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FEMaLe

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Legislation

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Rules of Application (RAP) – Commission Regulation (EC, Euratom) No 1268/2012 of 29 October 2012 on the rules of application of l Regulation (EC, Euratom) No 966/2012 of the European Parliament and of the Council on the financial rules applicable to the general budget of the Union (OJ L 298, 26.10.2012, p.1).

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Abbreviations

Abbreviation	Description
CSO	Civil Society organisation(s)
EC	European Commission
EU	European Union
RRI	Responsible Research and Innovation
WP	Work Package(s)

Executive summary

The project FEMaLe responds to the specific challenge put forward in 'SC1-DTH-2018-2020: Personalised early risk prediction, prevention and intervention based on Artificial Intelligence and Big Data technologies', which, in the present case, concretely relates with the digital transformation in endometriosis health and care nexus. The project flags the interconnectedness of needs related to the disorder, its governance regimes and of the biophysical and societal contexts in which these needs ripen.

The project FEMaLe aims at facilitating the science, societal and policy arenas responsiveness to the new wave of experience, expertise and knowledge needs that are occurring from the innovative inter-sectoral approach of the project, building upon complementary research and innovation initiatives currently tackling the challenges of the aforementioned nexus which are emerging around the globe.

The project intends to be one of the prominent commitments to support the European Commission on the search for innovative avenues to explore, recognize, pilot and generate pioneering responses to identified challenges in the EU context.

The main aim of the guidelines for 'code of practices', introduced by the present document is to propose to the participants of project FEMaLe a framework for the conception, production, test and validation of all anticipated outputs, especially the key deliverables.

The guidelines provide a short overview on the current context, highlighting the fact that notwithstanding how prevalent endometriosis is, and how considerable its impact on those affected, it receives a small part of the society's attention compared to other comparable common and systemic disorders (e.g., diabetes, psoriasis, migraine, etc.), and how endometriosis has been the focus of remarkably modest curative research and even less social scientific studies.

This provision delivers a series of specific information starting to describe the background upon which the project FEMaLe is rooted which is the European landscape of endometriosis considering societal drivers, the pan-European research panorama, relevant national initiatives and how they link with the pan-EU agenda, the economics of endometriosis (market, innovation arena, product, services and systems), and the societal panorama interlinked to this long-term chronic health condition.

Then, the concept of the EU idea of Inclusive, Innovative and Reflective Societies (IIRS) is explored, considering it is driven by the ambition to structure Europe in a changing world, to propose a IIRS framework for the project FEMaLe. This framework is organised around the following key pillars: principles (e.g., the principles of European medical ethics from European Council of Medical orders, etc.), outcomes (e.g., via Responsible Research and Innovation good practices, etc.), and integrity (e.g., advancing research integrity practices and policies, etc.).

Then, the guidelines demonstrate how WP2 tackle specifically identified focus areas which are ethics, gender and inclusion, RRI and Open Science, and how it links the project FEMaLe activities with the EU's agenda on IIRS. A specific set of activities are delineated for each of the aforementioned focus areas, for instance how the project FEMaLe Advisory Boards on Ethics, the Ethics Advisory Board (ETAB), led by IAAD (P10), contributes to steering activities and correlated outputs.

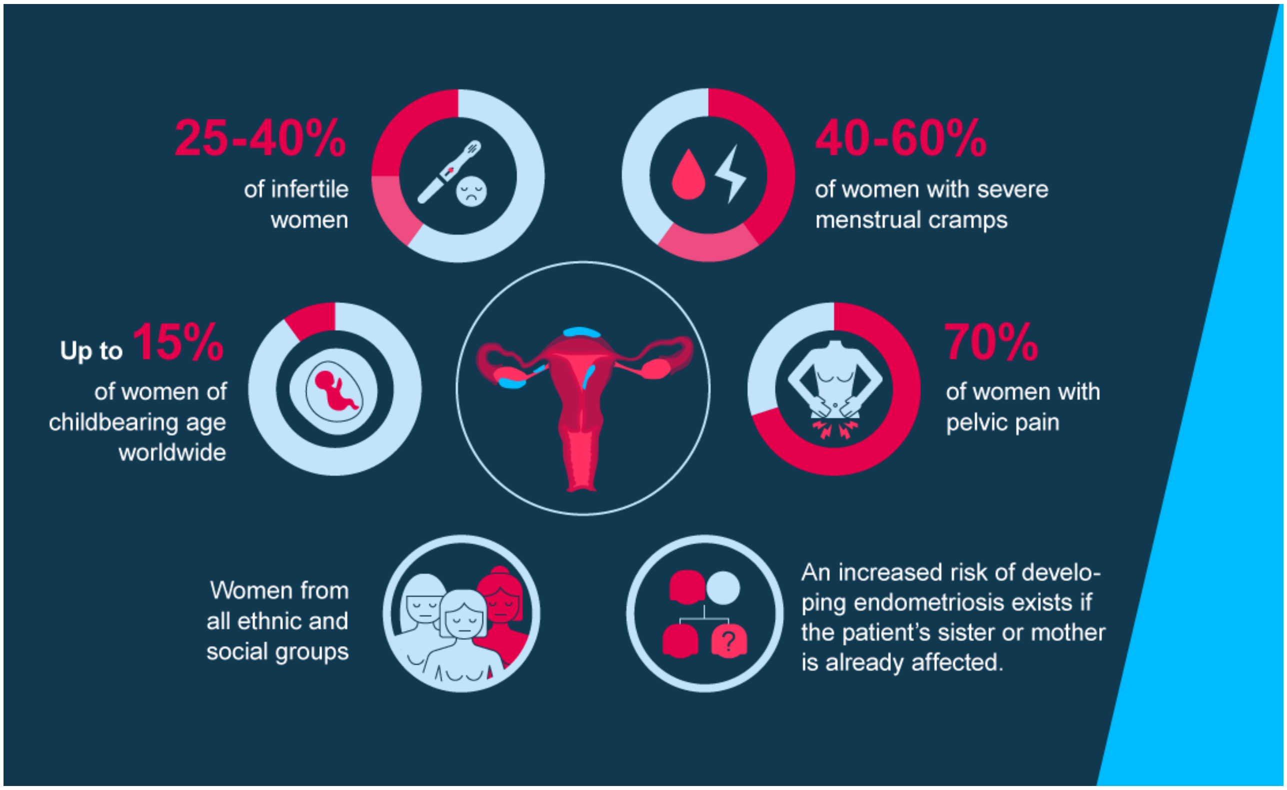
Finally, the present provision underlines the project development cannot be isolated from the powerful network of interlinked initiatives, thus cooperation and interchange are among the most reliable means to ensure an improved and accurate impact and value in the activities that the project aspires to implement. The project FEMaLe will systematically build upon recognised evidence, especially generated is the pan-EU panorama, and also interlink with pan-EU and UN pertinent services.

1. BACKGROUND

Revealed in 1860 by Karel Rokitansky, this disease is still not accurately understood. Questions concerning how it appears, what triggers it and notably how to prevent it persist unanswered. Endometriosis is an illness affecting women, in which the endometrium (the tissue that lines the inside of the uterus or womb) is present outside of the uterus. Endometriosis most frequently occurs in the lower abdomen or pelvis, but it may ensue anywhere in the body. Symptoms of endometriosis comprise lower abdominal soreness, pain with menstrual periods, pain during sexual intercourse, and trouble becoming pregnant. Oppositely, certain women with the disorder may not reveal any symptom. [3] The precise number of women suffering from endometriosis is undetermined. However, it is estimated that 10% of women worldwide are affected (actually an estimate that has historically ignored adolescent girls and trans, non-binary and intersex individuals), an estimated 200 million worldwide. [4] Endometriosis is seen in in a very variable proportion of women, depending on the region in the world, their medical history (e.g., surgery for pelvic pain, for infertility, etc.). [5] The exact occurrence is unknown since the diagnosis requires laparoscopy, a surgical diagnostic procedure used to examine the organs inside the abdomen with a laparoscope (small camera), to visualize and biopsy endometriosis lesions. Diagnostic delays occur as numerous symptoms are highly comparable to other frequent health disorders. Endometriosis relates with a variety of symptoms, such as period-related pain (dysmenorrhoea), period-related or cyclical urinary symptoms, etc. [6]

Figure A shows a global overview on the current understanding on endometriosis. [7]

Figure A – Who is affected by endometriosis?



