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FEMaLe

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D2.2: White paper on ethical health and care systems

1. Introduction

Ethical health and care systems refer to systems that prioritise ethical principles in their operations, policies, and decision-making processes. These systems aim to provide high-quality care and support to individuals while upholding values such as respect, dignity, fairness, and autonomy.

Some examples of ethical health and care systems include those that prioritise patient-centred care, shared decision-making between healthcare professionals and patients, and informed consent. Other ethical considerations include confidentiality, privacy, and data protection, as well as ensuring equity and access to healthcare services for all individuals.

Ethical health and care systems also emphasise the importance of ethical leadership, training and development of healthcare professionals, and a culture of ethical practice in healthcare organisations. They recognize the importance of ethical values not only in the delivery of care but also in the broader social and cultural context in which healthcare is provided.

FEMaLe (Finding Endometriosis using Machine Learning) project encompasses the design, validation, and implementation of a comprehensive model for detecting and managing individuals with endometriosis. The goal is to facilitate shared decision-making between patients and healthcare providers, enable the delivery of precision medicine, and drive new discoveries in endometriosis treatment. The overall objective is to deliver novel therapies and improve the quality of life for patients with endometriosis. Ethical considerations are crucial in such healthcare systems to ensure that patients receive high-quality care that is consistent with their values and preferences while being treated with respect and dignity.

This report is thus created to talk about ethics in healthcare systems in general, explain the existing solutions and describe the current challenges. Furthermore, the cases in FEMaLe project, and how the partners are handling the ethical issues are discussed and some of the main issues are explained. Finally, the propositions for further steps are provided.

The rest of this document is structured as follows: in 1.1 the state-of-the-art solutions and existing ethical regulations for healthcare systems are explained both in Europe and in the United States. According to such existing solutions, potential needs are explained in 1.2.

In Section 2 the aim of this document is reminded again. Then, the different perspectives of ethics in healthcare systems are defined in section 3, and the challenges that such systems should handle on each of these perspectives are discussed in 4. In section 5, we particularly discuss cases in FEMaLe project.

At the end, the recommendations and suggestions for filling the gaps in this regard are explained, and finally the document will be wrapped up by a conclusion.

1.1. State of the Art

Interdisciplinary ethics committees play a vital role in discussing ethical questions within various fields. Over the past three decades, two types of ethics committees have emerged as dominant within healthcare institutions: research ethics committees (RECs) and healthcare ethics committees (HECs). RECs primarily review medical research that involves human subjects, whereas HECs focus on addressing moral issues that arise in patient care [1].

It is worth noting that regulatory structures have been established at both international and national levels for RECs, but HECs have received much less regulation. This difference in regulatory oversight is significant and highlights the need for more attention to be given to the ethical questions that arise in the delivery of healthcare.

1.1.1 Ethical implications in the United States

The United States has a long history of addressing ethics in healthcare systems. Some of the major initiatives include:

- **The Belmont Report**: This report was published in 1979 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. It provides ethical principles and guidelines for the protection of human subjects in research. The three primary areas of application were stated as:
    - Informed consent.
    - Assessment of risks and benefits.
    - Selection of human subjects in research [2].
- **The Health Insurance Portability and Accountability Act (HIPAA)**: This is a federal law, passed in 1996, includes provisions for the protection of patients' privacy and security of their personal health information. It generally prohibits healthcare providers and healthcare businesses, called covered entities, from disclosing protected information to anyone other than a patient and the patient's authorised representatives without their consent.
- **The Patient Bill of Rights**: This document, first published in 1998 by the American Hospital Association, outlines the rights of patients in healthcare settings, including the right to informed consent and the right to participate in decisions about their care. This is not a federal law, but rather a document that outlines best practices for healthcare providers and institutions. Some states have adopted their own versions of the Patient Bill of Rights with additional protections for patients. Additionally, healthcare organisations may have their own policies and procedures that incorporate the principles of the Patient Bill of Rights.
- **The Affordable Care Act (ACA)**: This law, signed into law by President Obama and colloquially known as Obamacare, passed in 2010, includes provisions for the expansion of healthcare coverage and the protection of patients from insurance company abuses, such as denial of coverage based on pre-existing conditions.
- **The National Institute of Health (NIH)**: This government agency provides funding for research and sets ethical guidelines for the protection of human subjects in research.
- **The Joint Commission**: This independent organisation accredits healthcare organisations and has developed a *Code of Conduct* that outlines ethical principles and standards of behaviour for its employees, commissioners, consultants, surveyors, and contractors.

