection of biological samples from all newborns, regardless of social and economic status [10].

3.3.2. Abuse of Control and Violation of Privacy

Despite demonstrated public support for biobanks, some within the academic, governmental, and public realms have also expressed cautions associated with the ethical, legal, and social implications of these [6,42,44]. Perhaps the most important issue that should be taken into account when discussing biobanks and, specifically, forensic use of biobanks, is

confidentiality [13,30,31]. These concerns include data privacy, from the return of results to participants and accidental results (IFs); data sharing and secondary use of samples; informed consent; sample ownership; and the benefit of sharing [43].

Additionally, de Groot et al. [31], following the deontological perspective, represent confidentiality as a duty, the maintenance of which goes beyond the consequences. As a deontological argument, the authors bring respect for the patient's autonomy, privacy, or a promise of maintaining trust [31]. So much so that, as reported by Dranseika et al. [30], if donors are informed about potential forensic use, they may be reluctant to donate their materials to research; however, if they are not informed about this, they cannot decide whether research participation is in their best interest and whether the resulting privacy and confidentiality risks are acceptable to them [30]. Tamburrini motivates the importance of privacy as the protection of what people consider important in life, "as the intimate sphere or conditions for autonomous judgment" [10]. Therefore, concepts such as privacy and individual autonomy are closely interconnected and understood as the right of individuals to be respected as agents fully able to make and implement their own decisions [10].

Since these are forensic DNA databases, the possible violation of privacy becomes a crucial issue. In the ethical debate on forensic DNA databases, Machado and Silva [11] consider ethical challenges as potential threats to a series of civil rights, such as the right to privacy, freedom, and moral and physical integrity; the dignity of persons; and the presumption of innocence. However, the authors also place privacy at the center of the debate regarding the preservation of samples and profiles of individuals arrested but then acquitted, representing it as a violation of the right to privacy under the European Convention on Human Rights [3,10,11].

In the European Convention on Human Rights [54], the European Court ruled that the concept of private life also includes the physical and psychological integrity of a person. The guarantee offered by art.8 [54] aims to ensure privacy both in a wider sense (such as the protection of one's physical and psychological integrity) and in a tighter one (such as the protection of confidential information) [10].

Ethical standards that regulate biobanking are promulgated by two declarations of the World Medical Association (WMA). The Declaration of Helsinki (1964) [16] lays down ethical principles for medical research involving human subjects, including the importance of protecting the dignity, autonomy, and privacy of research subjects. In concordance with the Declaration of Helsinki, in 2016, the declaration of Taipei [17] provided ethical considerations regarding health databases and biobanks (specifically collection, storage, and use of biological materials, as well as identifiable data) that should contribute to the benefit of society, in particular, public health objectives [34,44].

In 2009, anonymization, which is the removal of all personally identifiable information, was proposed as a solution to privacy issues. Although this technique pursues the laudable aim of preventing abusive and discriminatory use of genetic data, the scientific community tends to underline that complete anonymization is never entirely possible since genetic data is one of the most reliable means of personal identification [3,40]. Bathe and McGuire [40] describe this process as an imperfect solution, a double-edged sword. On one hand, it is able to solve privacy problems; however, on the other hand, it can put at risk the scientific value of the biobank since the data becomes more difficult to control and validate. More recently, in 2022, Paris [3] expanded this concept by stating that anonymization techniques significantly hinder the progress of scientific research. They, in fact, do not allow those conducting the study to either contact the patient during the clinical course, update personal and health information, or acquire new ones [3]. Not to mention that anonymization precludes any influence of donors on the use of their samples [40]. Cambon-Thomsen also questioned the anonymization of samples as a useful solution to ethical and legal problems by reviewing double coding as the preferred option [41].

As specified by Jahns et al. [24], particularly in the case of genetic information, complete anonymization is inherently impossible to attain since it typically entails removing the link between a pseudonym and the donor's or patient's personally identifying information.