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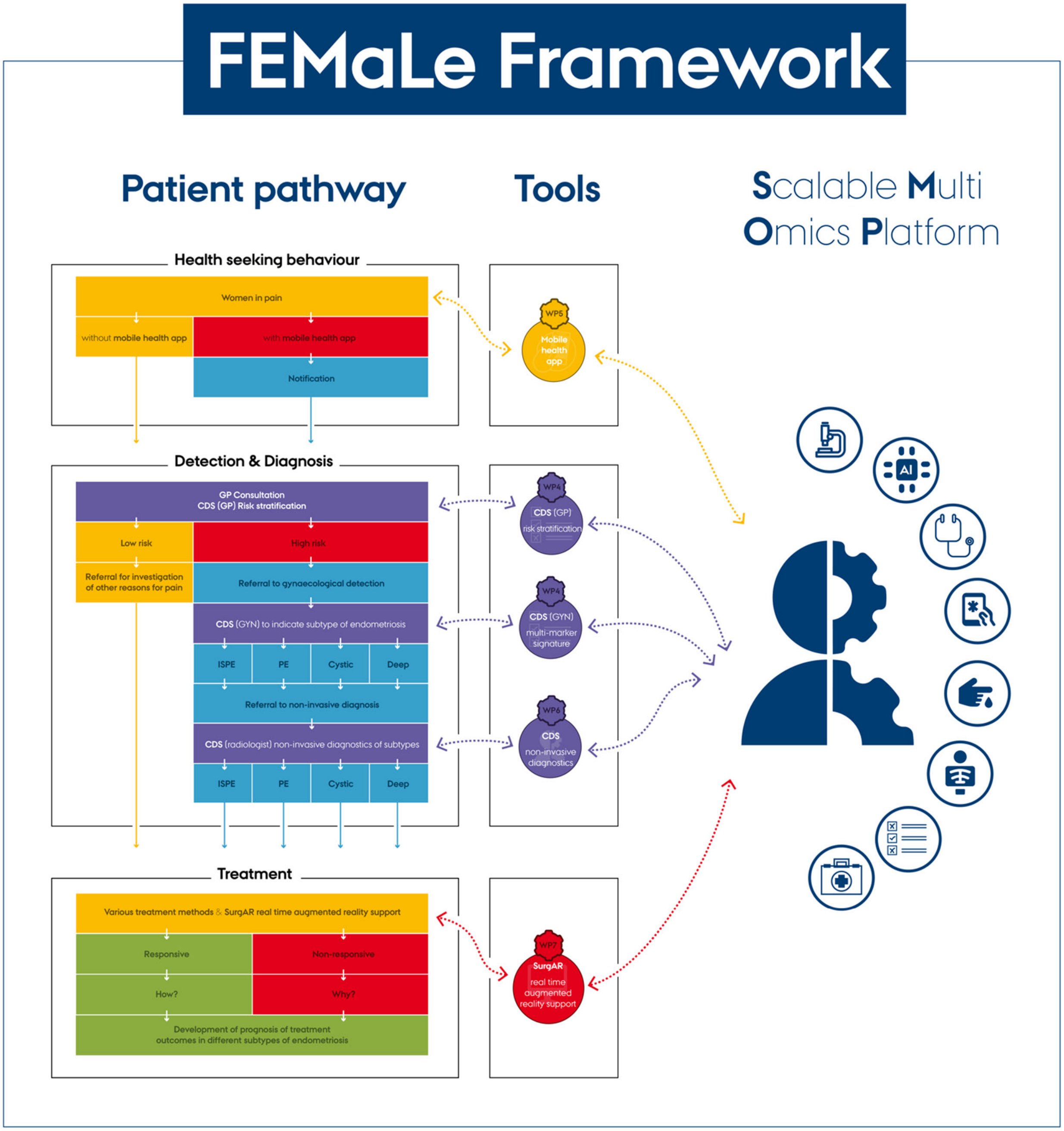
[3] ESHRE guideline for the diagnosis and treatment of endometriosis, Kennedy S, et al. in *Human Reproduction*, June 2005.
[4] Endometriosis Awareness 2021, endometriosis.org, 2021.
[5] The frequency of endometriosis in the general and selected populations: A systematic review, Parazzini et al. in *Journal of Endometriosis and Pelvic Pain Disorders*, July 2020.
[6] Avoiding diagnosis delays in endometriosis, the Medical Defence Union (MDU), October 2020.
[7] Who is affected by endometriosis?, Bayer AG Pharmaceuticals, 2021.

The project FEMaLe builds on the growing need to reduce diagnostic delay and introduce non-invasive, definitive diagnostic methods for endometriosis, facilitated by precision medicine and patient-shared data through a Scalable Multi-Omics Platform (SMOP). The project concept is driven by megatrends (increasingly ageing population, unharnessed health data value creation, and diagnostic delay) and will reconceptualise 'P4 Medicine' to deliver a comprehensive model for personalised early risk prediction, prevention and intervention for people with endometriosis, based on big data technologies. This will drive discoveries in endometriosis treatment to deliver digital therapies and improve quality of life.

Figure B – Framework of the project FEMaLe



1.1 The European landscape

1.1a – Societal drivers

Dr Chrysoula Zacharopoulou [8], Founder of "Info-Endometriose", is a French gynaecologist highly engaged in the endometriosis nexus [9], now Member of the European Parliament for France, stated "*Contrary to popular perception, menstrual health is not just a "women's issue" but an issue of gender equality and social justice.*" [10]

Though highly driven by pioneering technologies such as Artificial Intelligence, the project FEMaLe is organically driven by social sciences and humanities criteria. For instance, the consortium recognises societal factors, such as clinical gender bias and inequities in the treatment of pain based on gender, may contribute to the under-prioritization of endometriosis research funding. In particular, the project develops a framework for inclusiveness and diversity in societal engagement under the header of healthcare-related ethics, gender equality and inclusion, RRI and Open Science. Citizens are engaged and involved in all pertinent activities for the development of anticipated outcomes, in particular throughout WP2 to WP5 and WP8. FEMaLe builds upon participatory process across all WP to ensure relevant stakeholders' needs and requirements are met. This is done by actively involving end-users, individuals, groups and communities to ensure taking their perspectives into account, values, beliefs and knowledge into consideration and improve their compliance regarding the use of technology. In broad terms, the targeted audience incorporates unorganized public globally. The unorganized public is subject to information campaigns and educational programmes per scheduled activities within WP9. When activating the unorganized public, a balanced representation of principles, education and cultural background is ensured considering distributed socio-demographic diversity. In formal engagement activities and processes, partners practise a random selection strategy to account for gender, seniority, occupation, education and geographical diversity.

1.1b – The EU research arena

EU-funded researchers are exploring pathways to tackle endometriosis, such as studying the molecular mechanisms underlying endometriosis [11], or identifying simpler diagnosis and potentially more effective treatments [12], or tackling endometriosis diagnostic delay [13], etc., in the promise of achieving new therapy opportunities for the millions of women around the world who suffer from this chronic inflammatory disease. A vast series of developments are currently in progress at pan-European level either tackling endometriosis specifically or indirectly via possible examining and linking with possible consequential symptoms such as infertility. For example, the French National Institute of Health and Medical research (Inserm) develops in the fertility nexus.[14] Research activities also address the challenges inherent to modelling endometriosis, which are linked to its multifactorial nature, a context which impedes the recreation of its pathology and the recognition of clinically applicable metrics to evaluate medication.[15] A significant number of initiatives aim at determining the triggers and drivers of endometriosis to assist expand our knowledge of its diverse forms and to support inform innovative therapies, medication and non-invasive biomarker discovery programmes.[16]

Remarkably, the scientific community are also driven with the motivation to recognise a common framework for the development of research and innovation actions at international level. A recent international consensus development study concludes that "*Using robust consensus science methods, healthcare professionals, researchers and women with endometriosis have developed a core outcome set to standardise outcome selection, collection and reporting across future randomised controlled trials and systematic reviews evaluating potential treatments for endometriosis*." [17]

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[8] Chrysoula_Zacharopoulou, Member of the European Parliament for France, 2021

[9] Chrysoula Zacharopoulou's research and affiliations, researchgate.net, 2021

[10] Endometriosis: an invisible and neglected disease that affects 180 million women, Zacharopoulou C., womendeliver.org , April 2018

[11] Molecular Mechanisms of Endometriosis (MOMENDO), project funded by the H2020 Programme (ID: 691058), 2016-2019

[12] Non-invasive clinical markers for diagnosis of endometriosis (GLYCOMENDO), project funded by the H2020 Programme (ID: 843862), 2019-2021

[13] Translational Research on Endometriosis (TRENDO), project funded by the H2020 Programme (ID: 101008193), 2021-2025

[14] Fertility and endometriosis: a research update from Inserm, Inserm press office, April 2019

[15] Fertility and endometriosis: a research update from Inserm, Inserm press office, April 2019

[16] WERF Endometriosis Phenome and Biobanking Harmonisation Project (EPHect), World Endometriosis Research Foundation, 2013-2021

[17] A core outcome set for future endometriosis research, Duffy JMN et al. in *British Journal of Obstetrics Gynaecology*, March 2020

1.1c – National initiatives

In addition, a number of national initiatives are takin place to raise awareness but also to structure a roadmap towards effective pathways for better understanding the condition and therefore provide accurate answers. For instance, the French Minister for Solidarity and Health Dr Olivier Véran recently promoted a strategy that will revolve around "*five major topics in order to get to grips with the fight against this disease in the most complete way possible, working in improving its detection, patients' care pathways, and treatments by reinforcing medical research and communication to make this disease known*". [18] [19] A survey was recently conducted in in Germany, Austria and Switzerland considering endometriosis is a significant encumber for healthcare and social security systems. The study tackles specifically quality indicators for the treatment of the disorder. [20] The table 1 (below) proposes a series of national initiatives offering possible synergies with the project.