1.1.2 Ethical implications in Europe

Europe has a long history of addressing ethics in healthcare systems, with many initiatives aimed at protecting patient rights, promoting ethical research, and ensuring access to high-quality healthcare. These ethics can be different among different countries due to differences in healthcare organisation, laws, and economic, social, cultural, religious, and moral values. However, the more general implications which are inspiring for all EU countries are listed as follows:

- **The European Charter of Patients' Rights (ECPR)**: This document, adopted in 2002, outlines 14 fundamental rights for patients in the European Union, including the right to access healthcare, the right to informed consent, and the right to privacy and confidentiality. The ECPR is not a binding legal document; however, many European countries have used the Charter's principles to guide the development of healthcare policies and practices that prioritise patient rights and needs. An examination of the legislative bodies of EU member states revealed differing degrees of incorporation of the 14 rights outlined in a recent analysis [3]. The rights to information, consent, care quality, and prevention were found to be more frequently addressed in existing national laws than the rights to avoid pain, the right to innovation, and the right to respect patients' time. The protection of patients' rights varies across countries due to differences in healthcare organisation, laws, and economic, social, cultural, religious, and moral values. The effective implementation of the ECPR also varies across the EU, with some countries lacking specific provisions but applying laws related to informed consent, privacy, and access to health records to healthcare situations [4].

- **The General Data Protection Regulation (GDPR)**: This regulation, implemented in 2018, sets standards for the protection of personal data in the European Union, including health data. The GDPR requires healthcare providers and organisations to obtain informed consent for the collection and use of personal data, and to implement appropriate security measures to protect data. The GDPR was adopted on 14 April 2016 and became enforceable beginning 25 May 2018. It applies to any organisation that processes the personal data of individuals within the EU.

- **The European Code of Conduct for Research Integrity**: This document, published in 2011 (the most recent version published and translated to all official EU languages in 2017), sets ethical standards for research conduct in the European Union for all EU-funded projects. The code emphasises the importance of honesty, transparency, and respect for research participants and their rights [6].

- **Ethics Guidelines for Trustworthy AI**: this was published by the High-Level Expert Group on Artificial Intelligence (AI HLEG), which was appointed by the European Commission. The guidelines were published in April 2019 and updated in June 2020. The guidelines are not legally binding, but they provide important guidance and recommendations for policymakers, businesses, and other stakeholders involved in the development and deployment of AI systems.

1.2 Potentials and Needs

In recent years, there has been a surge of innovation in health technologies driven by new medical breakthroughs, innovative scientific approaches, and the emergence of digital health technologies. This has led to pioneering methods of drug development and disease diagnosis, as well as the rise of 'big health data' and new forms of networked care. As a result, European health systems are predicted to undergo significant transformation.

Despite the significant potential of these technological innovations, much of it has yet to be fully realised. Furthermore, the rise of new health technologies is accompanied by a profound shift in the way individuals engage with health matters, whether as patients, citizens, or consumers. This shift is reshaping the healthcare landscape and presents new opportunities and challenges for the healthcare industry.

The FEMaLe project incorporates participatory processes, advanced computer sciences, state-of-the-art technologies, and patient-shared data to deliver three main outcomes:

A. Mobile health app for individuals with endometriosis
B. Three clinical decision support (CDS) tools for healthcare providers. These include a risk stratification tool for general practitioners, a multi-marker signature tool for gynaecologists, and a non-invasive diagnostic tool for radiologists.
C. Computer vision-based software tool for real-time augmented reality guided surgery of endometriosis.

These outcomes are designed to facilitate the detection and management of endometriosis, promote shared decision-making between patients and healthcare providers, and improve the quality of life for individuals with endometriosis. The project utilises cutting-edge technologies and patient data to create personalised interventions and precision medicine.

All the mentioned reasons can bold the importance of establishing good ethical standards in the healthcare systems. This will ensure that all partners within the project will adhere to the standards, and it will create an environment where all decision-making follows an established set of rules and regulations.

2. Aim

In this white paper we will discuss the importance of ethical considerations in FEMaLe project. Then we define the different aspects to which ethics apply in healthcare systems in this project.

The problems and challenges of these aspects are described. The existing solutions are first studied, and the recommendations are given for further actions. the following criteria are the main objectives:

A. Identify the problems and challenges of partners in all the defined ethical aspects,
B. Recognize the most important ethical domain,
C. Recommend solutions to better structure an ethical healthcare system.

3. Definitions

Here the different aspects of healthcare systems in which ethics are applied are defined.

