

## STATEMENT OF THE RICORS COORDINATOR

**RICORS CODE**  
**RD21/0012/0001**

**Thematic area:** Primary care, chronicity and health promotion

**RICORS Leader:** Elisa Llurba Olivé

### RICORS STRUCTURE AND OBJETIVES

Importance and scope of the RICORS at national and international levels.

Max. 1 page

The RICORS Maternal and Child Consortium aims to provide a comprehensive and synergistic plan that encompasses hospitals and primary care, and is meant to improve women, maternal and infant health, while avoiding long-term consequences of perinatal and developmental complications. Hence, it will develop specific programmes for pregnancy and child surveillance to be applied in the Primary Care setting, that identify those mothers and offspring at higher risks for specific conditions, and to provide management strategies and protocols, to reduce the burden of disease through prevention, early detection, adequate management and correct referral.

Cardiovascular disease is the first cause of death in developed countries. Maternal characteristics such as obesity and malnutrition, and environmental factors such as air and noise pollution, have been associated with adverse perinatal outcomes in the short and long-term. Specific mechanisms underlining maternal and foetal programming are not well understood, however there is evidence that pregnancy and perinatal outcomes related to placental diseases such as preeclampsia, growth restriction or prematurity, are associated to greater cardiovascular and metabolic risks later in life, for both mother and child. Likewise, prematurity and growth restriction, and other risk factors such as congenital heart defects, perinatal hypoxia or neuro-infections, benefit from early interventions such as breastfeeding, strict follow-up of neurodevelopmental milestones, evaluation of sequelae in other target organs (i.e. kidney), some of which are not currently addressed in primary care.

In the current proposal, we address knowledge gaps, and provide a greater insight about: (i) promoting maternal health (nutrition and exercise) in obese and diabetic women to improve perinatal and infant outcomes; (ii) identify women at risk for placental complications of pregnancy (preeclampsia and intrauterine growth restriction), implementing a primary care screening program in the first and third trimesters of pregnancy; (iii) improve cardiovascular health in women by early identification of risk factors according to obstetric outcomes, and to provide integral primary care follow-up after pregnancy; (iv) elucidate the role of environmental factors, green spaces and noise pollution in pregnancy outcomes at the community level; (v) early detection, community support and treatment of women that use or abuse drugs and alcohol during pregnancy, with family-care support for both mother and child to avoid long-term consequences of addictive behaviours; (vi) to early detect short-and-long-term neurocognitive, developmental and sensorial consequences of late Prematurity; (vii) to develop early-primary care tools for the identification of children at risk for neurodevelopmental disorders; (viii) explore the impact of a policy of maternal breastfeeding promotion in child development; (ix) evaluate the impact of lifestyle strategies to improve cardiovascular and metabolic health in those children with high-risk (intrauterine growth restriction, maternal diabetes, obesity); (x) implement protocols to aid in prevention, early detection, monitoring and sequelae of childhood chronic serious diseases (cardiac arrest, paediatric stroke, brain trauma, post-cardiac surgery, neuro-infections, long-term hospital stay); (xi) prevention, early detection and follow up of paediatric patients with chronic renal and digestive diseases in primary care; (xii) To include (a) patients' experiences and point of views in the design of policies to improve different aspects of maternal and children health through social science methods will be used to reinforce and implement participation from users and patients in developing care strategies and guidelines and (b) include e-health technologies to improve detection and follow-up of different maternal and children chronic conditions, at the primary care level. These innovative and substantively different approaches overcome the limitations of previous work. As such, this proposed project will provide a major incremental step in driving the field forward, by opening new horizons with respect to detecting these conditions earlier life (and treatment), and informing the mechanisms and efficacy of these interventions to improve maternal-children health.

The RICORS Maternal and Child Network will focus on strategies developed from preconception, prenatal and postnatal stages, with strategic groups from all Spain that have expertise in the different areas, to extract expert advice applicable to the primary care setting throughout the country. It will bring together a multidisciplinary team of obstetricians, paediatricians, midwives, nurses, epidemiologists, family care practitioners, nephrologists, cardiologist, psychologists and anthropologists, who will cover different aspects of this project, defining a new pregnancy and child cohort over 46 health centres in Spain, composed by hospitals and primary care facilities, that will work as a team to achieve the objectives of this consortium. This will allow to generate evidence-based consensus protocols and recommendations that can be applicable not only in Spain, but in other countries, in order to exercise preventive medicine for women and children in primary care facilities throughout Europe. Therefore, this proposal combines a huge motivation with a consolidated expertise in the field, is in full coherence with our field of knowledge and previous work, and it actually represents the culmination of 15 years of work of the team as a whole with the inclusion of new investigators from primary care and other fields with a clear change towards translational medicine and patients views and experiences for its implementation in primary care.

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## POTENTIAL IMPACT

Describe the dissemination plan and the strategy for the transference and exploitation of results to the society. Describe the potential impact on patient-based health outcomes and National Health System (portfolio of services, national cohesion)...