Table 1 – National panoramas on endometriosis and possible synergies (non-exhaustive)

Country	**National initiative**	**FEMaLe contribution areas**
Denmark	Endometriosis Society *(Endometriose Foreningen)*	Project deliverables from WP1 to WP9
Denmark	Easter Run (5 km), Sports Universe	WP9
Denmark	Meet FEMaLe on Facebook	WP9
Hungary	Endometriosis Society *(Együtt Könnyebb Női Egészségert Alapítvány)*	Project deliverables from WP1 to WP9
Hungary	Lucy App (menstrual and fertility calendar)	WP5
Hungary	Endometriózis Magyarország (Facebook, 7790 people like this)	WP9
UK	Endometriosis UK	Project deliverables from WP1 to WP9
UK	Endometriosis.org (Global forum for news and information)	Project deliverables from WP1 to WP9
France	Conferences on endometriosis awareness in the Auvergne region	WP9
France	European Endometriosis awareness week	WP9
France	Endometriosis:creation	WP9
France	EndoFrance	Project deliverables from WP2 to WP9
France	Info-endométriose	WP9
France	ENDOmind	WP9
France	Fondation pour la recherche sur l'endométriose	WP2 and WP9
Latvia	Endometriosis Society (Latvijas Endometriozes biedrība)	Project deliverables from WP1 to WP9
Sweden	7th Society of Endometriosis and Uterine Disorders congress	WP9
Sweden	Instagram account, @endometriosdoktorn (Dr. Anna-Sofia Melin)	WP9
Sweden	The Endometrix Blog	WP9
Turkey	Endometriosis Society (*Endometriozis ve Adenomyozis Derneği*)	Project deliverables from WP1 to WP9
Turkey	Medical Park Hospital, Gynecology and Obstetrics Dept., Istanbul	WP3 and WP9
Norway	Endometriosis Society *(Endometrioseforeningen)*	Project deliverables from WP1 to WP9
Scotland	Endometriosis Friendly Employer campaign	WP9
Scotland	EXPPECT Endometriosis Service	WP3 and WP9
Serbia	Endometriosis Society (Žuto uže)	Project deliverables from WP1 to WP9

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[18] Endometriosis: a disease studied to be soon understood better, www.sortiraparis.com, March 2021

[19] Engagement of the French Ministry for Solidarity and Health regarding endometriosis, *Direction Générale de l'Offre de Soins* (DGOS), March 2021

[20] QS ENDO Real – A Study on the Reality of Care for Patients with Endometriosis, Zeppernick F. et al. in Geburtshilfe Frauenheilkd, February 2020

1.1d – Economics

FEMaLe proposes and extensive set of exploitation of results and among them businesses, either on one enhancement dimension, e.g., partners engaged in the project such as SurgAR, but also on other dimensions which are the potential for start-ups and acceleration processes.

The endometriosis market landscape must also be examined under frameworks encompassing healthcare-related ethics, gender balance and equality, RRI and Open Science, and to some extent inclusion as well, understood as the fair access to treatments via public healthcare services. The global endometriosis market is forecast to reach $ 2.42 Billion by 2026, according to a new report, driven by an increasing focus on clinical trial. [21] A geographical analysis shows Europe accounts for the largest number of clinical trials by region, with France accounting for the greatest number of clinical trials in Europe. By country, the United States of America (USA) account for the largest number of clinical trials.

The endometriosis market is a fragmented market with top five companies accounting for only 40% of the market share: Pfizer, Bayer, Eli Lilly, AstraZeneca. Partnerships and acquisitions are the key strategies followed by the major companies in the industry. Some of the recent industry developments include Pfizer has received US FDA approval for Depo-Provera for treatment of endometriosis. AbbVie has received U.S. FDA Priority Review for Investigational Oral Treatment Elagolix for the Management of Endometriosis with Associated Pain. [22]

Pharmaceutical giants are also exploring cooperation mechanisms such as Evotec and Bayer who are developing joint efforts to generate efficient, non-hormonal endometriosis therapies. Their work is based on creating small molecule antagonists which block the P2X3 receptor, known to hold a substantial part in soreness instigated by endometriosis. [23] The momentum for a pioneering therapy in endometriosis within this wide-ranging alliance outline evidently embodies a role model for other spheres of significant unmet therapeutic need where, through increased research and development proficiency, more achievements on goal are created to advance pipeline yield.

Innovation pathways are on the rise and brought to the public attention via a variety of channels, such as for instance the recent EU Prize for Women Innovators 2020 for Cécile Real (France), co-founder and Chief Technology Officer of Endodiag [24], a company which develops early diagnosis solutions for endometriosis, and also takes part in endometriosis research by developing diagnosis solutions focused on patient screening and individual endometriosis characteristics. Endodiag is comprehensively driven by human values and consideration of the individual.

Innovation is brought to a vast number of dimensions from tech-based approaches or more conventionally drug therapies. Laboratoires Pronutri (France) recently introduced a new complex showing a 66.1% reduction in pain in women with endometriosis of AFSr (see footnote 25) stages II, III and IV in a maximum of four months (clinical study published in Minerva Ginecologica, October 2020 and Genesis, June 2020). [25] The company states 91.3% of women regain their quality of life.

Regarding tech, the attractiveness of fertility tracking apps such as 'Clue' and 'Ava Health' that initially motivated the attention of worldwide investors in 'femtech' startups catering for a number of disregarded women's needs regarding certain disorders. However today, as the marketplace expects to be worth a projected $ 48 Billion by 2025, attention is expanding in new fields exceeding fertility tracking and into areas such as endometriosis. Anya Roy, cofounder of Syrona Women (research-based femtech), declares *"[Investors are] looking for the next big thing in femtech*", pointing out to two predominantly spheres which are under scrutiny: menopause and endometriosis, suggesting these conditions are long ignored by the healthcare arena. [26]

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[21] Europe endometriosis market and competitive landscape, Research and Markets, April 2020
[22] Endometriosis Drug Market, Size, Share, Outlook and Growth Opportunities 2019–2026, Naveen Kumar, Medium, March 2020
[23] Excelling Together for the Benefit of Women Suffering from Endometriosis, Bayer-Evotec Strategic Alliance, April 2020
[24] EU Prize for Women Innovators 2020, September 2020
[25] Endometriosis : innovation in the reduction of the main disabling symptom, Sandra Laplane, in *Nice-Matin*, March 2021
[26] 'Femtech' moves beyond the fertility app, Amy Borrett, sifted, March 2020

1.2 Project FEMaLe

The future of advanced predictive models helping people with complex multifactorial diseases involve big data analytical tools capable of analysing large populations and more shared decision making.

The framework 'P4 Medicine' (predictive, preventative, personalized, participatory) was developed to detect and prevent disease through close monitoring, deep statistical analysis, biomarker testing, and patient health coaching to best use the limited healthcare resources and produce maximum benefit for all patients. However, we have seen only few feasible examples over the past 10 years. The project 'Finding Endometriosis using Machine Learning' (FEMaLe) project revitalises the concept to develop and demonstrate the *Scalable Multi-Omics Platform* (SMOP) that converts multi-omic person population datasets into a personalised predictive model to improve intervention along the continuum of care for people with endometriosis. The project designs, validates and implements a comprehensive model for the detection and management of people with endometriosis to facilitate shared decision making between the patient and the healthcare provider, enable the delivery of precision medicine, and drive new discoveries in endometriosis treatment to deliver novel therapies and improve quality of life for patients.