3.1. Data Ethics

Data ethics refers to the moral principles and guidelines governing the collection, processing, storage, and use of data. Here are some of the key ethical aspects of data:

- **Privacy**: Individuals have a right to privacy, and the collection, processing, and use of their personal data must be done in a way that respects their privacy rights. This means that data must be collected and used only for the intended purpose, and individuals must be informed about how their data will be used.
- **Confidentiality**: Data must be kept confidential and protected from unauthorised access, use, or disclosure. This is particularly important when dealing with sensitive information, such as health records or financial information.
- **Data quality**: Data must be accurate, relevant, and up-to-date. Organisations that collect and use data have a responsibility to ensure that the data is of high quality and that it is used appropriately.
- **Informed Consent**: Individuals must be informed about how their data will be collected, processed, and used, and they must give their informed consent for this to happen. This means that individuals must have a clear understanding of what they are agreeing to and the implications of providing their data.
- **Transparency**: Organisations that collect and use data must be transparent about their data practices. This includes providing clear and understandable explanations of how data is collected, processed, and used, as well as providing access to individuals to their own data.
- **Equity**: The use of data must be done in a way that is fair and equitable. This means that data must not be used to discriminate against individuals or groups based on their race, gender, age, or other characteristics.

3.2. Ethics in policies of a healthcare system

This ethical domain requires a comprehensive approach that takes into account the unique ethical challenges of the healthcare industry. Here are some steps that can be taken to apply ethical principles in healthcare policies:

- **Identify Ethical Issues**: The first step is to identify the ethical issues that are relevant to the policies being developed. This might include issues related to patient privacy, data security, informed consent, equity, and access to healthcare.
- **Consult Ethical Guidelines**: There are many ethical guidelines that have been developed specifically for healthcare, such as the ones mentioned in section 1.1. These guidelines can be consulted to help ensure that policies are consistent with accepted ethical standards.
- **Involve Stakeholders**: Policies should be developed with input from a wide range of stakeholders, including healthcare professionals, patients, and other community members. This can help to ensure that policies are sensitive to the needs and perspectives of all stakeholders.
- **Consider Impact on Patients**: Policies should be developed with a focus on improving patient outcomes and protecting patient rights. This means considering the potential impact of policies on patients and ensuring that policies are consistent with the principles of beneficence (doing good) and non-maleficence (not doing harm).
- **Develop Clear Policies and Procedures**: Policies and procedures should be developed that clearly articulate how ethical principles will be applied in the healthcare system. This might include procedures for obtaining informed consent, guidelines for protecting patient privacy, and protocols for responding to ethical dilemmas.
- **Monitor and Evaluate Policies**: Finally, policies should be regularly monitored and evaluated to ensure that they are achieving their intended goals and that they are consistent with ethical principles. This might involve conducting regular audits or surveys to assess patient satisfaction or tracking key performance indicators to evaluate policy effectiveness.

3.3. Ethics in Research

Ethics in research for healthcare systems encompasses various aspects that aim to protect the rights, well-being, and dignity of research participants, as well as ensure the integrity and validity of the research process. Some key aspects include:

- **Informed Consent**: Researchers must obtain informed consent from participants, ensuring that they have been fully informed about the nature, purpose, risks, and potential benefits of the research. Participants should have the autonomy to freely decide whether or not to participate and should be able to withdraw their consent at any time.
- **Privacy and Confidentiality**: Researchers have a responsibility to protect the privacy and confidentiality of research participants. Identifiable data should be securely stored and access to participant information should be restricted to authorised individuals.
- **Risk-Benefit Assessment**: Ethical research requires a careful evaluation of the potential risks and benefits associated with the study. Researchers should minimise risks to participants and maximise the potential benefits while maintaining scientific rigour.
- **Protection of Vulnerable Populations**: Special attention should be given to the protection of vulnerable populations such as children, pregnant women, prisoners, and individuals with cognitive impairments. Additional safeguards may be required to ensure their well-being and minimise any potential harm.
- **Ethical Review and Oversight**: Research involving human participants should undergo ethical review by independent research ethics committees or institutional review boards. These bodies evaluate the ethical implications of the research, assess the risks and benefits, and ensure compliance with ethical guidelines and regulations.
- **Data Management and Transparency**: Ethical research involves proper data management practices, ensuring data accuracy, integrity, and responsible use. Transparency in reporting research findings is important to facilitate knowledge dissemination and prevent publication bias.
- **Conflict of Interest**: Researchers should disclose any potential conflicts of interest that could compromise the integrity, objectivity, or impartiality of the research. Financial, professional, or personal conflicts should be addressed and managed appropriately.
- **Responsible Conduct of Research**: Researchers should adhere to high standards of integrity, honesty, and professionalism throughout the research process. This includes proper study design, accurate data collection and analysis, and responsible reporting and publication practices.