Describe the contribution of the RICORS to national and international standards Max. 2 pages (10,700 characters)

*Potential impact on patient-based health outcomes and National Health System (portfolio of services, national cohesion)...*

This project belongs to the RICORS thematic area one: Primary care, Chronicity and Health promotion. And within this, Maternal and Child Consortium goals are included all seven descriptors of this application, that are; chronic diseases and multimorbidity, promotion of health with gender perspective, health services, e-health, prevention and attention to addiction and investigation and implementation and maternal and child health: First of all, there is not greater prevention of chronic diseases and multimorbidity than the one started already from the intrauterine and early-childhood period. We plan to prevent relevant health diseases such as cardiovascular disease (CVD), impaired neurodevelopment, obesity, diabetes and inflammatory chronic conditions in children that have long-term consequences and determine mayor impacts in accumulated quality of life years. Indeed, the adverse consequences related to the early developmental period have the potential to negatively affect not only one life, but two (the mother and offspring), and possibly next generations. Thus, the main objective of this proposal is on searching effective strategies to promote an optimal intrauterine and children environment (epigenetic, toxic, environmental and nutritional), and break the maternal-foetal intergenerational pathology cycle. Secondly, it addresses gender and children inequalities of health access and gather therapeutic solutions by promoting a personalised and family-centred end users', gender and ethnic sensitive approach toward mothers, fathers and children. A whole WP is dedicated to women, parents and child needs and experiences. Social science methods will be used to reinforce and implement participation from users and patients in developing care strategies and guidelines. In addition, gender perspective would also be taken into account in three main objectives that aims to improve maternal outcomes by implementing solutions at a primary care setting to prevent preeclampsia and cardiovascular disease latter in life, the number one cause of death in women, that have classically lacked enough research attention compared to CVD in men. Third, promotion of health services is another of the aims of this consortium. It addresses one of the main gaps that actually exists within the National Health Service in Spain which is the different care that is provided at hospital and primary care settings in relation to maternal and child health. All the initiatives that we plan to promote within this consortium have a unique objective that is to achieve an equal, pragmatic, easy to implement, cost-effective, patient-centred and quality program for maternal and child health in primary care settings around Spain. Four, it also addresses the attention of addiction in pregnancy with all its specific characteristics, both medically, social and from the child perspective that constitutes a major challenge extremely difficult to solve if not under specific and expert approach. Fifth, within WP derivable we have included the design and validation of different e-Health solutions for improvement of diagnostic, prediction, management or monitoring of different health issues included in this proposal. Six, investigation and implementation of innovative tools and solutions to address our objectives is another key point of this initiative. We are convinced that the results of our investigations would be rapidly applied to women and children in the majority of primary care settings all over Spain. It is important to highlight the huge interest and commitment raised towards our project in the scientific community, patients associations and industry as it is proved with 17 letters of interest included in the application.

Therefore, our proposal perfectly addresses the objective of this Health Institute Carlos III (ISCIII) call in relation to primary care, chronic diseases and health promotion, targeting a unique population such as pregnant women and children. Therefore, this project is not only extremely relevant, but could also fulfill all the requisites and needs underpinned in the ISCIII RICORS call. Pregnancy and childhood research and policy implementation have been traditionally omitted in Primary Care Health Centers. The organization of mixed consortiums in our RICORS proposal will undoubtedly contribute to the normalization of combined and effective research and application of newly developed preventive, diagnostic and therapeutic achievements in the field of primary care attention to pregnant women and childhood.

*Describe the contribution of the RICORS to national and international standards.*

The world is facing first pandemic since a century. While it has uncovered vulnerabilities in our social and economic systems, it has also provided new impetus, visibility and recognition of the critical role that health care systems and health professionals play in responding to the needs of people, serving society and underpinning economy.

The work programme 2021-2022 of cluster 1 'Health' is directed towards two Key Strategic Orientations (KSOs) for research and innovation set by Horizon Europe's strategic plan 2021- 2024. The KSO-D of this plan is 'Creating a more resilient, inclusive and democratic European society'. Research and innovation supported under this destination should contribute to the impact area 'Good health and high-quality accessible healthcare' and in particular to the expected impact 1 of cluster 1 'health': citizens of all ages stay healthy and independent in a rapidly changing society thanks to healthier lifestyles and behaviours, healthier diets, healthier environments, improved evidence-based health policies, and more effective solutions for health promotion and disease prevention.

This proposal is in line with this idea as its main objective is to improve adult health by promoting healthy life-style and target interventions during prenatal and early-childhood that are known to be main contributors of children and adult chronic diseases and that hamper society quality of life. Moreover, this project also bears in mind four ideas reflected in the new Recovery Plan of the European Union. On the one hand, the digital transformation of health and care. Secondly, to contribute to give insight in the consequences of ambient pollutants in maternal and children health, and give more reasons for making the European Union the first climate-neutral continent by 2050, with zero pollution and zero waste. Third, it is in line with the European Union efforts to involve users - like patients and healthy citizens, health care professionals providers and payers, public health authorities and regulators, researchers or innovators from academia and industry - early in the knowledge generation or technology development process such that research and innovation activities are adjusted to the users' particular expectations, needs, constraints and potential. The RICORS Maternal and Child project aim to use social science methods that will reinforce and implement participation from users and patients in developing care strategies and guidelines. Finally, social transfer of the research is guaranteed thus, thus proposal include real setting and primary care interventions that would be rapidly translate to real users and professional solutions to improve health.