The project relies on participatory processes, advanced computer sciences, state-of-the-art technologies, and patient-shared data to deliver:

a) mobile health app for people with endometriosis;
b) three clinical decision support (CDS) tools for healthcare providers (risk stratification tool for general practitioners, multi-marker signature tool for gynaecologists, and non-invasive diagnostic tool for radiologist etc.), and;
c) computer vision-based software tool for real time augmented reality guided surgery of endometriosis.

Health maintenance organisations (HMO) expect to be able to reduce overall cost of treatment by at least 20%, while improving patient outcomes, using CDS tools. The SMOP is based on open protocol, embedded in all ethical and legal frameworks, to enable tailored and personalised usage to improve the lives of patients across Europe beyond the project period. FEMaLe is a prestige project for a range of precision medicine applications from novel R&D and improved clinical trials design through to practice-based CDS tools for use by healthcare providers and patients and augmented reality-based support tool guiding surgeons.

FEMaLe is a citizen-driven initiative, and civil society organisations present in the consortium (P6 and P16) secure solid and extensive engagement via commonly practiced channels (e.g., social media, awareness-raising events, etc.). Evidence-based public health campaigns and training programs for healthcare providers improve knowledge and address the stigma associated with endometriosis.

The project FEMaLe develops a framework for inclusiveness and diversity in societal engagement under the header of healthcare-related ethics, gender balance and equality, RRI and Open Science. Citizens are engaged and involved in all pertinent activities for the development of anticipated outcomes, in particular within WP2 to WP5 and WP8. FEMaLe builds upon *participatory process* across WP3 to WP8 to ensure relevant stakeholders' needs and requirements are met. This is done by actively involving end-users, individuals, groups and communities to ensure taking their perspectives, values, beliefs and knowledge into consideration and improve their compliance of using the technology. In broad terms the targeted audience incorporates unorganized public globally.

The unorganized public is subject to information campaigns and educational programmes per programmed activities within WP9. When activating the unorganized public, a balanced representation of principles, education and cultural background is ensured via distributed socio-demographic diversity. In formal engagement activities and processes partners practise a random selection strategy to account for gender, seniority, occupation, education and geographical diversity.

1.3 Societal impacts

A number of studies has revealed to what extent endometriosis and the remaining symptoms in the therapies aftermaths still impact the quality of life in women who has suffered with the disorder. A study engaging 931 women from Europe and the USA reveals endometriosis had impacted on work in 51% of them and in 50% on relationships at some point of their lifetime. Most reported occurrences were dysmenorrhoea, painful menstrual periods (59%), dyspareunia, painful intercourse (56%) and chronic pelvic pain (60%). Quality of life declined in all eight-scale profile of functional health and well-being (SF-36v2) compared with norm-based scores from a general US population. Multiple data variables analysis indicates that a series of co-morbidities, chronic pain and dyspareunia have an objective negative impact on both the physical and mental dimension of the SF-36v2. [27]

1.3a – Workplace

With an average time to diagnosis between 7 and 10 years and considering both direct and indirect costs, the annual national economic weight in terms of lost work, therapy and healthcare expenditures, the effective impact of endometriosis on work and employment is rather well estimated in a series of studies. [28] Key findings from a world-wide cross-sectional study and survey conducted in 2012 in Europe, UK and the USA show that the overall cost per woman with endometriosis per year is estimated 9.579,00 euros, considering the main part of expenses, e.g., 6.298,00 euros being correlated with employment leaves, with the financial weight of endometriosis being comparable or even higher than other chronic disorders such as heart conditions and diabetes. [29]

Remarkable initiatives highlight awareness-raising developments on the significance of endometriosis in the workplace, such as Endometriosis UK and the 'Endometriosis Friendly Employer' scheme to qualify employers to develop towards recognising and strengthening support for women with the disorder. Employers who engage in the programme assist break the taboo and stigma around endometriosis and provide improved employment environments where all employees are comfortable communicating about necessary practical adjustments. [30]

1.3b – Quality of life

Soreness considerably affects women's experience of endometriosis and therapies to tackle pain may not suffice to encompass all consequences in the medium and long term, and psychological intervention has been proven significant by a series of studies. [31] Key findings from qualitative data indicate that endometriosis effects negatively on women's lives in vast number of dimensions such as social life, social interactions and future plans, impacting women's subjective wellbeing, and that endometriosis substantially contributes to intensifying the risk of psychological comorbidities. [32]

Other initiatives reveal that anxiety, depression, poor sleep, Body Mass Index (BMI), education background, form of endometriosis, and dyspareunia have a causality effect on women's sexual function (SF). In a study, four major drivers had above average scores in reducing the SF of endometriosis patients: sleep quality, anxiety, pelvic soreness, and depression. [33] The incidence of comorbidities is a key component which occasionally turns early diagnosis challenging. Healthy lifestyles e.g., correct BMI, frequent physical activity, quality of sleep, diet and nutritional regimes, and a correct pharmacotherapy and surgical therapy, visibly may improve the pain conditions and lifestyle of the patients.

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[27] The significant effect of endometriosis on physical, mental and social wellbeing, De Graaff et al. in Human Reproduction, October 2013

[28] The direct and indirect costs associated with endometriosis: a systematic literature review, Ahmed M. S. in *Human Reproduction*, April 2016

[29] The burden of endometriosis: costs and quality of life of women with endometriosis and treated in referral centres, Simoens S. et al. in *Human Reproduction*, May 2012

[30] Endometriosis Friendly Employer scheme, Endometriosis UK, March 2021

[31] Impact of endometriosis on quality of life and mental health, Facchin F. et al. in *Journal of Psychosomatic Obstetrics & Gynecology*, August 2015

[32] Examining subjective wellbeing and health-related quality of life in women with endometriosis, Rush G. et al. in *Health Care for Women International*, March 2018

[33] Influential factors on sexual function in infertile women with endometriosis, Youseflu S. et al. in BioMed Central Women's Health, May 2020

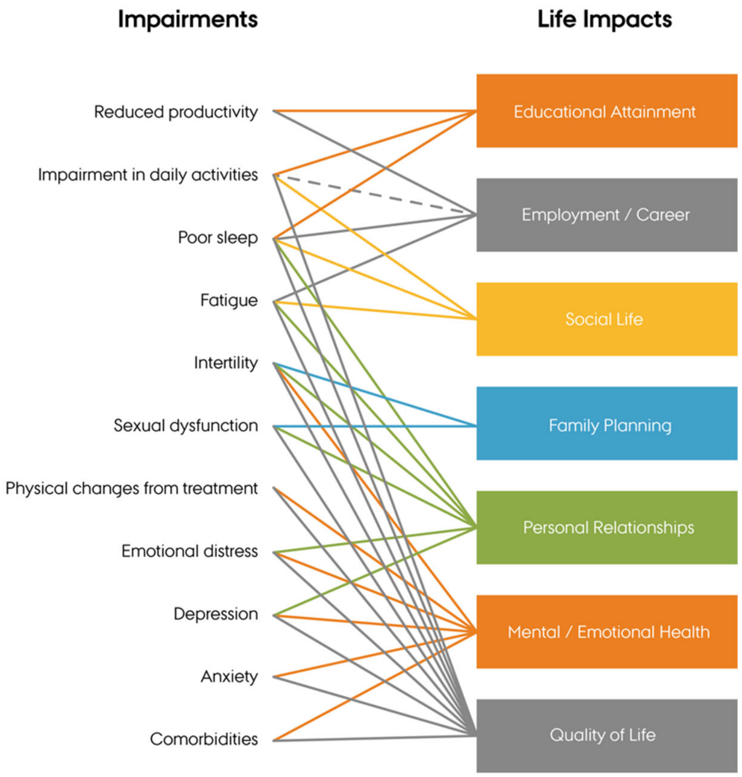

Figure C – Correlated impacts of endometriosis-associated impairments [34]

1.3c – Social, societal and political drivers

Experts from a series of specialties and backgrounds claim that expanding the social science of endometriosis is vital for two key objectives: what can be understood on how to improve the experiences of those affected, and what challenges can be recognised regarding politics and society more globally. Authors cross-examine the consequences of dismissing endometriosis as a 'woman's curse', consigning it to a cloudy realm of taboo which strengthens outdated beliefs of gender, sex, and gender expression, and to some extent, inclusion. Sociology have been the main field of proficiency driving social scientific studies of endometriosis, and, in recent years, a noticeable increasing body of work done in this area is observed, as well as a continuing broadening of the disciplinary arena of the work. The aforementioned contributions display in what manner social sciences and humanities studies can propose a fine-grain insight of how endometriosis impacts on people's lives, and also on broader interlinked inequalities, for instance a study applying the 'Endometriosis Health Profile-30' (EHP-30) [35] suggests local discrimination, taboos and international authority bodies influence the diagnosis and treatment of endometriosis. [36]

WP2 provides an actionable framework (knowledge and facilitators) to implement roundtable discussion and other types of even to tackle specifically policy changes to foster innovation in the field.

