Draft proposal for a

European Partnership under Horizon Europe

Fostering a European Research Area for Health Research (ERA4Health)

Version 21 December 2021

Summary

Majority of Investments in Biomedical and Health research at EU level belong to Member States. Around 10% of this budget could be considered for joint and collaborative research. This Partnership brings the opportunity to increase the European collaborative research funding, eliminate redundancies and reduce fragmentation by creating the seed of a **joint funding body** for the flexible joint programming of health related research and innovation programmes. ERA4Health will effectively involve public funders of health research in the European Research Area that jointly identify and implement a common good/best practice funding strategy in priority areas on various **health interventions addressing important public health needs**.

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[1] https://www.era-learn.eu/documents/final_report_ms_partnerships.pdf

The ERA4Health SRIA will be only approved and adopted by the Management Board once the Partnership is eventually launched. For more information on the whole process see Annex II.

The following countries have expressed their support and interest and have contributed to the development of this draft version either by participating in the Working Groups, in the dedicated survey (see more information in section 2.2) or the discussions in the plenary meetings: AT, BE, DE, CR, DK, EE, FR, HU, IE, IL, IT, LT, LU, NL, NO, PL, PT, RO, SP, SE, TW, UK.

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Content

1. Context, objectives, expected impacts

1.1. Context and problem definition

1.1.1 Policy context: the European Research Area

The European Research Area (ERA) was launched in 2000 to address the fragmentation of the EU's research and innovation system. The ERA aimed to promote:

- optimal transnational cooperation and competition, including research infrastructures
- an open labour market for researchers
- gender equality and gender mainstreaming in research
- optimal circulation, access to and transfer of scientific knowledge including knowledge circulation and open access
- international cooperation

The Commission published in 2007 a Green Paper summarising its progress[2]. In 2008, the Council of the European launched of the 'Ljubljana process'. The European Commission confirmed its engagement in the ERA with its ERA communication in 2012[5], with an ensuing renewed partnership between Member States, the Commission and research stakeholders adopted in Council conclusions. The Council's 2015 publication of an 'ERA Roadmap'[3] aimed to increase Member State participation, as they are expected to implement the necessary reforms to establish the ERA, but are considered to have been the partners less involved to date. The activities developed at European level under the ERA concept led to more integration of national research systems, coordination and interoperability in Europe, especially on research infrastructures, researchers' careers and mobility, **joint programming of research programmes** and public-private partnerships[4].
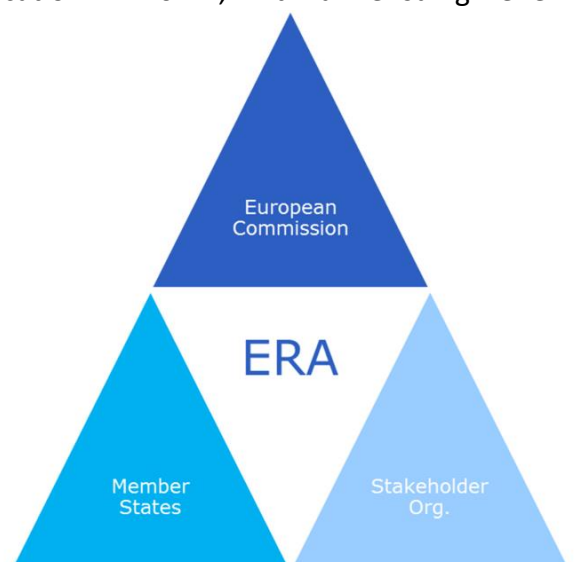
Over the last two decades, a wide range of ERA-related policy reforms and initiatives have been successfully implemented, contributing towards the overarching objective of realising the ERA. However, strong barriers to reaching an optimal situation remain. Firstly, the divisions of research competences between European, national and regional level have not been clearly defined. Secondly, the diversity of national research systems and the gaps in R&I investments and performance between the leading and lagging European regions hinder distribution of common resources and complicate setting the right balance between competition and cooperation. Moreover, using cooperation tools to foster national research policy coordination has introduced more complexity and more fragmentation of some European R&I eco-system.

The need for a **new ERA paradigm** is recognised in the European Leaders' agenda 2019-2024 which underlines that 'we must devote investment to people's skills and education, do more to foster entrepreneurship and innovation and **increase research efforts, in particular by addressing the**

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[2] The European Research Area: New Perspectives. COM (2007) 161
[3] ERAC Opinion on the European Research Area Roadmap 2015-2020 (ERAC 1208/15)
[4] The European Research Area: Evolving concept, implementation challenges (2016). ISBN 978-92-823-8859-4

fragmentation of European research, development and innovation'[5]. This new ERA paradigm must take place in close interaction with all the relevant R&I stakeholders, as well as, with the wider society, to provide a greater focus on outcomes and impacts to ensure that ERA delivers benefits for the society.

ERAC recognized in its 2019 opinion that, following the Horizon 2020 interim evaluation, investment in developing the ERA, an excessive number of Partnerships had developed, further contributing to the fragmentation of the ERA and pre-allocating too much national funding to previous EU level commitments, thus hindering national focus on national priorities.

The Council Conclusions on the New European Research Area[6] approved on 1st December 2020, calls on Member States and the Commission to prioritize investments towards the "New ERA" and reaffirms the 3% EU GDP R&D investment target. Invites Member States to set investment targets at national level, in particular with respect to public R&D efforts. The Council also took note of the Commission proposals to include a new 1.25% EU GDP public effort target to be achieved by Member States by 2030 in an EU coordinated manner and two new voluntary targets for Member States **to commit 5% of national public R&D funding to joint programmes and European partnerships by 2030** and to increase by 50% the R&D investment in countries that are below the EU R&D intensity average.

1.1.2 Elements for an ERA concept for Health Research

The members of "Fostering an ERA for Health" are committed to the 2030 Agenda for Sustainable Development to ensure healthy lives and promote well-being for all at all ages (SDG 3). The World Economic Forum 2016 has emphasized the value in health care as has the High-Level Strategy Group on Industrial Technologies of the European Commission (2017). In the United States, a consensus study report of the National Academies (2017) set out a path for global health, emphasizing the importance of international collaborative efforts, of improving R&D processes and developing digital health. The report of the European Commission's High Level Group on maximizing the impact of the EU R&I Programmes (2017), stressed the importance of a mission-oriented, impact-focused approach to address global challenges, to align EU and national R&I investment and to mobilise and involve citizens.

This partnership is fully aligned with the objectives of Horizon Europe and would contribute to achieving the following European Commission priorities:

- Promoting our European way of life
- An economy that works for people
- A Europe fit for the digital age

The partnership will contribute to priorities of the "*Communication on effective, accessible and resilient health systems*" (COM(2014) 215 final) by promoting actions on strengthening the effectiveness of health systems, increasing the accessibility of healthcare and improve the resilience of health systems.

The activities to be performed under the framework of ERA4Health are aiming to ensure:

- citizens' secure access to and sharing of health data across borders;

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[5] ERAC Opinion on the future of the ERA (1201/20)
[6] https://data.consilium.europa.eu/doc/document/ST-13567-2020-INIT/en/pdf

- better data to advance research, disease prevention and personalised health and care;
- digital tools for citizen empowerment and person-centred care

as stated in the "*Communication on enabling the digital transformation of health and care in the Digital Single Market; empowering citizens and building a healthier society*" (COM(2018) 233 final).

ERA4Health supports the objectives of the Commission proposal for the new EU4Health Programme (COM(2020) 405 final) as well as contribute to achieving the objectives of the Pharmaceutical Strategy for Europe[7], in terms of fulfilling unmet medical needs and ensuring that the benefits of innovation reach patients in the EU.

Investigator Initiated Clinical Studies

Clinical study means, for the purpose of this document, any systematic prospective or retrospective collection and analysis of health data obtained from individual patients or healthy persons in order to address scientific questions related to the understanding, prevention, diagnosis, monitoring or treatment of a disease, mental illness, or physical condition. It includes but it is not limited to clinical studies as defined by Regulation 536/2014 (on medicinal products), clinical investigation and clinical evaluation as defined by Regulation 2017/745 (on medical devices), performance study and performance evaluation as defined by Regulation 2017/746 (on in vitro diagnostic medical devices).

As indicated in the Forward Look on Investigator-Driven Clinical Trials produced by European Science Foundation[8] there are a number of areas where conditions for non-commercial clinical trials can be improved in Europe:

i. The **funding** aspect is a special problem because it is very expensive to perform large-scale clinical trials. For this reason, large-scale clinical trials are mainly undertaken by the pharmaceutical industry for diseases that affect large numbers of people. Rare diseases groups or new indications for established drugs are usually ignored. By the same token, funding for IICS was and frequently still is lacking, even though such trials are capable of increasing our basic understanding of diseases and improving healthcare. In addition, there is increasing pressure on clinical investigators to provide more routine clinical care services thereby decreasing the amount of time they can devote to research. Strategies for increasing the amount of research time available to clinical investigators and increasing funding and overall support for IICS are thus urgently needed.

ii. National and EC authorities have rules and regulations that govern clinical trials and these are interpreted differently by the different member states. This is an important obstacle for performing clinical research in Europe.

iii. In many countries there is a general perception that the attractiveness of patient-oriented research as a career has declined and that there is a shortage of qualified researchers. There is also a lack of incentives for qualified personnel to enter the field. An important obstacle to the development of an optimal strategy for non-commercial clinical trials is the issue of appropriate career structures in clinical medicine.

iv. Data ownership: in commercial clinical trials sponsored by the pharmaceutical industry, data are not owned by and open to researchers and the participating patients. While it is

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recognised that there are issues of intellectual property, the advancement of knowledge requires data to be shared and more needs to be done to address this.

v. Clinical and translational medicine requires a solid infrastructure comprising research centres and clinical trials units. These are centres of competence and excellence that are founded upon expertise and which provide access to patient-oriented research projects originating from the surrounding scientific community – academic scientists, investigators or industry sponsors. Professional staff trained according to good clinical practice, hospital beds, equipment devoted to patient-oriented research and standard operating procedures ensure that clinical studies are designed and conducted to the highest standards. In Europe there is a lack of enough of such infrastructure for clinical and translational medicine.