Research and innovation in maternal and children is an ideal field of application supported under this destination that will provide new evidences, methodologies and tools for understanding the transition from health to disease, from prenatal to adult life, at primary-care settings. This will allow designing better strategies and personalised tools for preventing diseases and promoting health. Specific measures will also be developed to educate and empower citizens of all ages and throughout their life, to play an active role in the self-management of their own health and self-care, to the benefit of an active and healthy ageing.

In a scenario where birth rate and vegetative growth are both decreasing in Spain, improving a healthier environment for the coming generations guarantees less health disruptions and healthcare costs. The potential results obtained from this proposal are directly applicable, since they imply the implementation of a new preventive concept of adult health conditions. The intervention package designed in the RICORS Maternal and Child project are innovative and low-cost, so it could be easily transferred to similar contexts, either with public or private funding. With all this in mind, if effective, these interventions could be implemented, improving cost-effectiveness of health systems and reducing the demands for mother, paediatric and adult health care.

*Raising public participation and awareness.*

Public participation and awareness is one of the main objectives of this initiative as displayed in WP 12. We plan to design infographics to inform maternal and infant of the results of our work. We plan to reach primary care services' doctors and caregivers with information about families' and children's perceptions of health needs. A short video to transfer research results among healthcare professionals, families, and community will also be produced to gather awareness among caregivers.

The expected results of this research are transferable to the organization, resource management, health services or health policies, generating synergies between research centres, exercise professionals and public and private health services. The knowledge derived from this research will be also transferred by means of the elaboration of consensus documents including guidelines about the development programs in pregnant women (for obstetricians, paediatricians, midwives, general

practitioners, cardiologists, etc.). Therefore, information will lead to modified clinical practice recommendations in order to improve maternal, offspring and children health.

The consortium are involved in a number of scientific activities with major public impact, are committed to stimulate public interest on the RICORS project and its goals. Scientific and medical results will be published and presented to the scientific and medical communities through the usual channels (journals, presentations at conferences, etc), according to the European Union Policies, patients associations will actively participate in the generation and diffusion of knowledge and information, and finally the stakeholders will disseminate results at industrial and commercial events.

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## ORGANIZATION AND MANAGEMENT

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The RICORS Maternal and Child consortium consists of 20 partners and 26 clinical associated groups with more than 300 investigators with common backgrounds, interests and expected impact. The management structure of the consortium has been designed with the primary aim of facilitating the coordination of partners and tasks, which are significantly diverse. This structure takes advantage of each partners' expertise's, while involving all partners in the progress of the project and in decision making (scheme 1-Memoria programa de investigacion doc).

The Programme Coordinator, who is Chief of the Obstetrics and Gynaecology Department at Hospital de la Santa Creu i Sant Pau, Barcelona, and principal researcher of the Women and Perinatal Research group in the Research Institute (<http://www.recercasantpau.cat/>), has in-depth knowledge of advanced and current standards to deliver medical care in pregnancy and has vast experience in design and accomplishment of clinical trials, methodology (molecular biology, genetic and mass spectrometry platforms), leadership and experience in advanced research studies and writing of clinical protocols.

The Assistant Manager to the Coordinator, will run financial and administrative tasks of the project and prepare the Reports for the Instituto de Salud Carlos III.

The Scientific Assistant will be an expert in laboratory and analytical methodology including statistical analysis. The Scientific Assistant will run the databases of the different work packages and supervise correct data input, validate data, perform statistical analysis and establish priorities.

The daily Management Team will be formed by the Programme Coordinator, the Assistant Manager and the Scientific Assistant to the Programme Coordinator, and will work in close connection with all Group Leaders.

The Direction Committee (DC) is composed by 50% of the PI and they have been elected collegially by secret ballot. It is form, apart from the RICORS coordinator would include: Keka Pallás, Fernando Cabañas, Lola Gómez-Roig, Oscar García, M Dolores Mesa, Gerardo Rodriguez, Elvira Larqué, Jesús López-Herce and Begoña Loureiro.

An external scientific advisory committee with national and international experts and patients association representatives, which will periodically advise and report on the activities of the network.

The Consortium is composed by two types of research groups:

20 Research Groups (RG) with 178 investigators.

26 Associated Clinical Groups (ACG) with 155 investigators.

The Project Management Board (PMB) is the overall joint decision-making body holding final responsibility for the quality of the results, major decisions regarding reporting, disputes, financial control, etc. It will be formed by one member from each group with equal rights for vote representation during joint decision meetings. The PMB will provide general coordination in scientific issues, and holds final responsibility for the Programme. The board will meet periodically and will hold teleconferences to assess the overall progress of the project. Work package managers will be responsible for the performance of their work package and the timely delivery of tasks, and deliverables.

The Associated Clinical Groups (ACG) Committee would be a group of researchers that will be elected from the ACG and would also have a member within the PMB.

In addition, longitudinal WP studies, including case activities and data collection, are arranged in sequential form in four blocks according to four main areas:

- Block 1 - Prenatal: coordination by Obstetric researchers of the participating groups (includes midwives, obstetricians, neonatologists, primary care physicians).
- Block 2 - Immediate postnatal period: coordination by Paediatric researchers of the participating groups (includes neonatologists, cardiologists, primary care paediatricians).
- Block 3 - Paediatric long-term follow-up: coordination by Paediatric researchers of the participating groups (includes primary care physicians, neuropsychologists, and paediatricians).
- Block 4 - Patient experiences and e-health technologies: Coordination by Anthropologists (includes midwives, paediatricians, psychologists, and primary care practitioners of the participating groups).