3.4. Ethics in Patient care

Ethics in healthcare systems with respect to patient care involves several important aspects, including:

- **Respect for Autonomy**: Healthcare providers should respect the autonomy of patients, which means recognizing their right to make decisions about their own healthcare. This includes obtaining informed consent, involving patients in treatment decisions, and respecting their values, beliefs, and preferences.
- **Beneficence**: Healthcare providers have a duty to act in the best interest of their patients and to promote their well-being. This involves providing effective treatments, alleviating suffering, and prioritising patient welfare.
- **Non-Maleficence**: The principle of non-maleficence means avoiding harm to patients. Healthcare providers should strive to minimise the risks and potential harm associated with treatments, procedures, or interventions.
- **Justice**: Healthcare systems should ensure fair and equitable distribution of healthcare resources, taking into account the needs of all patients. This includes addressing disparities, promoting equal access to care, and avoiding discrimination or bias in the delivery of healthcare services.
- **Confidentiality and Privacy**: Healthcare providers are obligated to maintain patient confidentiality and privacy. Patients should feel secure that their personal health information will be protected and not disclosed without their consent, except in situations where disclosure is legally required or in the interest of the patient.
- **Transparency and Truthfulness**: Healthcare providers should be honest, transparent, and provide accurate information to patients. This includes sharing diagnoses, treatment options, potential risks and benefits, and any limitations in care.
- **Continuity of Care**: Patients should receive continuous, coordinated, and appropriate care. This involves effective communication, collaboration between healthcare professionals, and ensuring smooth transitions between different healthcare settings.

3.5. Ethics in Societal Perspectives

The societal perspective of ethics in healthcare systems refers to the consideration of ethical issues and principles that arise at the broader societal level. It involves examining the impact of healthcare decisions, policies, and practices on society as a whole, and making ethical choices that promote the well-being and equitable treatment of individuals and communities.

From a societal perspective, ethics in healthcare systems focus on several key areas:

- **Access to Healthcare**: Ensuring equitable access to healthcare services and resources for all individuals, regardless of their socioeconomic status, race, gender, or other factors. This includes addressing disparities and working towards universal healthcare coverage.
- **Resource Allocation**: Ethical decision-making regarding the fair distribution of limited healthcare resources, such as organs for transplantation, medications, and healthcare facilities. This involves considerations of equity, efficiency, and maximising overall societal benefit.
- **Health Policy and Legislation**: Ethical evaluation and development of health policies and legislation that balance individual rights and societal interests. This includes issues such as public health interventions, vaccination policies, and end-of-life decision-making.
- **Public Health**: Prioritising population health and preventing disease through public health interventions, health promotion, and disease surveillance. Ethical considerations include balancing individual autonomy and privacy with the need to protect public health.
- **Research Ethics**: Ensuring ethical conduct in healthcare research, protecting research participants' rights, and considering the broader implications of research findings for society. This involves addressing issues such as informed consent, data privacy, and transparency.
- **Health Technology and Innovation**: Ethical evaluation and regulation of emerging healthcare technologies, such as artificial intelligence, genetic testing, and telemedicine. This includes considerations of safety, efficacy, privacy, and equitable access.

3.6. Ethical AI systems

The European Commission guidelines on AI ethics, released in April 2019, outline key requirements for trustworthy AI. These requirements are based on seven key principles and can be summarised as follows:

- **Human Agency and Oversight**: AI systems should be designed to augment human capabilities and decision-making, rather than replacing or undermining human autonomy. They should ensure that humans have the ability to understand, challenge, and override AI system decisions.
- **Technical Robustness and Safety**: AI systems should be developed with a focus on reliability and resilience. They should undergo rigorous testing and validation to ensure their safety, and appropriate fail-safe mechanisms should be in place to minimise risks.
- **Privacy and Data Governance**: AI systems should respect privacy and comply with data protection regulations. They should be designed to ensure the protection of personal data, and users should have control over their own data.
- **Transparency**: AI systems should be transparent, providing clear and understandable explanations for their decisions and actions. Users should have access to relevant information about how AI systems operate, including their limitations and potential biases.
- **Diversity, Non-Discrimination and Fairness**: AI systems should be developed and trained in a manner that avoids bias and discrimination. They should promote inclusivity, fairness, and equal treatment, considering the diverse needs and perspectives of individuals and avoiding unfair outcomes.
- **Societal and Environmental Well-being**: AI systems should contribute to the overall well-being of society and the environment. They should be aligned with sustainable development goals, respect ecological and social values, and avoid harmful or malicious uses.
- **Accountability**: AI systems and their developers, deployers, and users should be accountable for their actions. Clear responsibility frameworks should be in place, allowing for redress and mitigation of negative impacts caused by AI systems.