The new EU Clinical Trials Regulation on clinical trials[9] that is already in force and will be applied from 31 January 2022 promotes important changes to make Europe more attractive for clinical trials. As a new concept, it also introduces low-interventional trials (e.g. pragmatic trials to optimise treatment) with risk-proportionate regulatory requirements that needs public support since no commercial interest exist. In addition, promotes the following:

- Introduction of the concept of a patient's 'one-time' consent for use of data, tissues and biological samples, exclusively for the purposes of medical research, that extends beyond the trial itself, with the possibility for the patient to withdraw consent at any time. It is essential that this concept is implemented consistently within both the EU Clinical Trials Regulation and the EU General Data Protection Regulation[10], and also in all countries because some regulations, like ethical approval, will be the competence of individual national authorities.
- Strong transparency of clinical trial data through the publication of all studies, regardless of results, on a single website
- Streamlining of the application process, adding strict timelines for approval by Member States
- Creation of a single portal for data submissions that will reduce the bureaucratic burden on researchers, particularly for multi-country clinical trials
- Creation of an EU database identifying each clinical trial
- Opinions will now have to be issued within new legally provided timelines (while maintaining the role of ethical committees)
- Definition of ultra-rare diseases as a political concept introduced for the first time at EU level

Public to public (P2P) instruments in Health research

A number of achievements have been accomplished in an evolving European Research Area[11]. The interest of countries in participating and investing in P2Ps initiatives has been continuously rising since the launch of the first ERA-NET scheme in FP6. In an ERA-Net, national/regional agencies fund R&I projects (each country supports the participation of its scientists within a transnational project) and the Commission supports coordination of the network of funders. It is characteristic that in the period (2013-2017) in addition to the 28 EU Member States a total of 13 Associated Countries and 50 Third Countries have participated in P2P calls. This is more impressive considering that in the first five-years (2004-2008) the numbers were 24 Member States, 10 Associated

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[9] https://ec.europa.eu/health/sites/default/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf
[10] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0679&from=EN
[11] https://www.era-learn.eu/documents/era-learn-publications/era-learn-15-yr-brochure-aw2-web.pdf

Countries and only 4 Third Countries. This shows a strong contribution of P2Ps to the internationalisation of European research.

Accordingly, the level of national investments in P2P calls has been constantly increasing since 2004, and is almost Euro 8.9 billion (excluding EU contribution) in 2020 (including JPIs, FP7 ERA-NETs, Cofunds, Art. 185s and self-sustained P2P networks). The EU support of P2Ps across the different FPs has also increased significantly, from €380 million in FP6 (2.1% of the FP6 budget) to €802 million (1.4% of FP7 budget) in FP7. In Horizon 2020 it is estimated to reach approximately €2.5 billion (around 3.1% of the budget). This investment has mobilised national contributions that have increased exponentially over the years, i.e. €1.25 billion of national funding under FP6 and around €2.9 billion under FP7, to €6-8 billion in Horizon 2020 (Horizon 2020 Evaluation). The cumulative expenditure by the end of 2020 is €9 billion in more than 9,300 transnational projects[12].

In the figure below it is shown the cumulative Investment in Joint Calls, including EU Contribution, 2004-2020.
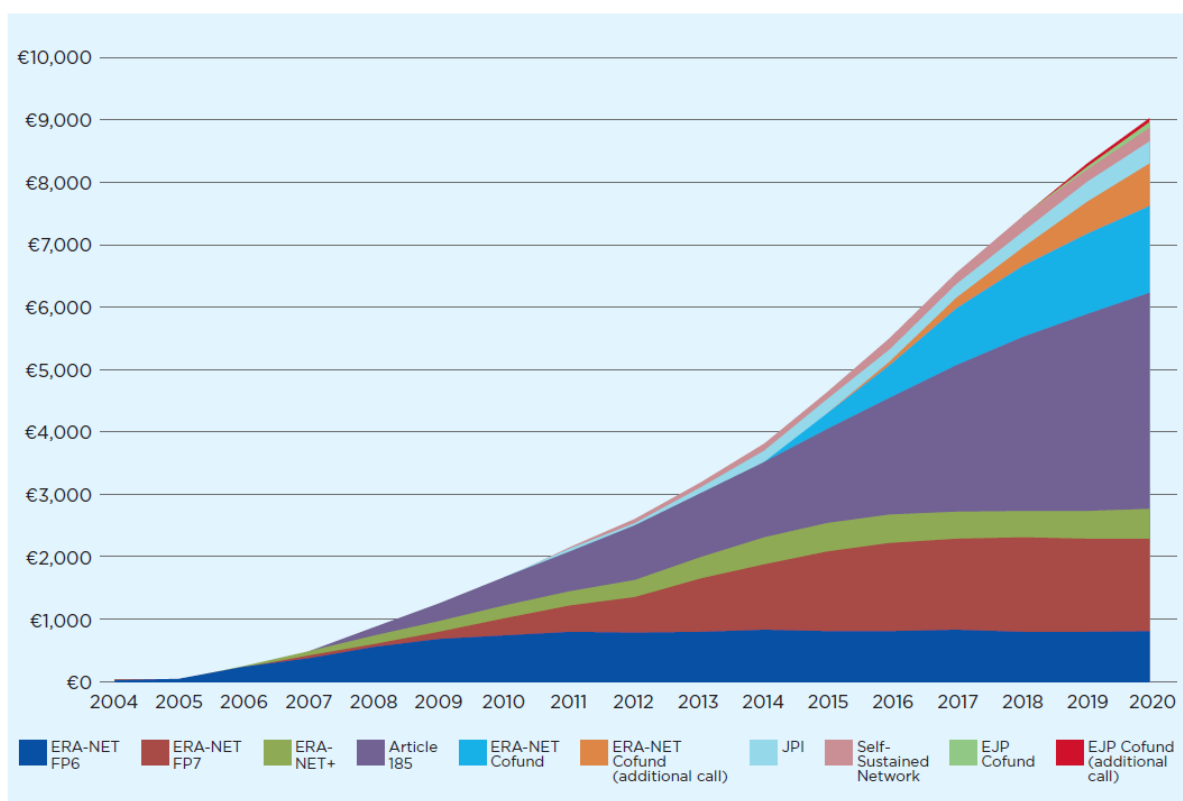
Biology and Health is an area where several pilots have developed a healthy eco-system of Public-private and Public Partnerships since 2003. The ERA-NET instruments, in their various forms, from the early ERA-NETs in FP6 to ERA-NET plus and ERA-NET Cofund, have been largely invested by European public funding agencies, national or regional research funders. Along with ERA-NETs, Article 185 TFEU and Joint Programming Initiatives were built. European Joint Programme co-fund action were also set up, with various configuration, encompassing or not ERA-Net-like capacities, and implementing multiannual programmes.

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[12] Annual Report on Public-Public Partnerships 2020 of ERA-Learn

Research fields covered during these years of ERA building where numerous. The figure below, extracted from ERA-LEARN website, aims at listing the P2P in the Health theme. Only active networks are shown.

	19	2020	2021	2022	2023	2024	2025	2026
Institutionalised Partnership	EIT Health-KIC							
ERA-NET-Cofund	ERA-CVD							
	JPI-EC-AMR							
			JPIAMR-ACTION					
	NEURON Cofund							
			NEURON Cofund2					
	ERA-HDHL							
	HDHL-INTIMIC							
	PhotonicSensing							
	EuroNanoMed III							
	FLAG-ERA II							
	ERA PerMed							
	JPCOFUND2							
	ICRAD							
	AquaticPollutants							
			M-ERA.NET 3					
			TRANSCAN-3					
EJP Cofund	HBM4EU							
	One Health EJP							
	EJP RD							
Article 185	AAL 2							
	EMPIR							
	EDCTP2							
	PRIMA							
JPI								
EIT - KICS	EIT Health							
FET - FLAGSHIPS	human brain project							
Other	ERIC							
	ETP							
	SEA-EU-NET (self-sustained)							
	EUREKA							
	19	2020	2021	2022	2023	2024	2025	2026

Nevertheless, this list helps to underline how the instrument, being versatile, allowed Countries, to mobilize national and regional money to work together on areas deemed worthy of specific support, in addition to the RIA or IA types of actions, in the successive framework work programmes. Topics selected for support, by Member States and Associated Countries, and by the Commission, after discussions at Thematic Committee level, could be either very cognitive and upstream research at the forefront of scientific breakthrough, consolidation around dedicated medical fields with a recurrent need for better mechanistic understanding and support for discovery of new measures for prevention, diagnostics or treatments, reactions to perceived new threats on public Health. Successful ERA-NETs could have extended life-time, while some attempt remained as single shots.

Funding of **Investigator Initiated Clinical Studies** is a significant concern. Organising multinational clinical trials is time-consuming and expensive. Although Framework Programme 7 and Horizon 2020 provided some grants for clinical trials but mainly phase II trials and not large phase III, **there is no pan-European funding agency comparable to the National Institutes of Health in the US**.