The Coordinator, the Direction Committee, the Assistant manager of the coordinator will set up the following tasks:

- kick-of consortium meeting within one month after resolution of the call;
- consortium trimestral teleconferences to discuss the progress of work packages;
- administrative procedures;
- Quarterly management conference calls with the consortium partners, providing agenda, venue and minutes;
- One Project Management Board meetings per year
- Follow up and close out actions arising from meetings, based on information provided by consortium partners;
- Other need-based meetings with stake holders, industry and associations representatives
- to develop and implement management tasks;
- to define, develop and assign scientific tasks;
- to advise and direct partners on developments necessary for projects;
- to monitor and supervise progress of scientific work;

- to ensure that partners perform and report their work in accordance with agreed procedures and quality standards;
- to coordinate preparation of periodic activity reports and communications for scientific issues;
- to schedule and approve dissemination activities, scientific workshops, meetings and training activities.
- Report to the ISCIII and provide all necessary documentation received from consortium partners

### **Consortium Agreement.**

The legal framework of the consortium will be represented by a Consortium Agreement (CA), to be signed during month 1. The CA will essentially contain the following points:

- the internal organisation of the consortium, its governance structure, roles and responsibilities, decision-making processes and management arrangements;
- specific arrangements concerning intellectual property rights, access rights, confidentiality and dissemination;
- specific arrangements concerning the exploitation of results;
- liability and indemnification;
- provisions for the settlement of internal disputes, including cases of abuse of power;
- any other provisions necessary to ensure a sound management of the project.

The CA will be in any of these points compliant with the general arrangements stipulated in the ECGA and follow a structure such as the DESCA model agreement.

Ethical principles followed in the RICORS Maternal and Child Consortium

The RICORS Maternal and Child project involve ethical issues on informed consent and data protection issues.

The partners are committed to ensure that the research carried out in this project is safe for humans and the environment (including biodiversity), taking into account any other concerns to ensure the safe and socially acceptable development and application of life sciences and biotechnology. This proposal thus raises no sensitive ethical issues relating to human beings, human biological samples or personal data (whether identified by name or not). In addition, there is a common consensus among the consortium that the highest standards of welfare must be employed. A partnership agreement regarding the ethical dimensions of this research project will be established between all partners, stating that participants will conform to current legislation and regulations in the EU and in the countries where the research will be carried out, as well as to international conventions and calls of conduct. This will be signed by all participants and embedded in the consortium agreement between partners.

Ethical principles in RICORS Maternal and Child Consortium will follow the WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI: Ethical Principles for Medical Research Involving Human Subjects

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, and amended by the:

29th WMA General Assembly, Tokyo, Japan, October 1975

35th WMA General Assembly, Venice, Italy, October 1983

41st WMA General Assembly, Hong Kong, September 1989

48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996

and the 52nd WMA General Assembly, Edinburgh, Scotland, October 2000

Note of Clarification on Paragraph 29 added by the WMA General Assembly, Washington 2002

Note of Clarification on Paragraph 30 added by the WMA General Assembly, Tokyo 2004

and conform to pertinent legislation of the European Union.

### **Consideration of gender aspects**

In addition, the consortium is committed to incorporating the principles of gender mainstreaming throughout the various elements of the project, in accordance to Articles 2 & 3 of the Treaty of Amsterdam (1997) and other EU policy directives. Every effort will be made to ensure that the consortium and its activities contribute to the promotion of gender equality wherever possible, and steps will be taken to ensure that none of the activities of the consortium contributes to gender inequality or aggravates existing gender inequality.

The distribution of genders in the RICORS Maternal and Child Consortium research teams is the result of the present composition of the partner groups. At the time of application the list of investigator have an outstanding women participation, the project Coordinator is a relatively young women, and 6 out of 10 members of the Direction Committee are woman. And, in general, the majority of investigators from the research and associated groups are women.

While keeping scientific excellence and expertise as the basic selection criteria, the RICORS Maternal and Child Consortium is willing to implement an action plan to reduce gender inequality and promote gender equality. The following objectives underpin the gender action plan: a) ensuring that women and men have equal opportunities to participate in the various aspects of the project; b) in addressing diversity, taking account of the different situations needs and interests of women and men in the consortium. The main specific actions planned are the following: a) the consortium is committed to incorporating a woman for the vacant role of Project Manager; b) special attention will be played to women recruitment during the launching phase of the project and advertising this action in all jobs advertised; c) the gender dimension of the project will be audited and monitored once a year and the results will be made publicly available in the RICORS Maternal and Child

Consortium dissemination web server; d) opportunities for mobility within the programme will take account of the different needs of women and men in order to enhance participation by women scientists.

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## IMPACT, INNOVATION, TRANSFER AND DISSEMINATION

Describe the potential impact of the programme and the expected scientific and technological contributions; detail the adequacy of the dissemination plan and the strategy for the technology transfer.

This section should include: potential impact on health outcomes for patients and for the backbone of the National Health System; for the scientific community (clinical guidelines or other contributions to national and international standards); patents.