Different Guidelines are being developed about the AI systems and the ethics [7], however, not a general standard is fixed yet to a large extent.

3.7. Ethics in commercial use perspectives

From this aspect, the new medical devices placed in the United states, and Europe should meet the requirements of the FDA (Food and Drug Administration) and MDR (Medical Device Regulation) respectively.

The ISO standard for Good Clinical Practices (GCP) is published by the International Organization for Standardization (ISO). It provides guidelines for the design, execution, documentation, and reporting of clinical studies involving medical devices. Adhering to GCP standards is crucial as it ensures the collection of high-quality data under ethical conditions and facilitates regulatory compliance both within the European Union (EU) and globally.

The European Union (EU) Medical Devices Regulation (MDR) mandates that clinical investigations adhere to Good Clinical Practice (GCP) guidelines and specifically refers to the ISO14155 standard. For market applications, the US Food and Drug Administration (FDA) accepts clinical data gathered outside the United States on the condition that GCP principles have been followed. The FDA acknowledges the ISO14155 standard for medical device trials, and other regions also recognize the GCP standard in a similar manner. Some key aspects covered by ISO 14155 include:

- **Ethical Considerations**: The standard emphasises the importance of obtaining informed consent from study participants and protecting their rights, safety, and well-being throughout the investigation.
- **Study Design and Conduct**: ISO 14155 provides guidance on designing the clinical investigation, including participant selection, study protocol development, and study site selection. It also addresses the responsibilities of the sponsor, investigator, and ethics committee.
- **Data Management**: The standard specifies requirements for data collection, handling, and storage during the clinical investigation. It emphasises the need for accurate and reliable data to support the evaluation of the device's safety and performance.
- **Adverse Event Reporting**: ISO 14155 outlines the reporting requirements for adverse events and other safety-related information during the clinical investigation. It promotes timely reporting and appropriate actions to mitigate risks to study participants.
- **Study Documentation and Reporting**: The standard provides guidance on documenting the clinical investigation, including the creation of essential documents such as the investigational plan, study reports, and final study results. It also covers the reporting of study outcomes to regulatory authorities and other relevant stakeholders.

4. Challenges

4.1. Ethical Concerns

Applying ethics in healthcare systems presents several challenges and problems that we are facing today. Here, we mention some of the most important ones. We will discuss them in relation to cases in FEMaLe project in section 5.1.

- In the aspects of data ethics there are several challenges. The increasing digitization of healthcare data raises concerns about **privacy** and **data protection**. Healthcare systems need to ensure the secure collection, storage, and sharing of patient data while respecting individual privacy rights. Striking a balance between data access for quality care and protecting patient confidentiality is an ongoing challenge.
- On the other hand, **protecting the privacy of data** has several limits. First your ability to derive value and insight from your data, and second it requires additional resources to completely remove the trace of the data. This second can be dependent on different parameters like the type of data.
- Another aspect of data ethics concerns the **quality, equity and variability of data** which is not an easy task to do. A collection of such data requires human resource, collaboration of different healthcare partners which might be working based on various standards.
- In the aspect of **ethics in policies** of a healthcare system, **the need of human resources** who are fully aware of the national and international laws is negligible. The policies should be discussed, tested and reviewed properly which needs a committee fully responsible.
- In **patient care** the **transparency and truthfulness** is now being questioned by professionals [5]. Sometimes this aspect of ethics may cause stress for the patient and may trouble the best interest of the patient. Moreover, from the aspect of **confidentiality and privacy** it is hard for organisations to avoid conflicts which might be caused by research ethics. The data which is served for patient care can be used for research in healthcare, however, to keep all the ethical aspects might cause a huge cost of money and energy for the researchers.