Studies on endometriosis, and more globally on healthcare and wellbeing matters observe a growing practice of cooperative mechanisms with the society at large, engaging and involving a variety of key actors, following Responsible and Research Innovation (RRI) recommendations, and the EC has been a key driver on this matter when considering finding schemes frameworks. [37] The project FEMaLe develops a framework for inclusiveness and diversity in societal engagement under the header of healthcare-related ethics, gender balance and equality, and RRI. Regarding RRI specially, WP2 generates a gender-balanced focus group comprising a vast variety of health professionals, educators, youth representatives and menstrual health activists, to contribute inclusively to the project development. [38]

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[34] Impact of Endometriosis on Life-Course Potential: A Narrative Review, Missmer A. et al. in International Journal General Medicine, January 2021

[35] Development of an endometriosis quality-of-life instrument, Jones G. et al. in Obstetrics & Gynecology, August 2001

[36] Quality of life measurement in women living with endometriosis, discoversociety.org, June 2020

[37] Responsible research & innovation, European Commission, 2014

[38] Responsible research and innovation: from science in society to science for society, with society, Owen R. et al. in Science and Public Policy, December 2012

2. EUROPE IN A CHANGING WORLD

WP2 main aim is to provide a comprehensive framework to secure the project development and results are aligned with the European Union idea of an inclusive, innovative, and reflective society. [39]

The WP generate reflection activities and debates on citizens needs and realities, values and expectations regarding innovation, policies, and public affairs, and to a certain extent research and development. Key areas connecting social sciences and humanities key principles, ethics, gender approaches, inclusion, RRI and Open Science are explored to develop a transparent and ethical framework to contribute to early diagnosis and treatment of endometriosis under the perspective of social sciences and humanities, e.g., life course public health, culturally sensitive population health programmes, community-based participatory research, bioethics, inequalities, public engagement, etc.

All in all, WP2 aim at overcoming EDTE barriers related to the society at large, to foster effectiveness in citizen-centered innovation, transparency, and participation.

2.1 IIRS enabler

The FEMaLe consortium recognises exploring and finding pathways for early diagnosis and, to some extent, therapies for endometriosis constitute a social challenge, and aim at incorporating pathways for the lessening of inequalities and social exclusion.

To that end, the project development is built around new approaches of innovation processes which provide participative environments and citizens engagement. The FEMaLe consortium recognises supporting IIRS "is a prerequisite for a sustainable European integration."

In addition, activities are organised to ensure interlinking relevant EU policies which are significant for the inclusive development of solutions, especially 'Europe 2020 – for a healthier EU' [40], the European Strategy on Bioeconomy [41] and the European Digital Strategy [42], to name but these few.

In addition of the seven 'EU2020 Strategy' flagship initiatives [43], the project FEMaLe integrates key recommendation from the following three pillars: the 'Innovation Union', the 'Digital agenda for Europe' and the 'Agenda for new skills and jobs'.

The project FEMaLe also incorporates the national dimension of IIRS. The table 2.1a (below) proposes a series of national initiatives on IIRS offering possible synergies with the project.

The international dimension as well is also explored by the consortium to identify key enabling recommendations to enhance further the global impact, transferability and IIRS component of the project.

These dimensions are represented in the project via the WHO strategy on research for health [44] and the WHO Global Strategy on Digital Health. [45]

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[39] Europe in a changing world - Inclusive, innovative and reflective societies (IIRS), Horizon 2020 Programme, EC, May 2014

[40] Europe 2020 – for a healthier EU, EC, June 2020

[41] European Strategy on Bioeconomy, EC, February 2012

[42] European Digital Strategy, Horizon 2020 Programme, EC, 2014

[43] European Digital Strategy, Horizon 2020 Programme, EC, 2014

[44] WHO strategy on research for health, change

[45] WHO Global Strategy on Digital Health, change

2.2 Good practices

IIRS approaches brings together a vast diversity of individuals addressing emergent and societal transformations towards more inclusion and participative processes. Engaging people from under-represented backgrounds, gender balance, good governance are only a few amongst the most compelling ones. A number of good practices propose developments according to the needs of these specific challenges and of the overall objectives of reflexivity, inclusiveness and innovation characterizing the EU agenda on IIRS. Citizens' engagement contribute to the dialogue about shared values and principles, and their adaptation to the changing needs of plural societies.

Project:	**Grant agreement ID:**	**Start date:**	**End date:**
OpenGovIntelligence	**693849**	**1 February 2016**	**31 January 2019**

OpenGovIntelligence [46] IIRS dimension is centered in Linked Open Statistical Data (LOSD). The project proposes a framework to develop a co-creation model and demonstrates how a systems approach towards Linked Open Statistical Data (LOSD-driven co-creation and innovation allows new and innovative services to be engineered in a way that allows for higher levels of public value to be created by encouraging co-creation. This aim is achieved by proposing general guidelines for public administrations, citizens and businesses for opening up and exploiting LOSD in a way that addresses the relevant challenges and facilitates the co-creation of innovative data-driven services through the direct participation of citizens and businesses.

Project:	**Grant agreement ID:**	**Start date:**	**End date:**
STARDUST	**774094**	**1 October 2017**	**30 September 2022**

STARDUST [47] IIRS dimension focuses on citizen-oriented cities and citizen's governance. The STARDUST project offers holistic approaches for transforming carbon-based cities into smart, highly efficient, intelligent and citizen-oriented cities, or "innovation islands". These approaches include both technical and non-technical solutions. 'Living Labs' activities develop in 'Lighthouse' cities and evolve around the concept of 'Smart Innovation Ecosystems', aiming at a higher degree of citizens' engagement and participation towards innovation. The project aims to improve a city's competitiveness, make a sustainable use of resources and engage in innovative and efficient behaviours and attitudes; all this, in order to support smart decision-making.

Project:	**Grant agreement ID:**	**Start date:**	**End date:**
Pharmawizard	**711824**	**1 December 2015**	**31 May 2018**

Pharmawizard [48] IIRS dimension develops on helping citizens to increase their knowledge about healthcare and to save money and time when purchasing drugs and in general any medication sold in a pharmacy. The project fosters the interaction of citizens and healthcare businesses with public administrations services, via mobile technologies, given the emerging new dynamics of change and opportunities, a unique and innovative mobile solution with a considerable novelty in the Health and Pharma ecosystem. The facilitates interactions between citizens and healthcare companies with government-operated healthcare systems (specifically services and official data and open data related to drugs, pharmacies, biomedicals and any consumer health product).

Project:	**Grant agreement ID:**	**Start date:**	**End date:**
IN LIFE	**643442**	**1 February 2015**	**31 January 2018**

IN LIFE [49] IIRS dimension directs interoperable, open, personalised and seamless ICT services. The project on existing knowledge and tested Active and Assisted Living (AAL) technology/services to support home activities, communication, health maintenance, travel, mobility and socialization, with novel, scalable and viable business models, based on feedback from large-scale, multi-country pilots. These interoperable services are integrated into an open, cloud- based, reference architecture, and tested in six Europe-wide pilots. IN LIFE is carried out with the perspective of comprising a range of different user profiles, considering also social-societal aspects (such as social inclusion or different educational backgrounds).

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[46] OpenGovIntelligence (ID: 693849), Horizon 2020 Programme, February 2016 – January 2019
[47] STARDUST (ID: 774094), Horizon 2020 Programme, October 2017 – September 2022
[48] Pharmawizard (ID: 711824), Horizon 2020 Programme, October 2017 – September 2022
[49] IN LIFE (ID: 643442), Horizon 2020 Programme, February 2015 – January 2018

3. IIRS FRAMEWORK

WP2 ideates and constructs the ethical framework of the project via structured workshops to debate upon the chosen key questions: principles, outcomes, and integrity. Principles and integrity tackle for both individuals and institutional developments, outcomes regarding the project's results. WP2 explores social sciences and humanities key principles, ethics, gender approaches, inclusion, RRI and Open Science as a privileged approach to encourage professionals to behave as anticipated by the society at large and their peers. Also, WP2 examines the complex interaction of policies and morality, and the insufficiency of policy frameworks as an ethical system. WP2 guidelines assist all participants make their research data findable, accessible, interoperable, andreusable (FAIR), to safeguard it is soundly managed.