Max. 3 pages (17,500 characters)

*Potential impact on health outcomes for patients and for the backbone of the National Health System:*

### (i) Contribution to scientific knowledge and advancement in its field.

As previously mentioned, the RICORS Maternal and Child Network aims to provide a comprehensive and synergic plan between hospitals and primary care, to improve women's, maternal and infant health, and avoid long-term consequences of perinatal and developmental complications. This proposal represents a pragmatic approach, both from the health system and clinical point of views. Scientific knowledge on fetal development, programming and maternal health generated in this project will be determinant for its transition to primary care practices. We are addressing the main causes of morbidity and mortality, such as cardiovascular, metabolic and neurological diseases, from prenatal and neonatal origin, with high impact in quality of life. Maternal and child health are one of the five health issues the WHO has highlighted as a priority for the next horizon agenda, however, research in this field is scarce, due to gender and child inequalities. It is for this reason that this proposal is of such importance, bringing together outstanding investigators and primary care midwives, obstetricians and pediatricians, in an unprecedented manner to ensure the translation and real-setting implementation of agreed protocols in a short period of time, using new, innovative e-Health solutions. Moreover, never before have children and women's point of views as patients been taken into account to address type of interventions and health innovations.

### (ii) Contribution to generate new tools, models or analysis systems that could enable improvement, boosting or creation of scientific research fields.

We believe that RICORS Maternal and Child Network generates, by definition, a new scientific interdisciplinary research field, where current notions of maternal and fetal programming merge with adult chronic diseases and disability. This will give new vision for primary care adult clinicians, which will be translated into further cutting-edge projects over coming years.

In the short term, some specific contributions of this project merit comment:

- Several work packages introduce important improvements in diagnosis and prediction of maternal and child chronic diseases, including preeclampsia, intrauterine growth restriction screening, and prediction of cardiovascular disease for both women and children.
- Likewise, new research fields are being developed, among others, maternal and fetal environment studies (both positive interventions, but also models analyzing toxic exposure) and their impact on neurocognitive development, cardiovascular and metabolic programming, and other chronic diseases.

### (iii) Contribution to improve the health and well-being of citizen.

RICORS Maternal and Child Network will generate sufficient new knowledge to have an impact in improving clinical practice for maternal and child care. However, the main impact lies in potential clinical implementation at Primary Care settings. While accepting the magnitude of the challenge, we are firmly committed to provide the system with clinical applications. We are convinced that e-Health solutions will be a reality in the coming years, and it will revolutionize current concepts, creating the need for social and professional interplay as pivotal factors towards a new era in the scientific and medical field, where limits between patients and care-givers are merged in new participating and empowered roles. We as a team are determined to overcome prejudging conditions and include women, parents and children's point of views and needs, aimed towards real solutions to improve care in all settings around Spain, achieving homogeneity and quality care. These clinical applications might change radically prognosis of perinatal conditions now associated with high rates of mortality and long term sequelae. We believe the state-of-the-art and our background in the field, combined with our expertise in innovative projects, maternal-fetal medicine, fetal programming, and critical neonatal/pediatric care, make realistic the ambitious goal of combining women and children's needs with outstanding clinical solutions applied in primary care settings around Spain.

### (ix) Inclusion of citizens, women, parents and children needs and experiences in research.

Spanish citizens are increasingly motivated and educated to use digital tools to manage their own and their family's health, care and well-being adopting healthier lifestyle behaviours and achieving better health and care outcomes during their own and their family's life-course. Consequently, they play a more active role in trying to know their health state and potential and they are able to follow up their health and that of their family by adopting healthy lifestyles at home, at work and in their community. They do so by trying to interact better with their doctors and carers, receiving

and providing feedback through diverse ways. At the same time, primary care services try to be increasingly integrative, open to diversity and inclusion, protective of sensitive health data, aware before the needs of their end users as well as affordable through different ways. So, we are in front at a quickly transition from treatment to prevention in healthcare and toward a more equal relations between doctors, health carers and their end users.

#### **(x) Contribution on digital solutions in maternal and child health problems.**

Digital technologies are recognized as capable to help citizens taking an active role in the management of their and their family health and well-being as well as to help health and care systems to promote and develop personalised and family-centred health and care models. Personalised approaches and the development of targeted interventions allow today that several medical conditions profoundly serious until now can be solve, attenuated, or turned to a chronic condition. Even more could be achieved if it is possible identify as early as possible individuals at higher risk or developing a particular condition considering two third of chronic diseases are thought to be preventable.

*Potential impact for the scientific community (clinical guidelines or other contributions to national and international standards); patents.*

The potential impact of the RICORS Maternal and Child Consortium project on public health and its contribution to research and innovation strategies for Maternal and Child health within Europe, represents the kern for its presentation to the general public. Information will be, initially, spread through the RICORS Maternal and Child Consortium web site. If results are achieved that have a direct impact on public health, their dissemination will be made using press releases, social network to reach a wider group of stakeholders, including e.g. patient organizations. To this end, the consortium will contact the Dissemination Department of every partner institution, which shall support the release and suggest the appropriate format and media in each participant country. The Coordinator and the rest of investigators leaders shall be also contacted in such cases, to explore the use of additional communication channels at the European and Latin America level towards direct contacts and stakeholders.

The Consortium will follow EC communication guidelines (e.g. as in the document “A guide to successful communications”) for dissemination in general and public awareness in particular, ensuring compliance with Article II.10 of ECGA.