4.1 Current Ethical Implications and their Gaps

There are several ongoing ethical implications in healthcare systems that have garnered significant attention and debate. Most of the regulations and guidelines which exist in the U.S and Europe are already discussed in section 1.1. According to the study that we did we can categorise the general aspects of current guidelines to the three following:

- The lack of existing a generalised guidelines: Different countries have different regulations based on their own healthcare systems and the implication of ethics might vary according to the culture, the healthcare system governing in the country, and other parameters. This can cause troubles in international collaborations. On the other hand, the novelty and the rapid growing caused by new systems (mostly AI) had made it difficult for the regulations to be updated.
- Instrumentalization of participants: Instrumentalization refers to the act of using individuals or groups as a means to an end, rather than recognizing their intrinsic worth and respecting their autonomy and well-being. Addressing the ethical implications of instrumentalization in healthcare requires a commitment to patient-centred care, respect for autonomy, informed consent, equitable resource allocation, and the mitigation of power imbalances. By upholding these principles, healthcare systems can ensure that participants are treated as individuals deserving of respect, dignity, and personalised care.
- Responsibilities which are imposed: The ethical guidelines are becoming more and more complicated because of the emerging aspects of healthcare systems. New regulations are made, or the existing ones are updated regularly, giving a large number of rules to follow. Through these ethical implications, responsibilities or burdens are assigned to both the professionals and patients.
    - Professional burdens: The professional cannot apply the best practices, since it might be affected by several ethical aspects like, patient autonomy.
    - Patient burdens: The patients are obliged to give consents to the care they are receiving, and according to the studies, they are not always fully informed about all the aspects of such concerns and might object to the results. The ethical implications do not provide a generalised and structured pipeline to solve the issue.
- Impact on the care given to patients: A question which can be raised in this regard is that if the current ethical implications are affecting the best care which can be given to the patients. We believe that this aspect should be particularly taken into consideration when establishing the new ethical rules.
- Lack of definite regulations on modern AI-based cares provided to patients.

5. FEMaLe

5.1. Cases

In FEMaLe project, we have identified five out of ten WPs that are concerned with healthcare systems. These WPs are studied to know how we are implicating ethics at the moment in the project. These WPs were interviewed through a questionnaire and the results are being provided here. Therefore, in this Section the way ethics are applied in each FEMaLe WP is explained and the problems are explained.

In Table 1 the objectives of the mentioned WPs are mentioned to give an understanding of how they are involved in healthcare systems.

WP#	Objectives	Ethical Aspects Involved
3	• To estimate the prevalence and geographical distribution of endometriosis-like symptoms in Denmark and the UK. • To develop a phenotype description for women with endometriosis-like symptoms. • To estimate the health related and social consequences of diagnostic delay.	Data, Research
4	• Clinical decision support (CDS) tool to Validate and refine endometriosis subtypes	Data, Research
5	• Translation and validation of Lucy App. • Develop the dietary and the lifestyle modules. • Practical and self-improving system for health monitoring.	Data, Patient Care, Research, AI
6	• To develop an algorithm to detect and classify endometriosis lesions from laparoscopic images. • To build an augmented reality software for the surgeons to help them detect and classify lesions during the surgery.	Data, Patient Care, Research, Societal, AI
7	• To develop an algorithm to suggest incision boundaries in laparoscopy. • To build an augmented reality software for the surgeons.	Data, Patient Care, Research, Societal, AI
8	• To teach patients how to manage and reduce the negative physical, psychological and social symptoms and consequences of endometriosis. • To prevent further development of chronic pain problems and improve the overall quality of life.	Data, Patient Care,

Table 1. The WPs involved in healthcare systems, and their ethical involvements.

5.1.1. Data Ethics

Apparently, all the involved WPs are involved in the ethical implications of data. Table 2, below, shows the aspects of data ethics that the WPs are handling. Please consider the fact that in WP4, the data is not collected, but they use datasets that they have previously collected on patients, and they generate new biological data (e.g., proteomic data). According to the type of data each WP collects, the application of ethical issues might vary in the method they use and also in the level of complexity. Considering the existing regulations, the WPs 3-7 follow GDPR regulations for the collection of data. WP6 and WP7 follow the Medical Device Regulations (MDR), and WP6 and WP8 follow the Clinical Trials Regulations.

The following are the summary of challenges that WPs are facing when applying the data ethics:

- Costly efforts to get the agreements to collect ethical data. International collaborations are difficult because of different rules concerning requirements of informed consent.
- MTA (material transfer agreement) that needs to be established to transfer data and usage by other partners.
- De-identifying the data to mask the identity of the patients is first very costly which requires new software and human resources.
- Additional resources are needed to build a secure platform for data management.
- Time-consuming procedures to follow every data aspect.

WP#	Privacy	Data Quality	Informed consent	Patient access to data	Equity
3	Yes	Yes	Partially	No	No
4	Yes	Yes	Yes	Yes	Yes
5	Yes	Yes	Yes	Yes	Yes
6	Partially	Yes	Yes	No	Yes
7	Partially	Yes	Yes	No	Yes
8	Yes	Yes	Yes	No	No

Table 2. The ethical aspects of data that WPs are considering.