ERA-NETs generally proceeded with a general scheme:

The main goal is the joint preparation and implementation of a research programme of common European interest. Many of the P2P's activities are related to reach this goal: definition of strategic research (and innovation) agendas; preparing the necessary call documents; setting up of a proposal submission system; checking the eligibility of received proposals; organising the

evaluation meetings; agreeing to a final funding decision within the group of involved funding organisations[13]. The operational activities and main features of P2P's include:

1. A scientific advisory board to refine expression of needs and areas of gap- filling/ optimal use of the cash raised by the Agencies
2. A decision-taking management board aligning the funders
3. Call operating systems based on national platforms made available for the community, with multinational call secretariat for operations
4. Calls were open calls, expecting a broad range of applicants and opening the possibility for newcomers to bring their expertise, skills and research capacities or infrastructures to the prioritized field

Call planning → Submission → Evaluation → Funding decision → After the call → Call planning

5. Selection of projects by international panels, usually using criteria based on relevance to the scope of the call, scientific excellence, potential impact, quality of construction and consortium to achieve the goals, dissemination scheme. Other criteria regularly incorporated were capacity building and widening, and gender equality
6. Process for project follow- up, dissemination and scientific animation
7. Performance indicators
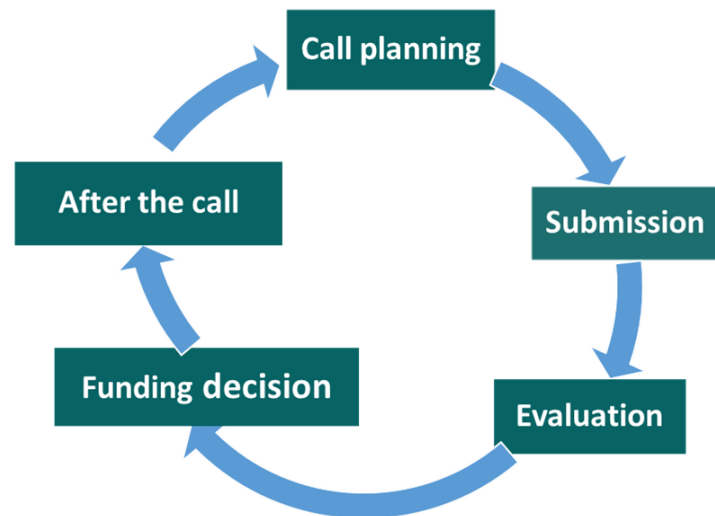
It is worth underlining that most funders are, by status, able to fund only national or regional research performing organisations, with sometimes restrictions or limitation of spectrum. Decision processes to validate engagement in a call and scale of that engagement vary from country to country, pending autonomy of said funders profiles, and also calendar schedules. Once decision has been taken to fund a project, each country interacted with its national research teams and institution to apply national rules for funding and follow- up.

Another remarkable point to emphasize, is that the ERA-Nets attracted non-European Union Countries, which could participate, on their own expenses, in the international ERA building. In this international setting and in some ERA-NETs, like in EuroNanoMed, the concept of **Responsible Research and Innovation (RRI)** has successfully been implemented and further developed[14].

Improving the European Research Area in Health research

Currently, several ERA-NET Cofunds are running in parallel with similar structures and actors (approximately 80% of all investment is made by 19 funding organisations from 10 countries) that are present in almost all these programmes (see Annex 1) including the European Commission

These ERA-NETs were in general focused each on specific scientific areas, and they all had similar bodies and activities (i.e. each one has: a specific Scientific Advisory Board, Capacity Building programmes, communication and dissemination actions, etc.). Whereas logistics around the open

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[13] Partnership Landscape related to Health Research. Description and Analysis (March 2018). ERA Learn
[14] Guidelines for Responsible Research and Innovation (RRI) in proposals to EuroNanoMed III

call processes were quite similar, handled by few actors, with shared call secretariat to exchange on procedures and best practices for calls. Following all these numerous networks has a huge impact in the participating funding agencies, in particular for those from smaller countries, that have to follow in parallel all these activities multiplied by the number of programmes in which they participate, including the attendance of numerous meetings, and in some cases to accept diversification of criteria.

> The Partnership "**Fostering an ERA for Health Research**" would aim to establish a flexible and much more effective coordination between most funding organisations of the numerous networks established in the European Research Area (ERA) for Health and Well-being. This will be done by centralizing those activities that are common or quite similar, while keeping the diversity needed for the scientific development in each of the thematic fields.

The Partnership ERA4Health will be an **instrumental platform** for joint programming of national research programmes. ERA4Health aims to compromise between three types of R&I funders:

- countries (and regions) which rather "fund rich", this having large and diversified R&I programmes, such as DE, FR and NL;

- those which are large, but rather "staff rich", allowing them to invest in meetings and coordination, such as IT, ES and PL;

- and the majority of countries which struggles to invest moneys and staff in such collaboration, despite their wish to do so.

This collaboration would mitigate the inequalities by orienting alternative scenario directly linked to further developments. Centralizing horizontal activities would reduce the overall operational costs and country/regions efforts which definitely would help countries and regions with less funding resources and less manpower dedicated to running these programmes. Implementing RRI related actions in the operationalisation of the Partnership and asking for RRI perspectives in the calls will so contribute to **achieve UN SDGs**.

Funding for Multinational Investigator Initiated Clinical Studies (IICS)

Despite the advantages of multinational clinical trials, just 3% of academic trials (vs. 30% of industry trials) involve more than one country. In Europe, the relative scarcity of multinational academic trials can be explained, in part, by restrictions with current cross-border funding options.

Significant support for clinical trial projects were made from 2014 to 2020 through H2020 Challenge calls such as, Health, Demographic Change and Wellbeing, which includes the Innovative Medicines Initiative (IMI) dedicated to public-private partnership projects (non-industry partners in consortia receive public funding, while companies contribute to the projects through in-kind contributions), Eurostars (Art. 185 for SMEs) and the European and Developing Countries Clinical Trials Partnership (EDCTP).

The European and Developing Countries Clinical Trial Partnership (EDCTP) is an example of a funding programme based on a combination of central, European funding and national sources. The budget comes from the European Commission, national member countries, and third parties such as private sector and other international partners (€683M, €683M and €500M respectively for 2014-2024).

The programme funds trials addressing malaria, tuberculosis, and HIV, as well as other poverty-related and neglected diseases in developing countries. All European and sub-Saharan African countries are eligible for funding, and partnership with private funders is possible. Proposed clinical trials should involve at least two European and one sub-Saharan country.

In general, national funding agencies do not accept cross border funding, inhibiting international collaboration. However, there are some exceptions:

- Innovation Fund Denmark, which has a total budget of 144M€, including 17M€ for projects on "individuals, diseases and society". Funding is available for clinical trials (about 20M€ over 7 years) with a significant share (12%) for international partners. The German Research Foundation (DFG) considers provision of a maximum of 20% of a clinical trial budget to sites in Austria, Luxembourg and Switzerland.
- An alternative strategy of creating a common pot for funding trials has been adopted by the Nordic Trial Alliance (NTA), running from 2013 to 2015 and covering Denmark, Finland, Iceland, Norway, Sweden, the Faroe Islands, Aland Islands and Greenland. The NTA budget comes from Nordforsk and national research councils. Funding supports multinational expansion of clinical studies whose funding is secured in the coordinating country. Supported trials must be run in a minimum of three of the member countries. These approaches have been successful in promoting research and competitiveness for the subset of eligible countries. 674 clinical trials across the region were initiated in 2015 with oncology the top therapeutic area. Over 50 percent of studies that year were sponsored by pharmaceutical companies compared to academic institutions, indicating pharma remains a force to be reckoned with. However, the numbers reveals that Phase IV studies were largely academic-sponsored while Phase I and Phase III trials were mostly conducted by industry sponsors.

Since cross-border funding is not possible for most funding agencies, countries have begun to join forces by coordinating national sources to fund multinational clinical studies using the ERA-Net cofund instrument. As previously mentioned an ERA-Net can cover a large number of diverse countries and combine national sources, with each country supporting the aspects of the project that occur nationally.

Existing ERA-Nets usually focus their call for projects on basic and translational research although there have been some examples where clinical studies have been funded, for instance on E-Rare-3 2016 call "Clinical Research for New Therapeutic Uses of Already Existing Molecules (repurposing) in rare disease" and in some others where clinical research is allowed but usually for very early stages (phase I or II) and tangentially to the core central part of the project.

The possibility of joining European funders for multinational clinical trials in this Partnership is an optimal solution for near-future financing of multicountry trials. In this model, proposals would be evaluated by a panel that would review the medical relevance and methodology of the trial protocol. The funding agencies would contribute a funding volume adapted to the cost of the trial. Moreover, the Partnership would allow expansion to countries outside Europe, creating an instrument with global potential.

1.1.3   Links to previous R&I Partnerships

Many public funders of research on Health and Well-being in the European Research Area are very experienced as partners in several ERA-NETs and Joint Programming Initiatives (JPIs). By contract,

these networking and joint programming activities are focused on specific priority areas with coordinated co-funding, but sometimes there are different strategies to align and leverage national funding. They depend on EU and national investments sometimes insufficient to achieve the desired scale and scope.

Current health-related partnerships funded under Horizon 2020 are:

- JPco-fuND-2 on Neurodegenerative Diseases; NEURON Cofund II on Neurosciences; Flag-ERA III (Human Brain project) which could cover a future Partnership on EU Brain Area;
- TRANSCAN 3 on Cancer, which might be mobilised to support the EU Mission on cancer;
- ACTION on Anti-Microbial Resistance;
- ERA-CVD on Cardiovascular Diseases;
- ERA PerMed on Personalized Medicine;
- EJP cofund on Rare diseases;
- EuroNanoMed 3 on Nanomedicine;
- plus, possibly, three networks having their centre of gravity on Clusters 2 and 5: ERA-HDHL and HDHL-INTIMIC (on Diet and Health, Cluster 2 and 5); CORE Organic Plus (on Organic farming, Clusters 5 and 2).

Public health research funders in the EU, support biomedical research and innovation in order to:

i. improve the knowledge and understanding of health, health promotion, and disease prevention and treatment;
ii. to develop new and better health therapies, technologies, tools and digital solution.

This implies a management and support to people's health and well-being as well as to prevent detect, treat and cure diseases.

Moreover, for researchers, ERA-NET calls represent a formidable opportunity to start building international connections and share research with European colleagues at an excellent level of scientific excellence. It also enables collaboration across borders with regards to innovations and RRI. The ERA-NET scale, usually somewhat smaller than classical H2020 RIAs, offers a very good start to develop networks and the expertise to work, then coordinate, at this international scale and then get access to H2020 calls.