#### **(i) Clinical guidelines**

##### **Main Expected Outcomes susceptible for clinical guidelines:**

- Maternal health (nutrition and exercise) recommendations and guidelines for obese and diabetic women to improve perinatal and infant outcomes.
- Primary care screening programs in the first and third trimesters of pregnancy to identify women at risk for placental complications of pregnancy (preeclampsia and intrauterine growth restriction).
- Early identification of obstetric risk factors to improve cardiovascular health in women, and primary care follow-up guidelines.
- Early identification of obstetric risk factors related to environmental factors, green spaces and noise pollution at a community level.
- Early detection, community support and treatment of women that use or abuse drugs and alcohol during pregnancy; clinical guidelines, and family care support recommendations for short and long-term management.
- Neonatal follow-up guidelines in primary care setting for at-risk children for impaired neurodevelopment especially targeting late preterm representing 7-8% of the newborn population (32.000/year).
- Recommendations and guidelines for promotion of maternal breastfeeding and human milk donation for nurturing preterm infants in the hospitals.
- To develop early-primary care tools for the identification of children at risk for neurodevelopmental disorders.
- Recommendations regarding lifestyle changes and strategies to improve cardiovascular and metabolic health in women and children with high-risk factors.
- Protocols and guidelines for prevention, early detection, monitoring and management of sequelae of childhood chronic serious diseases.
- Recommendations, guidelines and strategies for inclusion of patient experiences and point of views to design policies improving different aspects of maternal and child health management.
- Guidelines for inclusion of e-Health technologies to improve detection and follow-up of different maternal and child chronic conditions, at the primary care setting.

#### **(ii) Expected scientific and technological contributions**

This project will generate new knowledge and tools. The Exploitation Committee will analyze potential exploitation strategies; an exploitation plan will be updated throughout the network. When applicable, patent applications will be filed by partners involved.

#### **Main Expected Outcomes susceptible of IPR issues:**

- Use of angiogenic factors as a first and third trimester of pregnancy for the detection of at risk of preeclampsia women
- Digital App for implementation of life-style interventions to improve quality of life after preeclampsia in young mothers.
- A model of maternal and child environmental health program and a model of intervention unit about maternal and child environmental health.
- Early predictive biomarkers of neurodevelopmental outcome at school age.
- To develop FICare online platform and training materials, which will be translated into the required languages and cultural context, and to deliver training to both healthcare professionals and families.
- Digital APP for mothers promoting and monitoring breastfeeding.
- e-Health Assessment tool for the identification of nutritional and physical activity.
- e-Health Assessment tool for the surveillance of dietary and physical interventions for prevention of cardiovascular diseases in children.
- App for monitoring maternal and infant health and wellbeing.

#### **Strategy for technology transfer**

Management of IPR will be monitored by the Exploitation Committee and the Knowledge and Technology Transfer Offices (KTTOs) from institutions involved, ensuring that it complies with the General Agreement Rules with regard to dissemination, exploitation and use. Clear agreements on IPR rules among partners will be included in the general agreement. Interests of various companies within the industry on results from this network have been manifested with statements of interest from B Braun, ROCHE Diagnostics, Barcelona Health Hub, Mediktor and Philips, among others.

#### **Industry interested in technology transfer**

- ROCHE diagnostics
- Philips
- B-Braun
- Ordesa
- Ferring
- Barcelona Health Hub
- Mediktor
- Nestlé
- Masimo
- Siemens
- General Electric

**(iii) Training of new researchers** A fundamental impact of the RICORS Maternal and Child Network project will come through the training of young researchers in a multidisciplinary approach to predictions and prevention strategies designed towards maternal and child health. The consortium will provide young researchers with education and training on the scientific topics covered by the project, with a stress on multidisciplinary. This will often involve working visits to other sites within the network. Thus, the fellows will not only broaden their field of expertise but will also gain insight into the (combinations of) methods more appropriate to each problem. The young personnel hired within the consortium will be encouraged to present six-month reports of their activities to the Project Management Board (PMB), which will oversee the fulfilment of their tasks and of their training within the Network. Moreover, PhD students and postdoctoral fellows engaged by the network will be encouraged to participate in master-classes and international schools, as well as to present their work at targeted international conferences.

#### **(iv) Educational activities**

Other important expected impact of the Consortium is that of educational activities delivered in each WP that are

directed both towards health care providers and users (women, parents and children). A whole WP (12) has as a main objective promoting a personalised and family-centred maternal and infant informative material and digital tools.

In addition, in each WP there is a educational and dissemination plan for the translation of new technologies, protocols, guidelines and tools to care-givers in primary-care settings around Spain.