So, when a donor or patient wants their biological material to be destroyed along with all associated data, the anonymization process must wait until the biological material has been destroyed. However, data cannot be taken out of analyses of previously finished studies and/or published study findings [24].

With the goal to minimize this risk, in 2012, the European Commission published a document [55] describing the primary role of research biobanks, specifying the need to apply coding or anonymization to ensure donor privacy together with a new labeling process for specific conditions where clinically relevant information becomes known and can be provided to the patient [3]. In this respect, adequate governance of the biobank and oversight of research projects are fundamental concepts since it is also apparent that the violation of privacy cannot be neglected, nor does it present a solution. The authors agree that the adequate informed consent of the participants may represent a minimization of risk [14].

3.3.3. Post-Mortem Use of Biomaterial

In the examined articles, the ethical question that governs biomedical research is not only addressed when it involves living participants but also following their death. Additionally, de Groot et al. [31] also report situations where, during criminal proceedings, there is simply no alternative other than obtaining the medical tissue sample to provide unequivocal evidence. Nor is it an example when one assumes that the suspected deceased has been cremated (and, thus, exhuming a body is not possible) and there is no alternative to obtaining the suspect's DNA other than accessing his tissue samples stored in the hospital.

Tassé [19], Dhai, and Mahomed [9] stated that, given the recent growth in longitudinal population studies and long-term biobanks, the death of research participants is increasingly relevant. Recalling further is conducted not to underestimate this implication since genetic research can not only impact the participants but also their biological family members [19,45]. Samples and data that have been collected prior to the death of the participant with valid consent are also raising ethical and legal issues [19]. In any case, it is reasonable what Bak et al. [39] said about the fact that, even if consent has been asked during the participant's lifetime, this cannot be renewed for secondary uses of data after death. Most of the current research regulations have been constructed independently of any property rights of their own fabric. Although, in general, patients can refuse or consent to the donation of tissue, Cambon-Thomsen et al. [41] claim that, if the property right model were extended to material, cadaveric tissue could become the property of heirs [41]. In light of these issues, the authors questioned whether post-mortem use and sharing of identifiable research data was ethically permissible at all.

Even more confusing is the use of biological material and associated data after the death of the donor. Tassé [19], underline the importance of obtaining free and informed permission before conducting research, taking up what is contained in the Universal Declaration on the Genome and Human Rights [56]. However, the statement stipulates that if the participant is unable to give permission, it must be acquired in accordance with legal requirements and with consideration for the individual's best interests [19,56]. Hanold et al. [45] suggest that the information also contains a reference to what will happen to the biomaterial and data after the donor's death so that the donor can adequately consider the issue of post-mortem use at the outset [45].

On the other hand, as stated by Moraia et al. [7], when the consent does not foresee secondary research uses, the secondary use of already collected data may affect the autonomy and privacy of the research participant [7]. When consent to secondary use has not been required, the researchers should not be authorized, even if, on the other hand, there was no apparent possibility of harm to the dead participant [39]. Especially if we talk about secondary use of samples stored in biobanks, Wiskott et al. [34] highlight that, in the absence of the consent of deceased persons, guidelines are not always clear for the research activity and, above all, do not consider the impact of such secondary use on the biological family of the deceased [7,34].

Speaking of the return of the results, Bak et al., in 2020 [39], reported the opinion of Knoppers et al., according to which there is an ethical duty for researchers to return such results ("duty to warn") to participants, leaving, however, room for the right not to know. Therefore, in the context of the post-mortem disclosure of genetic information to relatives, several authors have advocated a passive disclosure policy where findings are returned only upon the request of the family, allowing active disclosure only in the case of high pathogenicity [39].