3.1 Principles

In this dimension of examinations, partners are expected to structure an ethical practice to:

a) identify ethical challenges and take proper action;
b) inform project participants of ethical concerns affecting patient care;
c) practice known code of ethics of the healthcare arena;
d) appraise outcomes of interventions to encourage ethical practice.

Principles, simply delineated, are principles which defines what is expected in terms of “right and correct and wrong or incorrect” regarding conduct. For instance, in the EU, professionals are held to ethical principles comprised within the “Principles of European Medical Ethics”. [50] Principles and ethical practice are incorporated into all aspects of the project development.

Naturally, we expect national codes to prevail above pan-EU recommendations and suggest taking the opportunity of project FEMaLe to explore pathways for alignment and improvement of current practices.

3.2 Outcomes

This is evaluating the results of the action with a holistic approach at each step of the process, considering all possible outputs (including collaterals). Likely the evaluation processes of research and innovation action initiatives targeting individuals, practices to resolve the project’s IIRS objectives are evaluated and measured in terms of their effectiveness to resolve the different segments of the IIRS dilemma, e.g., ethics, gender, inclusion, RRI and Open Science.

To that end we propose to identify and characterise a set of criteria for each of the aforementioned segments and assess outcomes via questionnaires and interviews. We propose to determine these criteria via multi-actors and citizens-driven approaches formatted in small groups webinars.

To that end, each partner identifies a group of 30+ actors from all areas pertinent to the project and engage them in the process to generate the criteria, IAAD proposes to generate a specific action plan [51] to implement these activities, that could be scheduled for May and June 2021. Consequently, evaluation grids are generated and implemented in a structured way.

To prepare this activity we propose to recognise key criteria recommended by the EC in all segments, for instance, and maybe more particularly, the Monitoring the Evolution and Benefits of Responsible Research and Innovation (MoRRI) [52], because it gathers a vast set of criteria comprising gender and societal aspects, Citizen Science questions, participatory processes, public engagement, open access, etc.

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[50] Principles of European medical ethics, European Council of Medical orders, January 1987

[51] File “D1.2_Action_Plan_FEMaLe_Rev.docx”

[52] Monitoring the Evolution and Benefits of Responsible Research and Innovation (MoRRI), the EC, October 2018

3.3 Integrity

The proposed approach on the research Integrity dimension of project FEMaLe, applicable to the way research and innovation action is conducted is to allows all participants to have confidence, substantial responsibility and trust in the practices and the outcomes of the activities. It equally relates to the scientific integrity of all implemented activities, and to the professional integrity of all participants, regardless their roles in the research and innovation action value chain. [53]

In addition, it is pertinent to embed the concept of integrity beyond its pertinence in the research and innovation sphere and ensure alignment with the reference framework of the European Horizon 2020 Programme, the EC flagship programme in that sphere. On the matter in hand, the programme is indeed structured on a vast number of European and international founding texts issued by a series of prominent bodies such as Science Europe, the OECD, the WHO, to name but these few.

3.4 National initiatives

The table 2 (below) proposes a series of national initiatives offering possible synergies with the project.

Table 2 – National panoramas on IIRS and possible synergies (non-exhaustive)

Country	**National initiative on IIRS**
Denmark	SUPER MORRI
Denmark	*HEIRRI (Higher Education Institutions & Responsible Research and Innovation)*
Denmark	GRACE (Grounding RRI Actions to Achieve Institutional Change in EU Research Funding and Performing Organisations)
Denmark	The Danish Code of Conduct for Research Integrity
Hungary	Hungarian National Social Inclusion Strategy II
France	National Charter for Research Integrity
France	The HRS4R Label Sorbonne University's policy for recruitment
Latvia	Background Report – Specific Support to Latvia
Sweden	VA (Public & Science), RRI Tools
Sweden	Responsible Research
Sweden	Act on responsibility for good research practice (2019:504)
Norway	Government's Action Plan for Business and Human Rights
Norway	The white paper 'Digital Life – Convergence for Innovation'
Norway	Research Council's definition of responsible research and innovation
Serbia	Intersection. Centre for Science and Innovation.

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[53] Advancing research integrity practices and policies, Science Europe, February 2017

4. DRIVERS FOR IIRS

WP2 tackle specifically identified focus areas: ethics, gender and inclusion, RRI and Open Science, and links with the EU's agenda on IIRS.

To some extents it also links with the ethical framework of the Horizon 2020 Programme, but not organically, this framework is under the strict supervision of a dedicated focus group, possibly under WP10 'Governance'.

The project FEMaLe Advisory Boards on ethics, the Ethics Advisory Board (ETAB) is led by IAAD (P10), and to facilitate simplicity, we propose to embed all 5 IIRS focus areas in the ETAB.

The ETAB would meet regularly during the year to actively contribute to the project development via sharing recommendations, steering activities, engaging external experts to provide insights on specific thematic, and beyond.

4.1 Ethics

Besides already mentioned key text on the endometriosis dimension (e.g., ESHRE guidelines, etc.), we trust paramount to also mention and emphasise on the pertinence of the declaration of Helsinki by the World Medical Association (WMA) in assisting determining an ethical framework for medical research involving human subjects [54] which last update is dated October 2013, during the 64th WMA General Assembly, held in Fortaleza, Brazil.

We propose to generate the 'Ethical Charter for Endometriosis', which is to be a distinct and comprehensive set of ethical principles expressly adjusted to the dimension of endometriosis, considering the unique characteristics of the disorder.

To that end, IAAD will conduct a comprehensive data collection via a variety of instruments such as text mining, Delphi method etc., and organise 5 webinars, in April, May and June (one for each selected IIRS thematic), with a panel of individuals, among which citizens and actors of the endometriosis arena (e.g., medical staffs, researchers, businesses and public health bodies).

The main outcome of these meetings is to establish the aforementioned list of ethical principles.

4.2 Gender and inclusion

The actual prevalence of endometriosis in the general population is unknown due in part to the societal normalization of pain and stigma around menstrual issues, but there is also a lack of disease awareness among patients, healthcare providers, and the public.[55]

Societal factors, such as clinical gender bias and inequities in the treatment of pain based on gender, have been well documented and may contribute to the under-prioritization of endometriosis research funding. The gendered prejudices, mistaken belief, bias, and merely poor information which are inherent to endometriosis have constantly frustrated a considerable number of women in their attempts to access therapy.

Endometriosis is specific for the biological FEMaLe gender, due to the central role of the endometrium and the ovarian-uterine-cerebral axis. Moreover, gender is of central importance in special cultural societies, where FEMaLe sexuality is suppressed, and pain problems related to the menstrual cycle are neglected.

In addition, medical treatment of endometriosis symptoms often involves oral contraceptives, and early studies indicate that this conflicts with the traditional power structure of the male-dominated families.[56] Research conducted are sparse on this topic, but it is suspected that a large number of individuals may be left without diagnosis and effective treatment.

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[54] WMA Declaration of Helsinki, World Medical Association, October 2013

[55] Prevalence of newly diagnosed endometriosis in women attending the general practitioner, Ferrero S. et al. *in International Journal of Gynecology & Obstetrics*, October 2010

[56] Contraception in ethnic minority groups in Bedford, Beard P. in *Health Visit.* , August 1982.

The consortium FEMaLe specifically reaches out to these groups with the newly developed CDS tools for early diagnosis and to include their experiences in the development of the project concept. The consortium trust to improve the acceptance of effective medical and surgical treatment, at best by increasing understanding in local communities.

Special efforts are needed to fulfil this aim as medical staff members of Western origin are easily misunderstood in ethnic minorities, due to lack of understanding of the cultural and religious context, especially when problems relating to sexual and reproductive function are of concern. In FEMaLe, we approach this potential problem by involving an endometriosis-specialised gynaecologist Negin Jaafar Nasrallah Negin from Aarhus University Hospital (P2). Her background in Middle East culture and detailed knowledge of Kurdish, Farsi/Persian, and Arabic languages and broad social media contacts allow us to introduce a subspecialist in marginalized ethnic women's sexual health problems.

Also, lesbian and bisexual women's health is critically understudied, [57] and it seems to differ a lot from heterosexual individuals in relation to health risks and healthcare use. The data available indicate that these women suffer from endometriosis to the same extent as heterosexual women,[58] but diagnostic delay as well as availability and acceptance of medical and surgical treatment are largely unknown.