#### *Detail the adequacy of the dissemination plan*

#### **Communication and dissemination activities**

- At month 2, a communication and dissemination plan will be created, including a focus group for patient point-of-views and an annual report.
- At month 3-6, we plan to set up a web site that play a central role for communication, training, and dissemination of results. Dissemination will be performed at various levels, including a News section reporting any major achievements. A RTD web platform integrating software tools, protocols and databases developed in the framework of the project, will be developed and made accessible to public and private interests under specified conditions.
- The consortium plan to be active in social network: facebook, twitter, instagram and tik-tok. Informative material for women, parents and children would be develop and disseminate for the wide public in different formats: video, podcast, articles and newsletters.
- At month 24, we will organize a Doors Open Day for women, parents and children, to gather impressions from a wider audience and obtain valuable feedback from the community.
- From a scientific standpoint, the experimental setup will be immediately shared with our research networks, including first and foremost the perinatal network in Spain -with which specific sub-projects will be explored-, but also the CIBER network, and our closest international collaborators.
- We will communicate project outcomes to wider audiences using various channels (i.e. website, social media, organized initiatives such as European Researchers' Night, and other local events), which will help us to introduce scientific information to women, mothers, parents and children.
- All partners have experience communicating to wider audiences and news media; i.e., Entre Mares'18 and '20, Researchers Night '20, television interviews and newspaper reports, local STEM programs.
- We will publish in high-quality peer-reviewed journals, share guidelines or recommend procedures and interventions; participate in international conferences and in our network societies (i.e., SEGO; SEMEPE; AEP; FMF, FIGO, ISUOG) meetings.
- Different national and international scientific societies have showed interest to disseminate results of these projects, some of them in outstanding positions such as:

- FIGO (*International Federation of Obstetrics and Gynecology*)
- SEGO (*Sociedad Española de Obstetricia y Ginecología*)
- AEP (*Asociación Española de Pediatría*)
- AEPap (*Asociación Española de Pediatría de Atención Primaria*)
- SENEo (*Sociedad Española de Neonatología*)
- BFHI-UNICEF (*Iniciativa para la humanización del Nacimiento y la lactancia-UNICEF*)
- SCOG (*Societat Catalana d'Obstetrícia i Ginecologia*)
- GERCPPYN (*Grupo Español de Reanimación Cardíaca Pediátrica y Neonatal*)
- AEBLH (*ASOCIACIÓN ESPAÑOLA DE BANCOS DE LECHE HUMANA*)
- SEH-LELHA (*Sociedad Española de Hipertensión*)
- SEN (*Sociedad Española de Nefrología*)
- *Asociación Española de Bancos de Leche Humana, amongst others.*

- Various patient associations and organizations have signed letters of support for the RICORS Maternal and Child Network:
  - EFCNI: *Diversas asociaciones de padres de prematuros, enfermedades raras, a nivel nacional y europeo*
  - *Fundación Save the Children*
  - AVAPACE (*Asociación Valencia de Ayuda a la parálisis cerebral*)
  - ATE (*Asociación de Pacientes con Atresia de Esófago*)
  - *Asociación Nacional de Infértiles*

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## ADDED VALUE OF SCIENTIFIC COLLABORATION AMONG THE DIFFERENT RESEARCH GROUPS AND MANAGEMENT OF THE INTELLECTUAL PROPERTY

Functional structure of the programme: describe the extension of the synergies and the added value to be obtained from the cooperative structure.

Scientific relationship between the different research groups in the proposed research topics: describe the ongoing scientific collaboration between different groups of the programme on the proposed objectives.

Describe the management of the intellectual property, in terms of previous knowledge, access rights, knowledge generated within the project and exploitation agreements.

Max. 2 pages (10,700 characters)

### Functional structure of the programme

Participating centres involved in the RICORS Maternal and Child Network are among the leading centres for research in fetal, maternal and child health in Spain. To be able to achieve the aims of this ambitious programme, and translate it to primary care setting, it is essential that centres of excellence are involved, who each have expertise in different specific areas, and who also have experience participating in multidisciplinary multicentre research, in order to achieve an adequate sample size of patients and standardize management protocols. Therefore, the cooperative structure proposed between centres will offer clear added value than a sum of individual projects:

1. Sample size and population: coordinated projects will ensure sufficiently large sample sizes for the specific pathophysiological groups described previously, with common diagnostic and inclusion criteria that will ensure applicability of our findings and external validation due to the multicentre nature of the projects.
2. Ability to perform the large prospective studies from the prenatal stage to early childhood that involve both maternal and foetal/child health. Few studies have tackled integration of prenatal, pregnancy and postnatal data, or attempted to evaluate repercussion of risk factors and interventions during these 3 stages.
3. Provide pre-clinical solutions, focused on preventive medicine that may be translated to primary care settings, with capacity for immediate external validation through the collaborative network.
4. Development of solutions focused on personalized medicine, since due to the sample sizes and multicentre nature of the network, statistical power will be sufficient to develop individualized risk algorithms, and therefore individualized prevention and follow-up strategies.
5. Establishment of synergies between high performance multidisciplinary research lines: It will bring together a multidisciplinary team of obstetricians, paediatricians, midwives, nurses, epidemiologists, family care practitioners, nephrologists, cardiologist, psychologists and anthropologists.
6. Creation of a single themed database and biobank, available for new studies associated to network projects, and other initiatives that may arise in the future.
7. Translational research and capacity building and competitiveness of the SNS. Long-term sequel from complications of pregnancy and early childhood are a world health problem. Complications of pregnancy affect 15% of pregnancies, but incidence of complications is under-reported, and follow-up of these patients in the Primary Care setting lacks specific protocols to detect early complications or risks, in both mother and child. The sum of specialized individual groups will provide an outstanding database with enough patients to obtain meaningful clinical answers, to generate protocols targeting problems described previously.
8. Creation of talent within the network, both in the research and clinical setting, in hospitals and primary care centres.
9. Dissemination of good practices through protocols generated by agreed clinical management, with mobility and transfer of technical, clinical and scientific knowledge among members.
10. Opportunity for new international initiatives and collaborations; availability of a national database and biobank will favour possibility to collaborate or enter in international initiatives, and expected results will qualify for new sources of international funding.
11. High social impact; results obtained will have a great impact on quality of life of these mothers and children. Development of these programs will allow adequate follow-up of mothers and children at high risk for cardiovascular, metabolic, neurodevelopmental and other chronic diseases. Expertise provided by the centres will be translated to social programs for support of these families, that will consist of educational campaigns for cardiovascular risk screening and detection in women, as well as knowledge of risk factors and screening programs for children in these areas.