The authors analyze their consent preferences in a US study from the perspective of research participants and their families. They noted that research participants' reasons to object to the sharing of findings in the event of their death included: having no relatives or not a good relationship with them, privacy concerns, and being uncomfortable burdening family members with potentially distressing information [39]. We refuse to neglecting the points made by Hanold et al. [45]: sometimes, the reputation of a deceased family member might affect the living person's private life and identity. Regarding the rest, relatives' reasons for preferring to receive genetic findings were found to be a sense of duty towards their deceased family member as well as their own interest in genetic knowledge [39].

Regarding the use of autopsy samples, the ethical–legislative issue is decidedly confusing. The importance of obtaining free and informed consent is enshrined and regulated by the Universal Declaration, even when the participant is unable to consent. Although this section focuses on research in the case of minors or incompetent adults, it is drafted in a sufficiently general manner to include research with deceased individuals [19]. In the review of international guidelines by Tassé [19], published in 2011, only four international guidelines and two biobanks discussed the fate of samples and data after death. Specifically, in the World Health Report (WHO) report of 2003 [57], it was mentioned that "the death of an individual who has provided a genetic sample or genetic information does not represent the end of the ethical responsibilities that are owed in respect of the samples or information" [19,39].

In the work of Tassé et al. [46], only 5% of studies explicitly abandoned consent for the use of data and samples after the death or incapacity of the research participant. In the remaining 49 studies, this issue was not addressed. Although some guidelines recommend a clearly articulated policy for biobanks about the effects of the participant's death or loss of legal capacity and included that participants should be informed of these, this solution cannot be retrospective [46].

Bak et al. [39] addressed the legislative issue by declaring that, in the United States, the research use of a deceased person's data is allowed (also outside of a consented research project) since it is not regarded as human subject research. Similarly, in the European perspective, the General Data Protection Regulation 2016/679 (GDPR) of the European Union (EU) does not apply to deceased persons [39,45]. Always in the European context, the European Convention on Human Rights of the European Court of Human Rights (ECHR) [54] has refused to recognize the right to privacy of the deceased. However, there is an indication in art.8 [54] that, in appropriate cases, when the reputation of a deceased family member affects the privacy of living persons, they may have a legal remedy [45]. Opposed is the Canadian approach since it does not differentiate deceased research participants from living ones and, therefore, requires substituted consent [39].

Regarding the legislative aspect, Hanold et al. [45] cite the OECD Guidelines on Human Biobanks and Genetic Research Databases (2009) [58]. Although this is a non-binding document, it recommends that biobanks should have a clearly articulated policy about what happens to the samples and data when participants become legally incapacitated or die [45].

3.3.4. Informed Consent Opens up the Secondary Use of Biobank Material for Forensic Research Purposes

Respect for the patient's autonomy is a fundamental principle of biomedical ethics, expressed through the collection of informed consent [9,31]. This allows individuals to

exercise their fundamental right to decide whether and how their body, body parts, and associated data can be used in research [9]. Although there are international guidelines that guide the researcher in the collection of consent to the use of biological material and associated data, there are still some situations that do not find a common interpretation. Surely, a crucial point is the collection of consent to the use of biological material and data belonging to a minor; according to the Council for International Organizations of Medical Sciences, consent for the donation, storage, and use of tissue samples must be given by their legal representative (generally the parents), with the possibility to withdraw consent at any time [4,46]. Tozzo et al. [4] also evidenced the fact that, in addition to the consent of the parent(s) or the legal guardian, the minor's decision must also be taken into account when she/he is old enough to understand the importance of donation or when they reach legal maturity [4].

Another widely debated point is represented by the use of biological material and associated data at a distance of time from the time of collection. Clearly, these additional researches cannot be covered by the consent given at the time of the first data collection, especially if the using permission was either limited or specific for a certain disease [7,9,41].