It is of paramount importance that FEMaLe reaches these vulnerable and marginalised groups and eliminate their obstacles in diagnosis and treatment. To assist with this, Gitte Bennich from the Copenhagen Capital Women's Clinic is affiliated to the project team. Gitte Bennich is active in the Danish LGBTQ Society and has a strong European network within sexual minorities.

The term 'gender dimension', as developed within the European Commission, means the integration of sex and gender analysis into research. The partners are fully aware of the importance of gender issues. The project complies with all relevant acts and directives at national, European and international level such as Council Directive 76/207/EEC [59], the Universal Declaration of Human Rights and as outlined in the EU gender equality law. As an active supporter of such acts, the project consortium integrates gender dimension recommendations and strategies to promote the active involvement of project personnel with fair distribution between the genders at both management and research levels. The project framework abides the latest guidelines on gender equality.

All activities planned i the project respect to gender. This includes consideration of gender perspectives in all stages of planning, implementation and evaluation of activities. FEMaLe is a gender-neutral initiative and secures activities implemented are driven to bring contributions to the eradication of gender discrimination in healthcare environments.

The consortium actively promotes and commits to furthering the careers of women in science, technology, engineering, maths and medicine, practicing learnings from the Athena SWAN gender equality scheme, now widely adopted in the UK. In addition, the project provides efforts to contribute to the enhancement of the Athena SWAN system, to tackle the paucity of research on the design and implementation of Athena SWAN action plans. The project activities forever support the women’s assertion and their role played in the healthcare value chains.

WP2 organises and implements workshops with women active in the entire healthcare arena. Based on the cooperation of all partners involved in the project, a guide of good practices is compiled to contribute to the reduction and, hopefully, eradication of gender discrimination in the healthcare arena. It is important to ensure that men and women are equally represented within groups of stakeholders and to ensure that their respective needs and interests are considered.

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[57] Lesbian and bisexual women's health is critically understudied, Eliason MJ.. in *British Journal of Obstetrics Gynaecology*, January 2017

[58] Lesbian and bisexual women’s gynaecological conditions: a systematic review and exploratory meta-analysis, Robinson K. et al. in *British Journal of Obstetrics Gynaecology*, November 2016

[59] Council Directive 76/207/EEC, The EU Law, February 1976

The partner countries within the project have different experiences about healthcare ethics, RRI, and gender approach. For this purpose, the project provides impetus for exchanges of good practices concerning the insurance of project ethics framework. Therefore, a constant communication among partners is ensured to enable sharing cultural experiences of their own countries. That will provide a solid framework of the project and allow to formulate models of good practices and possible directions for implementing these principles.

4.3 Responsible Research and Innovation

Responsible Research and Innovation (RRI) approach aims at improving the alignment between both the research sphere and its results, with the values, needs and expectations of the society globally. [60]

The consortium aims at providing a shared vision and characterization of RRI applicable to the endometriosis arena and proposes a comprehensive framework for its practice under research and innovation action (RIA) systems at pan-European level. The project FEMaLe builds the case that RRI and endometriosis are organically interlinked and must be acknowledged as a multi-disciplinary and multi-actor's strategy to promote mutual answers.

The co-creation and co-production of research and innovation outcomes provide emphasis on the endometriosis societal challenges, for which all members of the society share responsibility. RIA processes must be more responsive, reactive and flexible to tackle the aforementioned challenges. This ambition suggests, but not only, the practice of more comprehensive foresight and impact appraisals regarding pioneering technologies beyond their projected market-benefits and risks. The social benefits of these technologies must inclusively engage a large public and promote extensively mutual community values. To achieve this aspiration, a global paradigm shift must be implemented in a series of areas, namely in innovation and policy frameworks, and break away from giving prominence on the mentioned key technologies towards needs and results oriented strategies.

WP2 aims to map the RIA panorama and ecosystem addressing endometriosis in the project territories to generate an overview of the landscape, to identify relevant actors, and to recognize the inclusion of RRI in local and regional policy frameworks. The mapping practice is organized to provide prominent contributions to the technical and development WP (WP3 to WP8), via delivering an accurate clear set of information of the current background considering the actors and the relationships between them, enablers, obstacles, vulnerabilities, etc., and also policy instruments. WP2 activities aims to deliver intelligence to generate self-sustaining RIA ecosystems with the substantial integration of RRI models.

The mapping process is structured with the support of evidence-based practices and with recommendations from a vast number of experts, especially those organisations still engaged in developing initiatives such as those presented in the table 3 (below), which proposes a series of initiatives extending synergies with the project.

Table 3 – RRI good practices and possible synergies (non-exhaustive)

Project	Objectives and strategy	FEMaLe structured uptake
'RRING' H2020, ID: 788503	Generates a community of practice via a global mobilisation and access to an Open Access RRI knowledge basis	Multi-actors approach, RRI strategy recommendations, inclusive engagement of civil society and researchers
'EQUAL-IST' H2020, ID: 710549	Proposes structural changes to enhance gender equality within ICT-centered Research institutions	Gender equality plans approaches, EURAXESS synergies, guidelines, tools and rationale
'EU-Citizen.Science' H2020, ID: 824580	Build and advance a sustainable platform and mutual learning space supplying different tools	Knowledge Hub approach providing actionable intelligence on key findings
'HubIT' H2020, ID: 769497	Contribute to ensure ICT related innovation is responsible, inclusive and aimed at reversing inequalities	European framework model, policy recommendations, success indicators and assessment toolbox
'NewHoRRIzon' H2020, ID: 741402	Delivers a conceptual and operational basis to integrate RRI practice into the research and innovation arena	Societal readiness thinking tool, RRI.EX is a virtual experiences, pilot actions and social labs
'SeeRRI' H2020, ID: 824588	Framework for integrating RRI principles into regional 'Smart Specialisation' policy	SeeRRI Process strategy and instruments, method for active mapping, self-sustaining R&I ecosystems model

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[60] Framework for Responsible Innovation, Engineering and Physical Sciences Research Council (EPSRC), March 2020

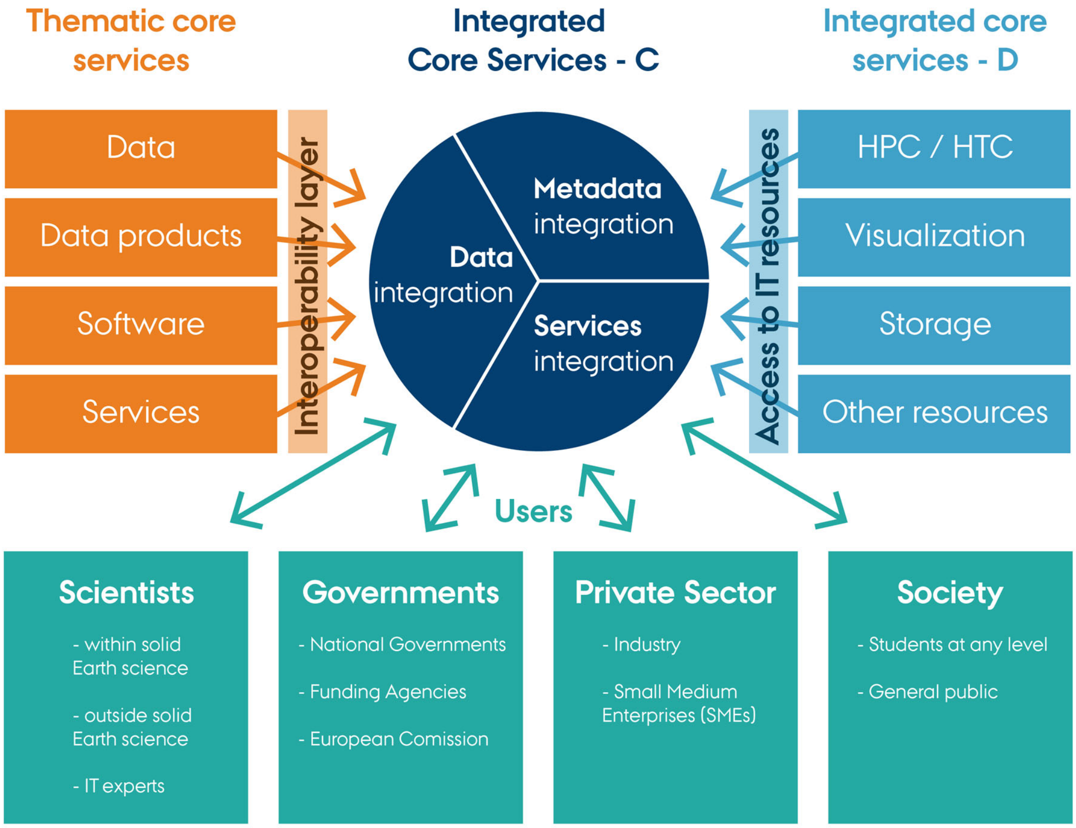
4.5 Open Science

Open Science is a series of measures intended to generate more transparent scientific processes and results more accessible. The main aim of the strategy is also to build a more replicable and robust science. This is done via the practice of pioneering technologies (for instance blockchain technologies), altering incentives (attitudes, motivations, disincentive, the role of patients, intellectual property rights, etc.).