### Scientific relationship between the different research groups in the proposed research topics

The programme will coordinate large projects in the field of Women and Child Health in Spain, focusing on strategies for preventing long-term consequences or complications in these populations. It has high value-added synergies, by combining complementary methodologies and approaches from different medical specialties and backgrounds.

There is a powerful and established synergy within the Maternal and Child Network that has the resources to develop twelve main objectives: (i) promote maternal health (nutrition and exercise) in obese and diabetic women to improve perinatal and infant outcomes; (ii) identify women at risk for placental complications of pregnancy (preeclampsia and intrauterine growth restriction), implementing a primary care screening program in the first and third trimesters of pregnancy; (iii) improve cardiovascular health in women by early identification of risk factors according to obstetrics outcomes, and to provide integral

primary care follow-up after pregnancy; (iv) elucidate the role of environmental factors, green spaces and noise pollution in pregnancy outcomes at the community level; (v) early detection, community support and treatment of women that use or abuse drugs and alcohol during pregnancy, with family-care support for both mother and child to avoid long-term consequences of addictive behaviours; (vi) identification of newly born infants at risk of neurodevelopmental impairment (prematurity, rare diseases, intrauterine growth restriction, perinatal hypoxia) and provision of ad hoc neonatal follow-up guidelines especially designed to be implemented in the primary care setting; (vii) explore the impact of an active promotion policy of maternal breastfeeding in child development; (viii) evaluate the impact of lifestyle strategies to improve cardiovascular and metabolic health in those children with high-risk (intrauterine growth restriction, maternal diabetes, obesity); (ix) implement protocols to aid in prevention, early detection, monitoring and sequelae of childhood chronic serious diseases (cardiac arrest, paediatric stroke, brain trauma, post-cardiac surgery, neuro-infections, long-term hospital stay); (x) prevention, early detection and follow up of paediatric patients with chronic renal and digestive diseases in primary care units; (xi) include patients' experiences and point of views in the design of policies to improve different aspects of maternal and child health; (xii) include e-health technologies to improve detection and follow-up of different maternal and children chronic conditions, in the primary care setting. In the last years, members of this group have obtained several national grants and are coordinating many clinical trials, being involved in international clinical trials. This group has generated more than 1200 original papers published in high impact factor international medical journals.

Twenty groups and 26 clinical associated groups from all around Spain, both from hospital and primary care setting, will carry out different WP tasks at the clinical level with common objectives and design.

Activities will include transverse platforms for execution of each project, with unique or shared responsibility between centres, requiring the following:

- Coordination for definition of joint protocols
- Monitor compliance with objective quantitative and qualitative measures
- Ensure dissemination of good clinical practices
- Integration of data in a central manner

Platforms provided will be as follows:

- Platform databases (coordinate by Lola Gómez-Roig): web platform RICORS Maternal and Child Network with integrated software tools, protocols and electronic databases developed.
- Platform for ultrasound image storage, including MRI, Doppler ultrasound and cardiac function imaging (coordinated by Elisa Llurba).
- Platform for biobank and biomarkers, with definition of sample standards, processing, units, databases, storage and project sharing (coordinated by M Dolores Mesa).
- Platform for neuropsychological monitoring (coordinated by Fernando Cabañas).
- Platform for cardiovascular monitoring and follow-up (coordinated by Patricia Fernandez for adults and by Gerardo Rodríguez).
- Platform for data analysis (coordinated by Max Vento).
- Platform for dissemination and educational activities (coordinated by Diana Marre).

#### **Describe the management of the intellectual property**

The programme coordinator will be responsible for coordination of dissemination and promotion activities, ensuring that results are adequately disseminated and there are no conflicts of interest among group members. The legal framework of the consortium will be represented by a Consortium Agreement (CA), to be signed during the first month. The CA will essentially contain the following points:

- a) Internal organization of the consortium, governance structure, roles and responsibilities, decision-making processes and management arrangements.
- b) Arrangements for distribution of partner contribution.
- c) Provisions for settlement of internal disputes, treats including cases of abuse of power.
- d) Any other provisions necessary to ensure a sound management of the project.
- e) Gender Aspects: This project already promotes gender balance in each research team, through equal opportunity hiring (in line with the *European Charter for Researchers and Code of Conduct for Recruitment*), flexible working family hours and maternity-friendly conditions, and work-life balance initiatives.

To this end, he will establish appropriate links with external agencies and bodies engaged in implementation activities. This strategy will allow scientific knowledge generated by the consortium to be actively disseminated amongst academic communities, to validate it, and amongst group members, to ensure it is valid. The full range of scientific, technological and product/process/system specific dissemination activities will be enabled without compromising the protection of the foreground IPR.