Tassé et al. [46], to overcome the hurdles created by the requirement for specific informed consent, proposed a multi-layered consent. This solution deals with the secondary use of genetic material by using a comprehensive consent form, which allows the subject to choose from a number of options in advance. Since 1995, new guidelines and amendments to existing ones have proposed solutions to the informed consent issue that include broad/blanket consent; multi-layered consent, with secondary use statements; recontact mechanisms; presumed consent/opting out; and waived consent [9,46]. Warner et al. [47] list multiple models of consent that have been endorsed: (a) specific consent, which provides for patients to be contacted in case of future studies; (b) tiered consent, in which patients decide the types of research for which their samples may be used in the future; (c) dynamic consent, which engages donors on an interactive basis; (d) blanket consent, which involves no restrictions at all for future use of donated biospecimens; and (e) broad consent, which combines general with the possibility of imposing some limits on research scope after review by a governance group [43,46,47]. According to the articles reviewed, the most common consent used in biobanking is the blanket consent and the broad consent.

However, such consent can only be implemented prospectively and, admittedly, some objected to the fact that this does not provide sufficient information and protection for donors' values [46]. Nonetheless, the majority of individuals surveyed in the article of Warner et al. [47] support the use of broad consent models. Virani et al. [43] demonstrate instead the success of "Permission to Contact" models, according to which all patients are asked for consent to be contacted later regarding future research opportunities. This type of dynamic consent is a more modern strategy that expands the authorization model outlined by Caulfield et al. [59] in a continuous, interactive process. Despite the authors having demonstrated that this method improves the number of participants eligible and available (80–94% of those approached agree to be contacted), many others find informed consent forms and aspects of research participation, such as risks associated, difficult to comprehend [43]. Other authors, such as Kurihara et al. [44], believe that the possibility of secondary use should be described in the study protocol and informed consent form. The authorization should be separately obtained from the consent to participate in the proposed primary research so that this does not interfere with the decision to participate in primary research. Such consent does not mean traditional "broad consent" but "valid" consent, as defined in the Declaration of Taipei [17,44]. In any event, as stated by Jahns et al. [24], the donor's withdrawal of consent causes all permits to lapse [24].

From a legislative point of view, Mungwira et al. [48] cite US federal regulations, which admit the collection and the storage of biological samples and data for future research without the need for a review by the institutional review board (IRB) as sources cannot be "identified directly or through identifiers linked to the samples and data" [48,49]. This concept was also taken up by Kondylakis et al. [50], according to who human samples are

not personal data; since the information contained in the material must first be extracted, the biomaterial shall be considered only as a carrier [50].

In the European context, most scientists are of the opinion that consent is acceptable for biological samples and data to be used for research out of the original research protocol [48]. In that sense, Gefenas et al. [51] announce one European position that accepts broad consent, optimizing it through strong ethical review and better communication with the participants. This thought is shared with Jahns et al. [24], according to whom it is essential that the donor is adequately informed about the broad extent of the future use of his/her biological material and related data, including the possibility of international medical research. Last but not least, even in the case of broad consent, the donor should have the option to restrict future use of specific research methods and/or fields, at least in part [24]. On the other hand, supporters of a stricter position based on the European Union General Data Protection Regulation (GDPR) prefer to use the public interest rather than consent as a legal basis for prospective collection and research on health data and biomaterials. This does not preclude the possibility of obtaining broad consent as an additional safeguard rather than as legal ground for the data processing. However, this option might be problematic as it might cause a research misconception among research participants if not properly explained [51].

Specifically, Paris [3] explores the legal approach to consensus in Italy, where art.110 of the Privacy Code [60] and the General Authorization of the Guarantor for the Protection of Personal Data n.9/2016 [61] provide that consent is not necessary when research is conducted on the basis of national or common law, in accordance with the European Regulation [62]. They also provide that consent is not necessary where contact with the data subjects is impossible or involves a disproportionate effort, which is likely to damage or hinder research. In addition, pseudonymization techniques are required and biological samples and data are only required to be retained for a period of time necessary for research purposes. Although, pursuant to art.110 bis [60], the Guarantor for the Protection of Personal Data may authorize the further processing of personal data, for scientific research purposes [2].