For funding agencies, it allows to sustain national researchers – most funding agencies only fund national laboratories or research performing organisations – but to allow their investigators to participate in projects representing much larger scope than their own local tasks, and to facilitate international contacts, access to research infrastructures or international facilities. The ratio of money invested / research funding in which the country is a partner is always largely positive.

By participating and committing more than one € Billion in partnership with the Commission over the last 20 years (ERA-NETs, Art 185 and 187, EJPs and JPIs), public health research funders in Europe have proven that they are interested, committed and able to unleash added value by working together and co-funding research collaborations at European level. They have also indicated a strong interest not only to continue current partnerships but also to create and explore new ones in priority areas of pre-clinical and clinical research. EU-supported partnerships in the health area are amongst the oldest and most effective ones. In particular, the nine ongoing Partnerships have invested some €500 million, leveraged by the €50 million of EU direct support.

Rationalisation of health ERA-NETs has taken place, with the following elements:

- national/regional funders have prioritised their involvement in ERA-NETs. Some ERANETs, and their addressed research areas have been given up (cancer guidelines, HIV/aids, paediatric medicines) but important research areas have evolved from this process (e.g. neurological diseases: JPND, NEURON; cancer: TRANSCAN; cardiovascular diseases: ERA-CVD; rare diseases: E-Rare), with continuous support of national/regional funders and the EC
- a general restructuring of the ERA-NET selection (and prioritisation) process by the EC, from FP6 (bottom-up) to FP7 (top-down, support for management) to H2020 (top-down, Cofund)
- in H2020, the EC has introduced defined criteria such as impact, leverage, EU added value, size of national/regional budgetary commitments which have to be met by a planned (new, to be continued) ERA-NET Cofund in order to be included in the EC's work programmes

Nevertheless, there is always room for improvement, two main **weaknesses** are observed:

- Participation and benefits of current Partnerships are variable depending not only on the impact of a given area on the national eco-system, but on the type of funder. In particular, smaller and resource poor countries struggle to participate in actions, even when such participation would both boost the ERA and the national research eco-system.
- Critical shortage in several actions of a common methodology among the different Programmes and JPIs and in their actions

Why is this initiative being proposed now?

As stated by the Scientific Panel for Health (SPH) "The European funding landscape is rich but the framework for health research has limitations, which, if addressed, would better serve health needs[15]". This Partnership seeks the opportunity to increase EU cohesion and to enable alternative adequate settings at different levels to accomplish a common EU ecosystem by positioning a challenging structure aiming to achieve a **common European Eco-System** for a reliable Interregional, and inclusive Health Research and Innovation strategy aligned to the national health programmes through EU. In addition, in a post-Brexit situation, this Partnership could **strengthen the EU strategic position** and help in attracting UK back towards the ERA orbit rather than spinning-off towards the NIH and US.

The timing of such a partnership is perfect. European research funding organizations, researchers, health and care system owners, policy makers, developers and innovators in the field of Research have skilled experience born by interacting together and running into difficulties.

Concerning the research itself, the time is ripe for further efforts to respond proactively to all evidence and accelerate the studies "from the bench to the bed" and *vice versa*, by treasuring the productivity carried out by the above mentioned ERA-NETs and JPIs. The results of the translational research should be applied into healthcare in responsible and sustainable way by implementing RRI and pursuing **co-creation, co-design and co-production methodologies**.

To bridge the gap between national and industry-sponsored clinical trials a new body should be set up to fund trials that will give healthcare providers the data to ensure patients get the best treatment and enabling them to allocate scarce resources for the maximum benefit. It takes a lot

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[15] Building the future of health research. Proposal for a European Council for Health Research (2018)

of time and energy to get funding for such large-scale trials which seek to answer important questions that are relevant to the treatment of thousands of patients.

The continuously growing arsenal of health interventions, whether it is a new pharmaceutical product, a medical device, a surgical intervention, or other measures utilised during health and care provision, reflecting the increasing demand for better quality of care by citizens, force decision makers of public health systems to optimally allocate limited resources in a well-informed manner. IICSs generate data on safety and effectiveness of a health intervention, often in real-world settings, and thus provide evidence to answer questions that clinicians face in their day-to-day practice in order to optimise the clinical management of patients beyond the context of marketing authorisation application for medicinal products. Such studies deal with potential diagnostic and therapeutic interventions that do not attract, or could go counter commercial interest. These clinical studies are critical to support endorsement of healthcare strategies (repurposing, comparative effectiveness, treatment combination or optimisation studies, personalised medicine trials).

By pooling existing resources, eliminating redundancies and reducing fragmentation, the implementation of multinational IICSs covered by this Partnership will benefit from better access to high number of study participants/patients, medical expertise and facilities, enhanced methodological standards; and shared costs, tools and procedures. IICSs often absorb large resources, that can be used more cost effectively and can deliver results faster. Thus, by synergising on public investments for IICSs in Europe under the common Partnership umbrella, researchers, clinicians and public health practitioners could identify and better align similar research questions related to, for example, the same active substance used in different medicinal products that investigator initiated clinical studies should address.

All these aspects will contribute to generate robust and reliable clinical evidence, increase the potential for broad implementation of research outcomes; prevent duplication of research efforts and allow broad uptake by health systems.

Influencing the EU Member States participation to shift the trend for a more inclusive EU-Ecosystem remains the actual response, in order to deliver high quality evidence based medicine that brings better clinical practice and high standards health care both available and affordable for citizens as well as to rendering health care systems more accessible and sustainable for all the European citizens.

What problems and/or strategic opportunities does the initiative aim to tackle?

In the evolution of the EU framework programs, newly added instruments have enriched funding opportunities and some actions have provided visibility to health research. Altogether, a set of dedicated instruments and calls for biomedical and health research provide opportunities for discovery research, for innovation and partnerships. The drivers and aims for each of these instruments vary and the downside of this rich landscape is the increasing complexity. Furthermore, despite the array of instruments, the main public investment in research still is in the national competence through national research programs and funding as reported for cardiovascular diseases or at aggregate level in the commissioned report by Deloitte, which furthermore highlighted the investment by industry. Despite this apparent wide offering, it is not sufficient – not in its scope, not in addressing health needs.

- Calls for collaborative research in SC1 Health are vastly oversubscribed, even more so than in the overall H2020 program. As a result, a substantial number of **high-quality research projects are not funded**. That oversubscription exists also provides evidence of the large potential for high quality health research in Europe.
- The **lack of sustainability** for collaborative projects leads to waste. EU projects often generate networks that maintain fruitful scientific interactions. However, the lack of continuation of funding undermines sustainability of the collaborative research and threatens data collections such as cohorts, biobanks and registries.
- **Future novel, emerging challenges** will need increased health research support, such as in public health and migration, implementation of a European digital health platform, and fighting major diseases in a mission-oriented approach.
- Access to health care in Europe is not equal throughout member states; participation in **health research is not equitable**. A more inclusive participation in health research would facilitate subsequent implementation of better health care.
- Major potential to advance health exists through building research programs on initiatives such as the European Reference Networks and linking R&I to health care. Such advance is severely hampered by the **lack of a strong cross-sectoral and cross-border collaboration**.

ERA4Health aims to tackle specific needs and opportunities at two different levels:

1. Health research as path to better health

a) Health, health care and health research form **a unique and interdependent ecosystem**. Health care is a national competence but cannot be separated from research. The rising costs in health care can only be managed through research underpinning decisions for implementation.
b) The use of **health data** creates a wealth of opportunities that are amplified by innovations in the digital space. Yet, this potential is currently underdeveloped and underused.
c) Health research is performed in a complex regulatory framework. Navigating the complexity of regulations in health research requires **coordination to meet the needs of society** and to facilitate health research to the **benefit of the patients**.
d) The potential of **precision medicine** raises expectations for further improvement of disease outcomes and increased quality of care but requires evidence and research into effectiveness and impact on overall health care. Health research at the EU-level can identify and address mechanisms that reduce **health inequality**.
e) In the present rapid evolution in societal structure, many changes have an impact on health. Meeting health research needs requires input from many disciplines including the social and environmental sciences, humanities and engineering, and this extends to health policy.
f) Health has no borders. Europe faces important public health threats, e.g. infectious disease, crossing borders of human and animal health. Health research needs a global and coordinated vision that is open to the world and takes a holistic 'One Health' approach.
g) Challenges in health require a **long-term commitment**. Chronic and degenerative disease, mental health, and the growth of co-morbidities are examples of major health issues that need a comprehensive and long-term view. The path from discovery to innovation and implementation is long.
h) Health and health care are pillars of the **social structure**, and a public and societal responsibility. Public funding must address challenges and needs of high public interest, including areas in which the industry is reluctant to invest if the product does not have an attractive market. Health research therefore needs **continued public investment**.

i) Health and health care are leading economic sectors. Several studies have documented the impact of research. EU developments in **digitalization, open science** and the support for creative, discovery science create excellent opportunities for innovation. However, a gap in **translation and implementation remains and requires dedicated support**.

j) The EU manages only one-tenth of the public research investment but is the major funder of impactful, collaborative research. Excellent EU programs push health research, but are not sufficient. This Partnership brings the opportunity to **synergize with European and national strategic initiatives** and a new model for impactful collaborations are needed to address the challenges for health.

2. <u>Fragmentation of European Research Area in Biomedical and Health Research</u>

The proposed Partnership fosters to run all the available resources (human and economic) at large scale and to reinforce and improve the flexibility of the relations and networking among the MSs at every level: Citizens/Patients Organisations, Research Centres, Clinical Health Care settings and Universities, Policy makers, Final users and Industries.

On the basis of our previous experience, we will develop common methodologies that will identify measurable indicators, define the current situation and provide evidences for the future taking into account the primary characteristics of each individual participant.