5.1.2. Ethics in Patient Care

According to Table 1, WP 5 and WP8 are directly involved with patient care. In this aspect both WPs are complying with 'Respect for patient autonomy', 'Confidentiality', 'Non-maleficence (not to harm)', 'Beneficence (promote their patients' well-being and to act in their best interests)', 'Justice (fair treatment without discrimination)', and 'Professionalism (maintain the trust of patients. Act with integrity, honesty, and transparency)'. Other WPs are indirectly involved in patient care. The ethical aspects applied to patient care are actually depending on the organisation in which they offer their output. Like in WP6 and WP7, the users are the hospitals who are going to use the AR product. So, the guidelines of patient care should be established, based on the hospital patient care.

5.1.3. Ethics in Research

All the involved WPs are conducting research and follow T*he European Code of Conduct for Research Integrity* [6].

5.1.4. Ethical AI systems

WPs 5-7 are involved in AI systems. An effort has been done since August 2022 to apply AI trustworthiness aspects in the work carried out as much as possible. Some issues like *human agency and oversight, robustness, diversity and fairness, age-independent users, fair systems, etc.* are being well-handled by the WPs. However, because of lack of clear and definite guidelines specific to the AI ethics of the FEMaLe project (as already mentioned), some of the following general challenges are observed:

- **Liability and accountability**: if an AI system makes a mistake or harms a patient it can be difficult to determine who is responsible, which can impact patient safety and trust in the healthcare system.
- **Transparency and explainability**: The complexity of how AI works is difficult to be explained to the users/patients. It is negotiable if it can even sometimes prevent the patient from receiving the best care, if all AI aspects are defined transparently to them.

5.1.5. Ethics in commercial use

In both the United States, the Food and Drug Administration (FDA), and Europe's Medical Device Regulation (MDR) system, AI applications in surgery are categorised as medical devices and are subject to regulatory standards. These medical devices are classified into four risk categories, which determine the evaluation and acceptance of new products. The AI-based surgical tool which is being developed in WP6 and WP7 is classified as Class 1, which encompasses devices that have minimal patient contact and contains minimum risk. Therefore, corresponding to such a class of tools, the ethical aspects are applied. Compliance with the ISO14155 standard helps to maintain high-quality data and make informed decisions regarding the safety and effectiveness of medical devices, while keeping the ethical aspects. When a product is ready for clinical validations, the clinical study protocols are sent to a French committee called CPP (Comités de protection des personnes) to be validated for a test in the target hospital.

6. Recommendations

6.1. General Suggestions

To ensure better implications of ethics in healthcare systems, several actions are suggested at the end of this report:

- **Establish Ethical Guidelines**: Develop comprehensive ethical guidelines specific to healthcare systems that outline the principles, values, and standards to be followed by healthcare professionals, researchers, and organisations. These guidelines should address key ethical considerations, specified to FEMaLe project so that all WPs have the same language when talking about ethics.

- **Ethical Training and Education**: Provide robust training and education programs on healthcare ethics for healthcare professionals, researchers, and administrators. Continuous education programs can help healthcare practitioners stay updated with evolving ethical issues.

- **Ethical Review Boards**: Establish institutional or regional ethical review boards to oversee research involving human subjects, ensuring that studies adhere to ethical principles. These boards can review research proposals, evaluate risks and benefits, and ensure compliance with ethical guidelines and regulations. Ethical review boards play a crucial role in protecting patients' rights and welfare.

- **Privacy and Data Protection**: Implement robust privacy and data protection measures to safeguard patients' personal health information. Adhere to data protection regulations and guidelines to ensure that patients' data is collected, stored, and shared securely and with their informed consent. Regular audits and compliance assessments can help identify and address any privacy or security vulnerabilities.

- **Informed Consent Process**: Strengthen the informed consent process by ensuring that patients have a clear understanding of the purpose, risks, benefits, and alternatives of medical interventions or participation in research. Healthcare providers should facilitate open and honest communication with patients, addressing their questions and concerns to support informed decision-making.

- **Addressing Biases and Health Disparities**: Identify and address biases and health disparities within healthcare systems. Promote equity in access to healthcare services, eliminate discriminatory practices, and implement measures to reduce bias in diagnosis, treatment, and resource allocation. Encourage diversity and inclusivity within healthcare organisations and research studies.

- **Ethical AI Integration**: Ensure that the use of artificial intelligence (AI) in healthcare systems adheres to ethical principles. AI algorithms should be transparent, accountable, and designed to minimise biases and discrimination. Ethical considerations should guide the collection and use of patient data, privacy protection, and decision-making processes involving AI systems.