In the article by Mungwira et al. [48], the perception of the secondary use of biological material is analyzed in the sub-Saharan Africa context. From a legislative point of view, in Malawi, The National Health Act of 2003 [63] requires research participants to provide informed consent before donating samples; however, the law does not contain guidelines on the reuse of such samples and data in research [52]. Generally, from the analysis of several studies via the authors, it seemed that, in the countries of sub-Saharan Africa, the majority of participants would consent to the reuse of samples without further consent, provided that the institutional review committee approves it. A smaller percentage of respondents said that the reasons for retention should be stated and that they would have preferred a separate consent [48,52,53]. Quite different, however, is the situation in Zambia, where the 2013 regulation states that "biological material and data can only be collected by the way it has been indicated in the research protocol" without secondary use [52].

Talking about informed consent, criminal proceedings, and forensic databases from a European perspective, Machado and Silva [11] specify that consent is not required when taking a sample from individuals who have committed a crime or are under investigation (for example, Austria, Denmark, Estonia, Finland, Latvia, Lithuania, Scotland, Slovakia, the Netherlands, and England and Wales); other countries (such as Cyprus, France, Germany, Luxembourg, Portugal, Republic of Ireland, and Spain) consider informed consent necessary for samples collected during criminal proceedings, even if coercive sampling is allowed [11]. Furthermore, the storage of samples from non-convicted suspects is even more problematic and described as a violation of privacy under the European Convention on Human Rights within the S and Marper v United Kingdom [2008] ECHR 1581 case [54]. This is why the authors wish to stress the importance, even during criminal proceedings, of always carrying out sampling in accordance with comprehensive information being provided to data subjects on the risks and foreseeable uncertainties arising from the collection

of DNA samples and the DNA profile, specifying the possible and unacceptable uses of the samples, as well as their retention time and how personal data are processed [11].

4. Discussion

From the state of the art, it is clear how, to date, human biobanks are an essential resource for personalized medicine, crucial in treating and preventing human diseases and improving health. When it comes to forensic science, several important advances have been made over the past decade. The "omics' era" made it possible to collect far more accurate and precise data to be used to define the post-mortem interval (PMI), causes of death, and intoxications from drugs and narcotic substances, along with biological age determination, evidence's nature, biogeographic origin, phenotypic characters inference, and other useful elements for personal identification. All this is made possible, thanks also to the possibility of acquiring, in addition to biological samples, a series of data relating to the individual regarding lifestyle, pathologies, sex, and age. This represents only a small part of the possibilities that could be offered to a forensic researcher who accesses the samples stored in a biobank, even if still some recent publications do not fully recognize its usefulness [13,23,34]. The purpose of forensic research is to identify useful new investigative tools and their applicability to a large and diverse cohort of samples. The researchers, to obtain the biomaterial needed, might utilize collections within their own institutions and work collaboratively with other institutions but also acquire samples from biobanks [64]. It is well-known and undeniable that forensic DNA databases are plagued by stigmatization and discrimination for representing a specific social category; however, it is necessary to emphasize how, also, the medical biobanks could be interesting when they were to be used for forensic purposes as the samples come from subjects who are potentially sick [10,11,31]. The stigmatization brings with it discrimination on several levels: government, healthcare, insurance, and, not least, business [40]. Although the problem exists, we believe that the risk of stigmatization and discrimination is rare and the process of pseudo-anonymization could prevent it altogether. The same cannot be said in research where the anonymization of biobank samples is not only not particularly appropriate in protecting the interests of individuals but can also have a negative impact on research, compromising it [65].