From the above mentioned weaknesses, some problems seem particularly important:

- Fragmentation of the European Research Area, lack of scale and scope
- Lack of staff by several countries to invest in EU Partnerships

And at the same time the Partnership offers **opportunities:**

- Opportunity to address major challenges jointly on a flexible basis having a single EU level Partnership deciding annually where and when to invest in (good/best practice) joint calls or actions would allow more countries to participate
- Develop a robust assessment for a common methodology of project evaluation that links all aspects (scientific, ethic, RRI, innovation, economic...)
- Gather a targeted engagement will serve to scale up retention for patient and citizen across EU countries by positioning them in our future actions (goals)
- Identify measurable indicators that define the condition at presence and provide evidence for the future
- Estimate findings and opportunities since the number of overlaps were observed

The Health related initiatives and the interaction of their stakeholders started to work together with a vision that shifted to the current scenario that still requires different **strategies** and many considerations among us:

- leading methodologies
- underlined the relevance of ethics and RRI at all stages
- early focus on IPR and regulatory requirements to enable innovations
- effectiveness for the GDPR that need to be addressed
- assess accurate measurable methods to monitor the activities adopted
- carry out settings to involve patient organization, end users and stakeholders
- promoting a gender perspective

- architect a usable platform to show and share the achieved results among all initiatives

And finally the envisaged **advantages** of this Partnership approach are seen as:

- One-stop-shop for many of the health related ERA programmes (existing and new ones)
- Calls with combine targeted actions to limit the gaps that could merit better investments (wide range of TRL levels, and fit to the purpose)
- Calls to improve the capacity building for a better positioning of the achieved results
- Effective intervention between policy maker and industry
- Efficient management
- Flexible and rapid response to deliver results

STRENGTHS	WEAKNESSES
• ERA • Alignment of EU public investment • Widening • SMEs • Programming and Evaluation Methodology • Capacity Building	• Fragmentation • Diverging approaches

OPPORTUNITIES	THREATS
• Leverage and Reinforcement of Health Systems • Increased impact • Citizen participation • Digital Europe • GDPR • International Cooperation	• Marginalisation of Europe • Innovation Drain • UK drift off • Chapels

A balanced approach between research and innovation is a central part of Horizon Europe. Full range of Technology Readiness Levels (TRLs) are considered from curiosity-driven research to commercially-driven innovation and support to market deployment, and within innovation, technological, non-technological and social innovation.

In many instances, new discoveries within basic research create the foundations for research and innovation impacts and lead to a wide range of innovations applicable to our everyday lives. Key Enabling Technologies (KETs), for instance biotechnologies and advanced materials, are crucial for Europe's competitiveness in strategic value chains. Developing and mastering KETs can contribute towards giving EU industries the competitive edge they need for industrial leadership in global markets and promise breakthroughs to solving global challenges and achieving a circular, resource efficient and climate-neutral EU economy. However, as indicated above, the type of funder participating in the network is influencing the type of performers developing the research and innovation activity. Particularly, in Health research networks, funding organisations that fund innovation are not deeply involved as the main objective (but not limited to) is funding pre-clinical research. An umbrella partnership with different kind of funders offer an easy and flexible tool to step in when the funding action targets higher TRLs or R&D closer to market.

1.2. Common vision, objectives and expected impacts

1.2.1. *Vision and core objective*

The EU manages only one-tenth of the public research investment but is the major funder of impactful, collaborative research. Excellent EU programs push health research and innovation, but are not sufficient. Synergy with strategic initiatives in member states and a new model for impactful collaborations are needed to address the challenges for health.

The final goal of research policy in the biomedical domain is better health, through knowledge and insight, translation and implementation. European values and a focus on health and well-being of every citizen must guide policy development. A long-term perspective, continuity and strategic investments can unlock the potential generated by the recent achievements. Public health as the ultimate goal requires a holistic view, beyond coordination and harmonization.

The partnership will ensure Europe is at the forefront of science and innovation in Health Research by 2050. Majority of investments in Biomedical and Health research at EU level belong to Member States and only 10% of the overall budget could be considered for joint and collaborative research (mainly from EU R&I Framework Programmes). This Partnership brings the opportunity to increase European collaborative research funding up to 20% by creating a **funding body for joint programming in priorities addressing European Health Needs**.

> ERA4Health PARTNERSHIP is defined as public funders of health research in the European Research Area that jointly identify and implement a common funding strategy in priority areas to advance health research and develop innovation. Whilst the European Research Area is at the core of the Partnership, the Partnership is open to international partners.

The goals and objectives of this partnership require an unique governance where EU catalyzes the relationship between research and innovation funding organisations (both biomedical/ health research funders and non-thematically oriented funders) and through them the entire R&D ecosystems including (biomedical research performance organisations clinical health settings and Health care systems, biotech SMEs and large companies, etc.) for a joint effort in the continued research and innovation cycle (from definition of priorities to uptake of innovation), which does not currently exist.

<u>Coherence and synergies in relation to major national policies, programmes and activities</u>

The proposed partnership will contribute to achieving the UN Sustainable Development Goals, in particular Goal 3 "Good Health and Well-being", and its sub-target on achieving "universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all", Goal 9 as ERA4Health contributes to foster innovation in a sustainable and responsible way and last but not least this Partnership promotes accountable and inclusive institutions at all levels (SDG 16).

ERA4Health is fully in line with the Orientations towards the first Strategic Plan for Horizon Europe and will also contribute to the following EU policies and policy guidelines:

1. The Political Guidelines for the new Commission (2019-2024)[16]:

   a. A **European Green Deal**. European citizens' health and the planet's health go together. "it is the quality of the air we breathe, the water we drink, the food we eat and the safety

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[16] https://ec.europa.eu/commission/sites/beta-political/files/political-guidelines-next-commission_en.pdf

of the products we use". Europe needs to move towards a zero-pollution ambition. A European Green Deal is a cross-cutting strategy to protect citizens' health from environmental degradation and pollution, addressing air and water quality, hazardous chemicals, industrial emissions, pesticides and endocrine disrupters.

b. **An economy that works for people**. Equal access to health systems has to be the most basic right for European citizens to prevent poverty and social exclusion especially in children and people with disabilities. Biomedical and Health research has a key role in developing costly effective treatments, affordable diagnostic tools and prevention strategies.

c. **A Europe fit for the digital age**. High performance computing, Big Data, genomics and AI are crucial ingredients for innovation that can help us to find solutions to societal challenges. It has a remarkable importance in the new health research strategies towards a Personalized Medicine. The rapid development of these new technologies may lead to new ways to prevent, diagnose and treat diseases. But these new tools also pose challenges in terms of uptake and appropriate transfer to practice within health systems and to daily medical and health care routines. In addition, the complexity of collecting, sharing and interpreting epidemiological and clinical data poses a further obstacle to reaping rapid benefits from big data collections. There are as well still privacy concerns and significant barriers to be addressed regarding cross-border data exchange for biomedical research and personalised care.

d. **Protecting our European way of life**. Investing in health research and capacity building is key in improving the perspectives of young women and men in their countries of origin.

e. **A stronger Europe in the world**. Europe needs more presence and active role at global scale that could only be possible by joining efforts. A Partnership that brings together the funding organisations that own 80% of total investment in health research in Europe will be a reference to other countries strategies.

2. **EU Health priorities: Europe's Beating Cancer Plan**[17]. Further research is needed in order to improve prevention against cancer. To be efficient and patient oriented, increased collaboration and teamwork within the health sector, and with other sectors, is needed. The different health professionals, e.g. radiologists, surgeons, oncologists, nursing staff, medical physicists and researchers, still work too much in separate sectors with insufficient collaboration or communication between them.

3. **European Health Data Space**[18]. Priorities in the Communication on enabling the digital transformation of health and care in the Digital Single Market[19]:
   a. citizens' secure access to and sharing of health data across borders;
   b. better data to advance research, disease prevention and personalised health and care;
   c. digital tools for citizen empowerment and person-centred care

4. EU agenda on effective, accessible and resilient health systems (the Communication COM(2014) 215; the State of Health in the EU; the European Semester);

5. The European Pillar of Social Rights (concerning access to health care).

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[17] https://ec.europa.eu/info/law/better-regulation/
[18] https://ec.europa.eu/health/ehealth/dataspace_en
[19] https://ec.europa.eu/newsroom/dae/document.cfm?doc_id=51628

To reach the main objective, the Partnership "Fostering an ERA for Health" will focus on the following overarching **Specific Objectives**:

> **SO1**. Support relevant medical research including clinical fields and intervention areas (prevention, diagnosis, treatment)

By providing a channel of communication between funding agencies and EU, the ERA4Health Partnership shall work as an efficient instrument to channel European Health research and innovation priorities to foster the excellence and competitiveness of the Health Research Ecosystem. Provided with an established policy decision-making process EU and national strategies converge into dedicated cofunded research programmes that support in the end transnational and traslational collaborative and multidisciplinary research and innovation projects.

It will support the generation of knowledge, which can provide the evidence base to inform interventions and disease prevention and, thanks to the use of appropriate tools, contribute to more effective translation of pre-clinical results and decrease the time required for new product development (e.g. complex in vitro setups models, relevant animal models). Taking into account the experiences made in the four quality Horizon 2020 ERA-NET addressing Cardiovascular Diseases (ERA-CVD), Nano Medical Technologies (EuroNanoMed) and Diet related diseases/Healthy Diets (related to the JPI "A Healthy Diet for a Healthy Life"), it will expand other priority areas addressing important public health needs. ERA4Health will have access to and make use of the evidence on the benefits and drawbacks of health interventions, in particular for optimising prevention strategies at an individual and societal level, clinical management, personalised medicine considering the patient from a holistic point of view (including socio-economical contexts), optimizing the decision-making processes especially considering concomitant treatment modalities and avoiding overtreatment.

An established instrument would also bring the opportunity to respond to urgent research needs in a flexible manner. In the recent COVID-19 outbreak, a number of funding organisations in Member States were able to launch national calls for projects aiming at developing new knowledge to combat the virus. This Partnership would have been an efficient tool to coordinate EU funding to promote coordinated and more ambitious research.