- **Collaboration and Public Engagement**: Collaboration among healthcare professionals, researchers, policymakers, and patient advocacy groups to address ethical challenges collectively. Involve patients and the public in ethical discussions and decision-making processes to incorporate diverse perspectives and ensure that healthcare systems align with societal values.

6.2. Proposals

At the end of this report, we propose a framework for the FEMaLe project to better manage the ethical aspects. We have already mentioned the general recommendations for establishing a framework.

Also, FEMaLe project partner EQuiP (the European Society for Quality and Safety in Family Practice) has published position papers since 2010, covering themes like ' Measuring Quality in Health Care (2010)', 'eHealth (2016)', 'Equity, a core dimension of Quality in Primary Care (Nov 2017)', 'Measuring Quality in Primary Health Care (June 2018)' and 'Family Doctors during COVID-19 Pandemics (March 2020)', to bring best quality care to patients.

The main proposals, based on the previous recommendations, for a common framework are the following:

- Promoting fairness in primary health care involves more than just addressing financial obstacles; it also requires actions that guarantee accessible and acceptable care for every patient. EQuiP advocates for **universal healthcare to ensure that everyone can access** the necessary promotional, preventive, curative, rehabilitative, and palliative healthcare services without experiencing financial hardship [8].

- Additionally, EQuiP emphasises the **significance of overcoming non-financial barriers**. This involves ensuring an equitable geographical distribution of high-quality healthcare facilities and medications, having skilled personnel available in appropriate locations, easily accessible well-equipped facilities, and providing services that are acceptable to all patients and patient groups [8].

- EQuiP highly recommends that **primary care professionals and practices assess the fairness of the healthcare they provide** and **implement quality improvement initiatives** that prioritise enhancing healthcare equity. This evaluation process should encompass analysing equity in various performance indicators such as vaccination rates and patient satisfaction. It should also involve critical incident analysis and self-evaluation of staff. The insights gained from an equity assessment should be utilised to customise care processes according to the specific needs of individual patients, as delivering identical care to all patients would result in inequitable healthcare provision [8].

- EQuiP emphasises the crucial **need for comprehensive training of all primary care professionals** in recognizing the significance of social determinants of health, providing community-oriented care, addressing diversity, and fostering interprofessional collaboration. It is essential that these training efforts are reinforced through continuous professional development programs, ensuring that healthcare practitioners stay updated and proficient in these areas [8].

- The primary objective of the **data collection process should not be solely focused on gathering information**. It is important to gather patient data on specific aspects of care only if it can effectively enhance patient care, prove to be cost-effective, and not require excessive time, staff, or financial resources beyond the potential benefits in quality improvement and/or increased patient safety. The justification for collecting patient information lies in its potential to positively impact the quality of care provided while considering resource constraints [9].

- We recommend the **use of new guidelines which are now more patient-centred** to provide guidance to clinicians who care for women with endometriosis. The fast-growing studies on endometriosis require the need for improving many aspects of the diagnosis of the disease and the treatment of endometriosis-associated symptoms. We find that following the classical guidelines might be unethical in some respects.

- We emphasise on the **use of non-invasive diagnosis according to new guidelines** like [10] which indicates that laparoscopy is no longer the diagnostic gold standard, and it is now only recommended in patients with negative imaging results and/or where empirical treatment was unsuccessful or inappropriate.

- We emphasise and **recommend the practitioners to agree on a unified classification system**. The advancement of non-invasive diagnostic methods and surgical therapy for endometriosis highlights the need for a universally applicable classification system that encompasses all aspects of the disease. Such a classification system, as the one suggested in [11], should be designed to be used by both surgical and diagnostic specialties. This would ensure consistency and facilitate effective communication and collaboration among healthcare professionals working with endometriosis.

7. Conclusions

This white paper focused on the ethics in healthcare systems. We have started by introducing the necessity of ethical issues in such systems and the solutions which are proposed internationally up to now.

As members of the EU-funded FEMaLe project, which aims to bring better care for females with endometriosis, we believe that a better understanding of the ethical aspects and in particular in the endometriosis care should be taken into world-wide consideration.

To achieve this, we start by some definitions, and we describe the existing challenges and the gaps which we find in the existing guidelines. We have then explained how different aspects of ethical issues are being handled in the FEMaLe project in all related work packages.

Finally, gathering all the mentioned information, we came up with some general recommendations and we propose an established strategy particularly to handle the healthcare ethical aspects in endometriosis.

We have started by providing some proposals in this regard which are based on our insight in the project, on the previous studies, and also on the consensus agreements between different stakeholders.

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