These possible negative effects on confidentiality, autonomy, and trust should be considered in light of possible benefits for criminal justice and forensic research. Trying to balance ethical injuries and benefits, we think that two topics are crucial: (1) whether there are alternatives to secondary forensic use of biobanks and (2) the urgency of the fight against criminality through cutting-edge research. Before discussing these two issues, it should be made clear that in many cases, the secondary forensic use of biobanks will not be useful to solve a crime in the first place but to define new and more accurate forensic investigative tools [31].

Notwithstanding, the potentials are widely recognized by the scientific community; the same can be said for the issues, especially those ethical related. Currently, almost all of these questions need to be clarified and analyzed in greater detail: from the rights of ownership with regard to personal data and biobanks, to the unequal distribution of risks and benefits among populations, to conflicts of interests involving the protection of individual rights [11]. Even more so, the public trust in biobanks is a vital prerequisite for their continued operation and related research. In order to promote reliability, the biobanks should be governed by the following principles of the protection of individuals, transparency, participation and inclusion, and, finally, accountability.

The right to privacy has evolved over time, starting from the concept of confidentiality to concretize legally in the so-called informative self-determination. Informative self-determination represents a broader idea of the right to the protection of personal data, including the concept of community privacy, understood as participation in a human and personal reality where data sharing affects the community, conditioning its political and health [61]. Therefore, the right of the individual is reconciled with the needs of society, a

series of conflicting rights that must be balanced among themselves as all being worthy of protection. In this sense, the need to prevent and combat crime must also be implemented without encroaching on unacceptable forms of surveillance of citizens [62].

The concept of privacy has evolved over time and, with it, the possible criticalities have appeared increasingly clear; on the other hand, the legislation remains fragmented, inaccurate, and not exhaustive [66]. The research on human biological samples has evolved since the adoption of the Declaration of Helsinki [16] so, today, the simple need to obtain informed consent for the collection, storage, and re-use of biological samples or data contained in biobanks is no longer sufficient and exhaustive. Unlike the Declaration of Helsinki, the Declaration of Taipei admits the multiple and indefinite uses of data or biological material collected and stored in biobanks, only with adequate consent [17]. In many cases, however, at the time of data collection, it is not possible to fully individualize the research purposes. Therefore, it becomes necessary the intervention of the GDPR [62] that states how donors could give their consent only to certain research sectors or parts of research projects [62]. In Italy, the situation is complicated by the Data Protection Authority [61], which generally determines how biological samples and generic data can be stored, in the absence of consent and in the context of different research projects, only where a similar research purpose cannot be achieved on samples and data for which consent can be obtained.

In this sense, with the GDPR, the thoughtfulness to provide a comprehensive legal framework, in which secondary regulation may act as an integration of and not as a surrogate of statutory law, became more concrete [66].

The GDPR should have supposed to lead to an effective regulatory harmonization throughout the EU, "forcing" the member States to intervene with regard to the processing of personal data for research purposes and biobanking where legislation is lacking; however, still today, from a legislative point of view, Europe is very divided. Sweden, as well as Spain, are using the public interest as a legal basis by abandoning the consensus, allowing the secondary use of samples stored in the biobank in the absence of any opposition. The UK is testing linkage methods in the creation of UK Biobank, a large-scale biomedical database and research resource, containing in-depth genetic and health information from half a million UK participants [67]. In Italy, in the absence of informed consent, the assessment of the impact of the study on data protection (DPIA) and the consultation with the Guarantor are foreseen. To solve this bureaucratic bug, in the literature emerge hypothetical solutions: the idea of joining the Swedish and Spanish procedure of the tacit agreement or providing lifetime consent for research and a disposition of one's body post-mortem for research purposes [68]. The hypothesis, in the interest of public health, patients, or to make the organization of the National Health System efficient, would be to follow the legislation on organ donation or the rule on early treatment provisions (DAT).

Models of consensus could be approved to date range, from the most permissive general consensus, to the most stringent-multilevel consensus, to the specific consensus. Dynamic consensus, through which an iteration is established almost continuously with the donor, could represent a suitable and ethically acceptable solution, even if reiterating requests and contacting the donor could make the situation more complex and tiring.