ERA4Health intends to be an open platform that follows specific standards and procedures, allowing the implementation of protocols related to biomedical research and application in health and care, taking an active participation on the co-design and implementation of co-funding strategies. A European Strategic Research and Innovation Agenda will be the basis for selecting priorities and implementing annual plans and activities. A robust Governance structure and effective decision making procedures would identify and prioritise topics of common interest and European benefit. Depending on the funding commitments and member's decisions several cofunded and consecutive calls running in parallel could be launched.

As previously mentioned, only 10% of the EU budget for health research could be considered for joint and collaborative research. Increase coordination of public research in ERA is at the core of ERA4Health activities. ERA-NET cofund actions in Horizon 2020 have one cofunded call with EU top-up funding, while the additional calls are financed without the support of EU funding. The average budget per cofunded call is 17 Million € (see table below). The additional calls are usually launched with a smaller amount.
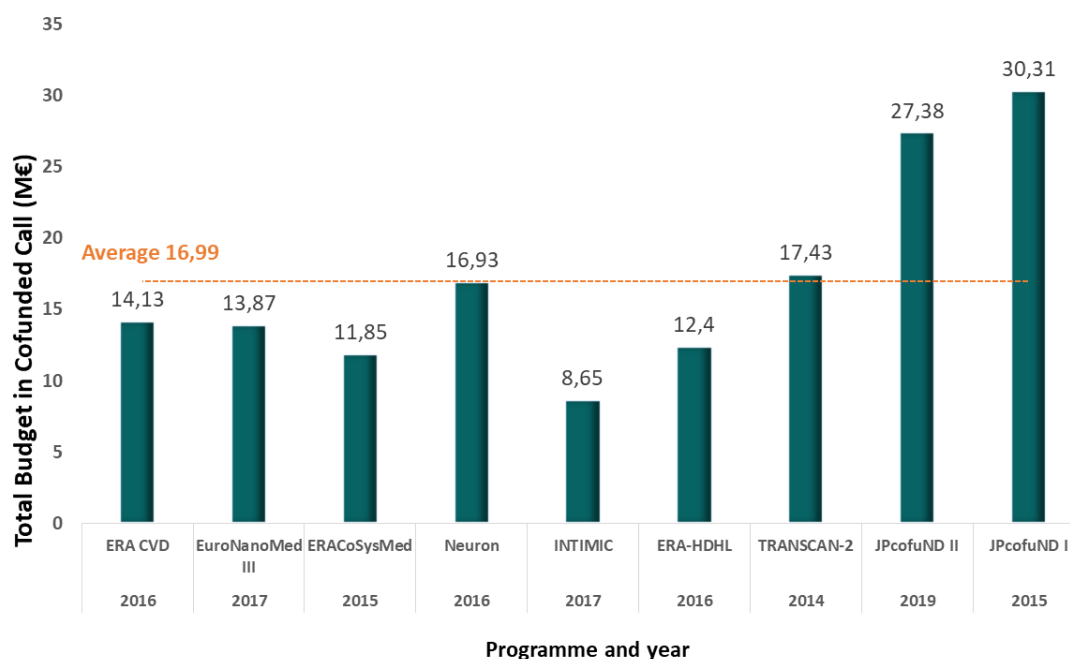
Rare Disease, Personalized Medicine and AMR are excluded.

During Phase 1 of ERA4Health (see section 2), it is envisaged the launching of at least 2 parallel calls cofunded with EU funding per year (at least 4 cofunded calls in 2 years) with a total budget of at least EUR 100 Million which includes 30% of EU funding would mean a relevant increase in the funding devoted to collaborative research projects in priority areas.

The Operational Objectives are therefore:

- Implement a Governance Structure and working procedures for priority settings that allow a flexible and inclusive decision making process that allows identifying topics for common interest and European benefit
- Elaborate Annual Work Plans
- Establish common operational procedures for the funding activities (i.e. evaluation procedures, call documents, monitoring)
- Launching calls for proposals on the identified research priorities
- Perform project monitoring that supports the fulfilment of granted project objectives

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SO2. Improve the utilisation of existing health technologies in clinical practice

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More public funding is required for academic clinical and translational research and more specifically, ERA4Health, will bring novelty in public to public partnership by establishing streamlined processes to conduct multinational **investigator initiated clinical studies** (IICSs) on health interventions. The value of these trials can be seen in the advances in cancer treatments, where over the years multidisciplinary approaches have been taken to work out the best strategy for treatment, ultimately resulting in much improved survival rates for many cancers. Several reviews have shown a great return on investment generated by such clinical research. The financial resources needed for multinational clinical studies including clinical trials need to be secured.

Due to the scale and the complexity of clinical trials, the peer review process is complex and has specific requirements – peer review of clinical trial applications usually involve an iterative process to optimise the trial design. As well as clinical evaluation, methodological and biostatistic

evaluation is also needed. Appropriate expertise is needed to assess properly the budget requirements of a trial.

There is a need to consider the diversity of studies that are not attractive for commercial companies, which include: long-term safety studies (especially those aimed at identifying rare but serious adverse effects) and efficacy studies; head-to-head comparisons, for example for superiority and non-inferiority studies; studies aimed at identifying medical endpoints relevant to real-life practice and the needs of patients; 'multi-modal' studies aimed at investigating, for example, various combinations of drugs with drugs, or drugs with devices and or surgery; studies to identify the most responsive sub-population as part of the broad move towards personalised medicine; studies in under-represented populations, such as children, the elderly and people with rare or understudied diseases; health economics studies; studies aimed at validating operational guidelines; meta-analyses using individualised patient data.

The Operational Objectives include:

- Analyse barriers and bottlenecks for launching and performing successful IICS
- Proposing solutions to overcome the bottlenecks and facilitate the organisation of transnational calls for IICS
- Launching calls for Investigator Initiated Clinical Studies
- Establish an efficient monitoring framework to follow-up the funded clinical studies

SO3. Build capacity, in particular in conducting IICSs at European scale

Europe is running out of well-trained physician-scientists (physicians who have trained in basic scientific research, "MD-PhDs") who are capable of working together and with other clinical trial professions. At the same time patient-oriented research is becoming increasingly multidisciplinary, with new technologies constantly appearing. In many cases young investigators are not being sufficiently well trained to cope with this multidisciplinary environment. In a worst-case scenario this situation leads to a real and damaging decline of patient-oriented research and related studies in Europe and greatly reduces the competitiveness of Europe in the field of clinical research and related research on drug development and diagnostics.

This objective includes the **networking of clinical research capacities and research infrastructures**, especially EU-funded ones. European Research infrastructures help to structure the scientific community and play a key role in the construction of an efficient research and innovation environment[20]. The transition towards customised health care is data knowledge-driven. By promoting interdisciplinary collaboration among Biomedicine Researchers, the Partnership ERA4HEALTH will seek the use and harmonization of the scientific equipment, knowledge-based resources, scientific data and any other infrastructure to achieve excellence in research and innovation.

The challenge of data- and knowledge- collection, management and stewardship is already beginning to be met by pan-European infrastructures like the ESFRI Research Infrastructures:

- ECRIN European Clinical Research Infrastructure Network

- BBMRI Biobanking and Biomolecular Resources Research Infrastructure

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[20] European research infrastructures (including e-Infrastructures), Work Programme 2018-2020.

- ELIXIR The European Life Sciences Infrastructure for Biological Information

- INFRAFRONTIER European Infrastructure for Phenotyping, Archiving and Distribution of Mouse Models

- INSTRUCT Integrated Structural Biology Infrastructure for Europe

- EATRIS European Infrastructure for Translational Medicine

- EU-OPENSCREEN European high-capacity screening network

- EuroBioimaging - The European Research Infrastructure for Imaging Technologies in Biological and Biomedical Sciences

The involvement of ECRIN is particularly important in this Partnership as key Infrastructure that supports clinical research in Europe.

Operational objectives include:
- Identify supporting measures for designing robust and feasible clinical studies
- Facilitates the use and access to services provided by European Research Infrastructures
- Create an expert group to support the activities devoted to IICS
- Facilitate the interaction of the stakeholders with a role in IICS (researchers, regulators, patients....) through Partner Search Tool for calls/LinkedIn account, organisation of networking events
- Include training and mobility programmes as part of the activities to be funded within the research projects and IICS
- Training activities for Early Career Researchers on the whole innovation chain and cross section topics (translatability, implementation of IICS, regulatory affairs, open data, etc...)

SO4. Implement and develop RRI in multiple ways (Partnership operationalization, calls, in project evaluation and monitoring)

ERA4Health will **implement and develop Responsible Research & Innovation (RRI)** and other cross cutting objectives in multiple ways from the Partnership operationalization to the implementation of calls or the project evaluation and will self-assure that research performed under the frame of ERA4Health respects RRI principles.

- ERA4Health will promote **research that anticipates and assesses potential implications and societal expectations** with regard to research and innovation, with the aim to foster the design of inclusive and sustainable research and innovation to ensure a true societal impact.

- ERA4Health will **engage with the society through citizens and patients** by giving a voice in the definition of ERA4Health scope and activities but also by communicating to them the major discoveries in the produced research. In addition, supported research will be citizens and patients, including children, centred.

- ERA4Health will **increase capacity building**, in particular in transnational IICS by providing a platform and tools to connect all stakeholders and by promoting formal

and informal science education at a wide range of levels (from students to early career researchers)

- ERA4Health will **ensure gender equality** in all ERA4Health activities meaning an equal gender distribution in its different governance bodies and consultative groups, funded principal investigators. ERA4Health will also support the inclusion of gender dimension in the funded research content.

- ERA4Health will **support research ethically conducted** with an ethic committee embedded in its governance bodies.

- **Promote open access and data sharing** including by adhering to the FAIR (findability, accessibility, interoperability, and reusability) data principles and supporting the development of adequate data governance structures. It will also support the establishment of the modalities of data sharing and exploration of health data (e.g., from health care records, disease and patient's registries, genomic banks) for new digital health technologies and tools. The social and economic benefits that health research data can provide to the health system are enormous (empowering patients, support for health professionals and policy makers in decision making processes, enhancing research quality and increased efficiency of therapy development by industries)[21].