The project FEMaLe proposes to develop with the 'Open Science' approach recommended by the EC, rooted in the following model: "*An approach to the scientific process that focuses on spreading knowledge as soon as it is available using digital and collaborative technology. Expert groups, publications, news and events*." This strategy is supported by the European Open Science Cloud (see Figure D below) which enable researchers across disciplines and countries to manage and exchange information in transparent way. Open Science can be firstly viewed as Open Access.

The concept of open access is causally linked to the following purpose: 'make the primary outputs of publicly funded research results - publications and research data - publicly accessible in digital format with no or minimal restriction as a means for accelerating research. FEMaLe is an Open Science driven initiative.

Figure D – The European Open Science Cloud (EOSC)[61]



FEMaLe participates in an open-access data pilot. The project will produce and maintain a data management framework, which will be managed by AU (Coordinator) and Correlate as part of WP10.

The plan is based on the principles of making data findable, accessible, interoperable and re-usable (FAIR) and will include information on the data standards that will be applied by the project, how the data will be exploited and how it will be curated and preserved.[62] Data collected will include results from the empirical assessment of end user needs, designs for the algorithms, software components and the integrated platform and the results of testing and validation studies.

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[61] The European Open Science Cloud (EOSC), the European Plate Observing System, March 2021

[62] The FAIR Guiding Principles for scientific data management and stewardship, Wilkinson M.D. et al. in Scientific Data, March 2016

5. SYNERGIES WITH EC SERVICES AND BEYOND

The project FEMaLe responds to the specific challenge put forward in 'SC1-DTH-2018-2020: Personalised early risk prediction, prevention and intervention based on Artificial Intelligence and Big Data technologies', which, in the present case, concretely relates with the digital transformation in endometriosis health and care nexus. The project flags the interconnectedness of needs related to the disorder, its governance regimes and of the biophysical and societal contexts in which these needs ripen. The project FEMaLe aims at facilitating the science, societal and policy arenas responsiveness to the new wave of experience, expertise and knowledge needs that are occurring from the innovative inter-sectoral approach of the project, building upon complementary research and innovation initiatives currently tackling the challenges of the aforementioned nexus which are emerging around the globe. The project intends to be one of the prominent commitments to support the European Commission on the search for innovative avenues to explore, recognize, pilot and generate pioneering responses to identified challenges in the EU context. Therefore, the project development cannot be isolated from the powerful network of interlinked initiatives, thus cooperation and interchange are among the most reliable means to ensure an improved and accurate impact and value in the activities that the project aspires to implement. The project FEMaLe will systematically build upon recognised evidence, especially generated is the pan-EU panorama, and also interlink with pan-EU and UN pertinent services.

5.1 EC services

In addition to its core objectives, among them substantially decreasing and even avoiding diagnosis delays in endometriosis, the project FEMaLe aims at contributing to the EU health agenda targeting 2 core interlinked areas of the EC: the public health and the digital arenas. However other pertinent areas are also in the project plan, especially the innovation action area, education, training and employment. We propose to create a specific focus group to lead communication with a series of EC services (listed below) and which main aim is to engage and connect with this services and explore all pertinent synergies from exchanging information, alignment, interchange and strengthening of the project development and anticipated results, joint participation in pertinent platforms (working groups, networks, etc.), alignment of pertinent communication, dissemination and exploitation of results activities. The table 4 (below) proposes the specific objective of synergies initiatives between the project FEMaLe and identified EC services and platforms.

Table 4 – Suggested synergies with EC services (non-exhaustive)

EC services and platforms	Role(s) and objective(s)	FEMaLe contribution areas
EU Public Health units	EU actions on health (policy, international cooperation, indicators and data, etc.)	Project deliverables from WP1, WP2, WP9
European Medicines Agency	Evaluation and supervision of medicinal products, medicine data, etc.	Project deliverables from WP3 to WP8
European Health Insurance Card	Pan-EU access to state-provided necessary healthcare (temporary stay)	Project deliverables from WP2 to WP8
eHealth : Digital health and care	Solutions using ICT to improve public health (products, services, systems)	Project deliverables from WP3 to WP8
A digital future for Europe	Building upon precedent initiatives enhancing the creation of a Digital Single Market	Synergies initiatives (joint-efforts on research and innovation)
EU4Health Programme 2021-2027	Fostering spinoffs, creating opportunities for advancement and exploitation of results	Project deliverables from WP1 to WP8
Employment, Social Policy, Health and Consumer Affairs Council configuration (EPSCO)	Increase employment levels, improve living and working conditions	Project deliverables from WP2 to WP8
European Health Committee (CDSP)	Foster Pan-EU co-operation to safeguard and improve the health of European citizens	Project deliverables from WP2 to WP8
European Labour Authority	Coordinates and supports the enforcement of EU law on labour mobility.	Project deliverables from WP2
European Agency for Safety and Health at Work (EU-OSHA)	Data management and dissemination to support safety and health at work	Project deliverables from WP2 to WP8

5.2 EC initiatives

The consortium generates a series of mechanisms to engage, connect and build upon EU-funded initiatives such as the projects MOMENDO [63], TRENDO [64] or GLYCOMENDO [65], to name but these few, and generate a series of joint-actions providing mutual benefits:

a) exchange of information on project developments via representations on each other's Advisory Board (proactive and mutual follow up);

b) alignment, interchange and strengthening of project results via the practice of joint case studies to identify corresponding case(s), upon which projects develop autonomously by implementing their respective approaches and methodologies; outcomes are compared and discussed in a join-examination processes;

c) joint participation in all pertinent platforms, networks and events on a reciprocity basis, also with alternated roles on a yearly basis;

d) alignment of pertinent communication, dissemination and exploitation of results activities.

Together with the partnership, IAAD identifies and compiles a catalogue of on-going initiative at pan-EU level, and co-creates a Synergies Action Plan. The comprehensive action plan effectively activates synergies between the project's partners and existing networks, projects, clusters, platforms, and interlinked EU bodies as well. Co-creation of a Memorandum of Understanding to secure an effective two-way uptake and exchange.

This activity may as well incorporate the reactivation of H2020 consortia engaged in projects recently ended or ending. The plan is implemented in each WP key activities to provide an effective leverage and uptake of key findings and learning from a vast panoply of sources, and a solid multiplication effect regarding the projection of the project results at national level and to other countries, incorporating the same diversity of actors from the pertinent arenas. Under WP2, this plan secures a centralized and global coordination of WP specific synergies activities.

5.3 International services

Though the main focus area of the project is pan-European it is of paramount importance for the consortium to consider and integrate a more global view of the international cooperation panorama on endometriosis, and, to that end, the consortium engaged and plan to engage more experts from the international landscape, in all fields of proficiencies pertinent to the purpose of the project. The table 5 (below) proposes the specific objective of synergies initiatives between the project FEMaLe and identified UN services. This engagement is especially realised via inviting the aforementioned experts to join the non-executive and steering bodies of the project such as the Advisory Boards.

Table 5 – Suggested synergies with identified international services (non-exhaustive)

UN services	Role(s) and objective(s)	FEMaLe contribution areas
World Health Organisation	Ensure universal health coverage, protect from health emergencies, improve health and well-being	Project deliverables from WP2 to WP8
UN's Sustainable Development Goals n.° 3, 5, 8, 10 and 17	Ensure healthy lives and promoting well-being at all ages, gender equality, etc	Project deliverables from WP2 to WP8
United Nations Development Programme - Health	SDG, human development, Six Signature Solutions and #NextGenUNDP	Project deliverables from WP2 to WP8

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[63] Molecular Mechanisms of Endometriosis (MOMENDO), project funded by the H2020 Programme (ID: 691058), 2016-2019

[64] Translational Research on Endometriosis (TRENDO), project funded by the H2020 Programme (ID: 101008193), 2021-2025

[65] Non-invasive clinical markers for diagnosis of endometriosis (GLYCOMENDO), project funded by the H2020 Programme (ID: 843862), 2019-2021

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