We believe that the agreement to participate in the Novara Cohort Study—NCS for whom the samples will be stored in the UPO Biobank [69]—represents a perfect example of informed consent for the acquisition of samples in a biobank. The UPO Biobank is an institutional biobank of the University of Eastern Piedmont, a multi-specialized university biobank of disease and biobank of citizenship [69]. It provides partially restricted informed consent; the use of data and samples is restricted to the study, which allows acquisition with the additional availability so that these can be used for other research indicated. In the event of similar secondary research being undertaken, donors will be informed by dynamic consent, allowing them to opt-out. We believe that this consent is an excellent example of comprehensive and complete information as the donor is required to give consent also on research in the medical legal field; the processing of their biological samples, even in

the event of a state of incapacity; and even the decision to be informed in the event of unexpected news/results.

From an operational point of view, another crucial issue remains that affects both hospital and population cohorts, namely, the difficulty of creating a connection with health data, even in the presence of explicit consent. This is due both to administrative and procedural complexity and to interoperability and data management problems. Data sharing in Europe is still very difficult due to administrative and ethical issues, which make linking health cohorts and databases problematic even in the presence of explicit consent. Without a solid relationship between care and research, the data collected by researchers cannot be used synergistically. In order for a biobank to fully express its potential, there must be data integration between multiple databases, free access to these to carry out analyses, as well as the possibility of using the data and evaluating their qualities.

Biobanks have enormous potential; in addition to being an interface between patients and biomedical research, they are data sets since the preservation of samples implies data preservation; however, medical data will continue to be underutilized if their problems are not solved regarding fragmentation and difficult access.

In summary, regarding the question of whether secondary forensic use of the biobank for forensic purposes is permitted or not, the availability of alternatives and urgency (temporal pressure and severity of crime) could be important factors to consider. It is safe to assume that the possible negative effects of the secondary forensic use of biobanks, regarding confidentiality, trust, autonomy, and justice, could outweigh the potential for solving crimes. But if we talk about forensic research, given the enormous potential that could arise from it, we cannot go beyond regulating the issue from a legislative point of view, especially considering that the desire has emerged to consider the possibility of secondary use of biobank samples for clinical research, even if the regulation still appears uncertain and fragmentary. The same rule should apply to the secondary use of forensic research, which cannot continue to be ignored.

5. Conclusions

In conclusion, biobanks today represent not only a tool for implementing quality research but also a service unit, a mediator between the needs and rights of those who donate to biobanks and researchers, institutions, and the entire community. The studies covered by this narrative review raise concerns that are in agreement with our thinking: ensuring quality, traceability, fair distribution, and supervision by a sense of scientific and ethical correctness is essential.

If the debate on the creation and use of biobanks has made great strides in recent years, much remains to be conducted regarding the use of materials stored in biobanks for research that is not only regarding health but also forensics. Surely, what is conducted by UPO Biobank in obtaining explicit consent for use in forensics (where forensic does not mean useful for judicial purposes but useful for research purposes) is an important first step; however, for this awareness to become public knowledge, it is necessary to open a debate on the subject involving not only forensic researchers but also researchers dealing with health, genetic and population research, citizens, bioethicists, and lawyers. It is essential for those involved in forensics research to have available: (a) adequate amounts of biological material to make studies increasingly in line with the demands of the scientific community, no longer limited to pilot studies with a few samples to be able to validate new techniques; (b) reduced timing and effort in the recruitment of participants in order to encourage and increase research also in the forensic field; (c) not only biological samples but also related data, increasingly needed in the omics' era, to identify new tools useful to answer questions of fundamental importance for the forensic profession (e.g., DNA methylation for age estimation; analyses of the microbiome in order to have data on geographical origin, lifestyle, and age; and the nature of evidence left, for example, at the crime scene).

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