- **Communicate and disseminate,** in particular to decision makers, **research outcomes** and citizen's and patients need for preventing, diagnosing and treating diseases. Communication activities aim at promoting the Partnership activities towards the broad public thus they will necessarily focus on the scope and impacts of the project for society, transforming the more complex jargon into contents addressing less technical audiences with the objective to guarantee outreach and enhance its visibility.

The Communication, Dissemination and Exploitation activities are rather transversal and instrumental to support ERA4Health objectives. They comprise activities for a proactive communications effort, which include maintaining a strategic calendar to prepare for important events, working with a network of communication contacts and strengthening the messaging both in terms of content and in the mode of communicating. Active promotion and communication activities will include online and non-electronic communication methods and tools as appropriate, special events as well as publications are core activities.

Operational Objectives:

- Involve society actors in the Strategic Advisory Board and make sure that consultation processes reach citizens and patients
- Support measures to involve patients in funded projects
- Produce communication materials to inform citizens and patients of ERA4health activities and research results from funded projects
- Monitor gender equality in all governance bodies, and pursue gender balance in scientific panels and consultative groups of ERA4Health
- Promote gender balance among the applicants in all funding actions
- Integrate gender dimension in the studies (only excluded in some relevant cases)

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[21] Understanding value in health data ecosystems: A review of current evidence and ways forward: RAND Corporation, 2017. Available from: https://www.rand.org/pubs/research_reports/RR1972.html

- Proposals of research projects and IICSs will be evaluated by an ethical committee and would need their approval before the funding selection
- Encourage the popularisation of the research topic in schools, middle and high schools e.g. events during the science days, or dedicated ERA4Health events
- A specific section for uploading documents developed by ERA4Health will be created in the ERA4Health website
- Elaborate guidelines for developing Data Management Plan for applicants. All consortia who will submit a proposal will have to integrate a data management plan
- Establish links with European Open Science Cloud[22], EOSC-Life[23] and Health Data Space[24] in order to facilitate the use of data and sharing data
- Elaborate a Dissemination, Exploitation and Communication Plan
- Implementing the dedicated website
- Create Social networks channel/account and feed them
- Dissemination of the success stories (research outcomes) from ERA4Health funded projects including the results of clinical studies that should be made available in public registers meeting the WHO criteria[25].
- Develop newsletters and other printed/downloadable materials

Expected outcomes

Achieving the four **Specific Objectives** should deliver the following outcomes:

SO1	• Research funders, policy-makers and the research community work together in an effective joint approach, including for identifying and prioritising topics of common interest and European benefit, thanks to a trusted governance and effective working modalities.
	• Generation of new knowledge and use of research results to develop evidence-based strategies and policies, and deploy good practices to European countries and regions;
SO2	• Access to and use evidences of the benefit and drawback of health interventions, in particular for optimising clinical management, repurposing, comparative effectiveness, treatment combination or optimisation studies, personalised medicine and avoiding overtreatment.
	• Countries cooperate better and use context-specific knowledge and evidence to make their health and care systems more sustainable and resilient with respect to upcoming needs and crises.
	• ERA4Health identify the main barriers to test health interventions at European level and facilitate the research community to conduct large-scale investigator-initiated clinical studies of various health interventions addressing important public health needs in a seamless way

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[22] https://www.eosc-portal.eu/
[23] https://www.eosc-life.eu/
[24] https://ec.europa.eu/health/ehealth/dataspace_en
[25] https://www.who.int/clinical-trials-registry-platform/network/registry-criteria

SO3	• ERA4health partners and relevant stakeholders build a more effective and integrated public health research system. Utilization of health services, preventative measures, technologies, tools and digital solutions are more cost-effective;
SO4	• Citizens are more knowledgeable to make better decisions for their own physical and mental health and well-being, monitor their health, and trust in knowledge-based health interventions launched by health authorities.
	• Health policies and actions for health promotion and disease prevention are knowledge-based, people-centred and thus targeted and tailored to citizens' needs, and designed to reduce health inequalities.

Overall Impact

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, notably to creating a more resilient, inclusive and democratic European society (KSOD) and promoting an open strategic autonomy by leading the development of key digital, enabling and emerging technologies, sectors and value chains (KSO-A). It aims to mainly contribute to the impact areas of the strategic plan: "Good health and high-quality accessible health care" which on top of that contributes to the Sustainable Development Goal 3 (Ensure healthy lives and promote well-being for all at all ages).

As indicated previously, this Partnership seeks the opportunity to increase EU cohesion and to enable alternative adequate settings at different levels by positioning a challenging structure aiming to achieve a **common European Eco-System** for a reliable Interregional, and inclusive Health Research strategy aligned to the national health programmes through EU. In addition this Partnership could **strengthen the EU strategic position** and help in attracting UK towards the ERA orbit rather than spinning-off towards the US.

Biomedical and health research at EU level needs to be more efficient to deliver better and of higher-quality solutions for prevention, diagnosis and treatment as well as providing better and equal access and affordable Health Care Systems to the citizens. A common vision based on a European Health Research Strategy and collaboration among countries and regions in Europe will be key in the leading role of EU in health research to make Science and Innovation community stronger and more efficient to tackle the existing and future challenges.

The expected impacts are described aligned with Horizon Europe (HE) Key Performance Indicators that are intended to track HE's progress:

More specifically, ERA4Health aims to contribute to two out of the six expected impacts as set out by the strategic plan, which are the following:

Destination 3 - **Tackling diseases and reducing disease burden:** Health care providers are able to better tackle and manage diseases (infectious diseases, including poverty-related and neglected diseases, non-communicable and rare diseases) and reduce the disease burden on patients effectively thanks to better understanding and treatment of diseases, more effective and innovative health technologies, better ability and preparedness to manage epidemic outbreaks and improved patient safety.

Destination 1 -**Staying healthy in a rapidly changing society:** 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.

In more details ERA4Health will lead to achieve the following impacts:
- improve the quality of research programming in the European Research and Innovation Area by building on best practices through networking European public funders of health research and will increase the outputs of the research and innovation discoveries for the benefit of society and economy.
- contribute to the transformation of healthcare systems in their efforts towards better health promotion and disease prevention while ensuring fair access for everyone to innovative, more patient oriented, sustainable (including from a fiscal point of view) and high-quality health care.
- contribute to living conditions that safeguard and promote health by positively impacting determinants of population health in relevant settings and on a variety of levels, including the local, regional, national and international level.
- increase knowledge on disease development and disease treatment that will lead to improved patient management and ultimately better health.
- effective, efficient, equitable, accessible, and resilient public health care systems that will be fiscally sustainable in the medium and long term. For example, the utilization of health services, preventative measures, technologies, tools and digital solutions will be more cost-effective.
- The generation of findable, accessible, interoperable and reusable data, which at the same time will ensure appropriate protection of patients' safety and rights, and data-driven approaches to confirm previous study or to respond to other research challenges and determine the effectiveness of other health interventions will reduce the research cost by avoiding effort duplication.
- Developed health strategies and innovations oriented towards public health needs in real-world settings will be more transferable and potentially useful as well as better accepted by end-users and will increase the scientific quality and societal relevance of produced knowledge, technologies and innovations, as for example by integrating an in-depth understanding of both genders' needs, behaviors and attitudes. In addition, health strategies and innovations will be easier implemented in other regions/countries, in particular in the countries with the poorest specific health indicators.
- Citizens are knowledgeable of disease threats, are empowered and make better decisions for their health.
- With clinical research, more patient-oriented, citizens adhere to knowledge-based disease management strategies and policies (especially for controlling outbreaks and emergencies).
- contribute to breaking the glass ceiling in the long term by increasing the participation of women in research and by making women have a voice by achieving gender balance in decision making.
- ERA4Health will contribute to the production of goods and services better suited to potential markets and will thereby contribute to the European economy.

The network platform integrating the whole research and innovation actors built by ERA4Health will offer rapid and coordinated responses to cross border health emergencies.

Impact Pathway

Destinations /Goals

- Tackling diseases and reducing disease burden
- Staying healthy in a rapidly changing society
- SDG 3 "Good Health and Well-being for People"

Specific Objectives

- Support relevant biomedical research including clinical fields and intervention areas (prevention, diagnosis and treatment))
- Improve the utilisation of existing health technologies in clinical practice
- Build capacity, in particular in conducting IICSs at European scale
- Implement, promote and develop RRI (ethical research, gender dimension, open access, dissemination)

Inputs

- National, regional and EC funding to implement calls and fund research projects
- Partners strategic commitment (in kind contribution)
- Shared Strategic Research and Innovation Agenda
- Multidisciplinary expertise

Activities

- Establish a robust Governance Structure and decision making procedure for priority setting
- Launching an implement JTCs and transnational IICS calls on common priorities
- Build supporting framework to overcome challenges in implementing transnational IICSs
- Establish links with existing initiatives for synergies and join activities
- Promote citizen and patient involvement, society engagement and facilitate interaction with stakeholders
- Promote RRI in all activities

Outputs

- Adopted SRIA to guide Annual Work Plans and **set** priorities for call topics
- Joint transnational research project portfolio
- Adequate framework and capacities for funding and performing multinational IICS
- New collaborative research networks
- Alignment of national/regional and EC research priorities
- Enhance the quality of research produced by involvement of citizens
- ECSs involvement in transnational projects

Outcomes

- Trusted governance and effective working modalities
- Research publications, position papers, policy recommendations
- Generation of new knowledge for applying new evidence based health interventions and policies
- Researchers conduct reliable large-scale IICS of health interventions (on PH needs)
- More effective and integrated PH research systems
- More cost –effective digital solutions, preventative measures and technologies
- Citizens empowerment
- Data and medata publicly available

Impacts

- A stronger Europe in the word through a fostered ERA for Health Research. More R&D, increased health financing, and strengthened capacity in health risk reduction and management.
- Good health and high-quality accessible healthcare thanks to more effective solutions for health promotion and disease prevention
- health care providers are able to better tackle and manage diseases and reduce the disease burden on patients thanks to better understanding and treatment of diseases, more effective and innovative technologies and preparedness
- People-centred Health policies and actions

Measuring progress

For the follow up of the general results of the Partnership, the most important recommendation proposed for European Commission in the report "A robust and harmonised framework for reporting and monitoring European Partnerships in Horizon Europe" is to create as a pilot a cost-effective solution to start collecting the partnership level data, so it´s important to know these indicators to address the results to them easily. In the final list, there are 14 indicators recommended for further implementation/discussion, out of which 11 could be operationalised immediately. In any case, these indicators should be connected with the specific Key Performance Indicators that measures the Partnership towards the objectives.

The progress of the European Partnership "Fostering an ERA for Health" towards reaching the specific objectives presented in this SRIA will be monitored by the Partnership members and the European Commission, along with the Health Programme Committee and Strategic Advisory Board, in order to implement the necessary adjustments to our activities and to the SRIA itself. The proposed indicators follow the recommendations of the EC. They are quantitative, qualitative and some would include anecdotal evidence.

Indicators of performance that might be used to assess Partnership objectives, activities and outputs:

Specific Objectives	Activities	Outputs	KPI
Support biomedical research including clinical fields and intervention areas	Robust Governance and decision making process Facilitate the interaction of stakeholders, knowledge exchange, open access and sharing research results Launching joint call for projects	Identification of priorities Alignment of research priorities Joint Transnational research projects portfolio National funding devoted to collaborative research	1. Adoption of AWP 2. Number of projects funded 3. Financial contributions, commited and actual
Improve the utilisation of existing health technologies in clinical practice	Build the supporting framework to overcome challenges in implementing IICS Launching calls for IICS	Adequate framework and capacities for performing multinational IICS Multinational IICS portfolio	4. Number of unexperienced Investigators selected for funding 5. Number of IICS funded 6. Financial contribution

Build capacity, in particular in conducting IICS at European scale	Share information and best practices Establish links with relevant stakeholders (ERIs and others) Support to ECS	Reduce fragmentation and create synergies with stakeholders ECS involvement in transnational projects and IICS	7. Activities with stakeholders 8. Number of ECS schemes implemented 9. Number of ECS in funded projects
Implement, promote and develop RRI	Implement ethical assessment Involve citizens (including patients) in E4H activities Promote gender balance at all levels Promote Science education initiatives Include open science measures in calls for projects and IICS Training activities on OA and data sharing	Researchers and Stakeholders are aware of the RRI impact of research and its effects on social justice/inclusion Visibility of the Partnership Research publications, position papers, policy recommendations	10. % of positive ethical assessments 11. Number of citizens involved in committees/projects/ consultations 12. % of women that are Pis/coordinators 13. % of women in review panels/committees 14. % of women as first authors in publications 15. % of projects with educational resource activities 16. % of projects delivering high quality DMP 17. use of existing/common shared databases and repositories 18.No of hits/members in contact lists, press releases, references in media, events, policy conferences, etc.

1.2.3. Collaboration with other partnerships and Union programmes

Synergies among Partnerships will result in better innovation governance, more public-public and public-private cooperation and improved R&I support in the countries & regions. More links and bridges between different programmes would facilitate:

- Use of same bodies to implement different funds to promote synchronisation and links at governance level
- Managing Authorities may identify Partnerships members as intermediate bodies for implementing their actions

For the ERA4Health partnership it is crucial to connect with other key players and initiatives in the health domain and beyond to increase the impact of R&I investments on the societal challenge that it addresses. To ensure coherence and complementarity of activities and leverage knowledge and investment possibilities, the partnership will establish collaborations with other European partnerships and missions under Horizon Europe as well as explore collaborations with other relevant activities at EU and international level.

Relationships within Health cluster candidate Partnerships seem obvious. ERA4Health will be instrumental in mobilising public investment as well as industrial contribution towards common goals in priority areas that perfectly complement Research and Innovation activities of other Partnerships. Thus, in practice, collaboration with all candidate Partnership is needed for setting up priorities, for avoiding overlapping and complementing R&I activities. In addition, there is a long lasting relationship with members that will participate in almost all the proposed Partnerships.

ERA4Health intends to build links with European partnerships in Health cluster[26], particularly with:

- **Innovative Health Initiative (IHI)**[27] aims to provide a collaborative platform for pre-competitive research and innovation where small and big companies can join forces with researchers, patients, healthcare professionals and regulators. A strong link will be created with this institutionalized European Partnership that will accelerate the development of scientific and technological innovations in the area of health (in a pre-competitive context). Moreover, the present partnership will provide the framework for unmet health needs from the idea to proof of concept for which IHI should develop technological solutions, while delivering the necessary evidence, cost-effectiveness analysis to support their translation into practice. We consider that a robust link with IHI constitutes a step forward in the development of ideas into market solutions and specific tasks and milestones will be described in our implementation description in order to enforce the relationship. This cooperation with partners specialized in e.g. pharmaceuticals, diagnostics, medical devices, imaging or from the biotech and digital industries will help speed up the development and uptake of innovation in public health.
- European **Partnership on Health and Care Systems Transformation** will develop methods and tools to embed technological innovations into health and care systems. The major link sets on their expected scientific impact, which invites them to work closely, especially in strengthen knowledge transfer and shared expertise on health and care systems research and innovation among EU Member States. ERA4health could complement the Partnership knowledge needs through launching call for projects. The second phase of ERA4Health with the implementation of Investigator Initiated Clinical Studies shall focus on new or improved

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[26] https://ec.europa.eu/info/research-and-innovation/funding/funding-opportunities/funding-programmes-and-open-calls/horizon-europe/european-partnerships-horizon-europe/candidates-european-partnerships-health_en
[27] https://www.imi.europa.eu/about-imi/innovative-health-initiative

health technologies that pursues a better, cost-effective, affordable, sustainable and efficient Health Care System.

- European Partnership on **Pandemic Preparedness** will be the research arm of the Health Emergency and Response Authority (HERA)[28] whose main activities will focus in increasing new scientific knowledge and technologies, design and develop countermeasures (such as vaccines), design new strategies for public health response and connect EU-wide infrastructures. The coordination between this partnership an ERA4health for implementing funding activities in priority topics is necessary for a quicker response in case of an emergency.
- **European Partnership on Personalised medicine** holds a great promise and several national and regional initiatives already support the advances of this area. This is why the Future Partnership Personalised Medicine can impact in all Health Cluster research topics. Both partnerships, seek to align priority setting and funding for research projects in which public funders of health research in the European Research Area jointly identify and implement a common funding strategy and the uptake of multidisciplinary research and innovation results into clinical practice.
- Synergies with the European Partnership on **Rare Diseases** would be an advantage, especially for implementing IICS (i.e. drug repurposing).
- Finally, the coordination with the European Partnership **ONE Health – Antimicrobial Resistance** could also bring complementary knowledge for the benefit of both Partnership's missions.

Before the start of some of these Partnerships an early collaboration needs to be developed with the existing networks as described in section 1.1.3.

Synergies with Partnerships in other clusters shall be also taken into account, namely:

(i)   the **Partnership of Safe and Sustainable Food Systems for People, Planet & Climate**. Research and Innovation will contribute to promoting sustainable and healthy diets. Both partnerships are somehow connected in the burden of malnutrition (undernutrition, over-nutrition and micronutrient deficiencies) and the prevention of diet-related premature mortality in Europe

(ii)   **Animal health: Fighting infectious diseases**. Emerging infectious diseases (EIDs) are a significant and growing threat to global health, global economy and global security and majority of EIDs (and almost all recent pandemics) originate in animals, mostly wildlife[29]. Current research in zoonosis focuses in the interface of the pathogen and the clinically ill person, emphasizing microbial detection, mechanisms of pathogenicity and clinical intervention strategies.

(iii)   **European Partnership on Artificial Intelligence, Data and Robotics.** The use and development of these technologies in biomedical research is a reality. In the area of healthcare and cancer: AI-powered digital technologies will lead the way in transforming the healthcare sector including the transition to new care models and, notably, value-based healthcare as well as new diagnostic methods and treatments, in particular in the area of chronic diseases.

(iv)   **Partnership Key Digital Technologies (KDT).** Photonics and software, advanced computing technologies, flexible electronics and bioelectronics are featuring

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[28] COM(2021) 576 - Introducing HERA, the European Health Emergency preparedness and Response Authority, the next step towards completing the European Health Union
[29] https://www.nature.com/articles/s41467-017-00923-8

increasingly in the digital transformation of the economy and society, and now need to be co-integrated to build complex systems and open up new avenues of application including Health Care systems. The [Health.E Lighthouse Initiative](#) champions a coordinated approach to produce new technologies for medical devices and systems more consistently and also ensures there is a broad scope of innovations that can benefit from standardisation of underlying technologies that bring down the costs of making it to the market. The EU produces 19.3% of the global Health & Care electronics and is the third region in the world after North America (41%), and China (20%)[30].

(v)   **European Science Cloud (EOSC)** is a co-programmed Partnership that will be at the core of Horizon Europe. ERA4Health will support the EU's policy of Open Science through the promotion and use of this digital platform. When implemented, it will allow the high-speed connectivity to transport and process data produced during research projects. Open science can lead to greater collaboration, increased confidence in findings and goodwill between researchers.

Besides the relations with European Partnerships, there are other European programmes that should be taken into account when defining activities and setting priorities such as the Cluster Health of HE for avoiding overlapping with the Work Programmes and the Cancer Mission, recently launched[31], that will support Member States, regions and communities on cancer control, even more so in light of the disruptive effect of the COVID-19 pandemic. It will enhance understanding of cancer, boost prevention, optimise diagnosis and treatment, improve quality of lives of patients and their families and ensure equitable access to care across Europe. The mission will put citizens, including patients, at the centre of research and innovation, and research and innovation at the centre of policy development. ERA4Health during Phase 2 will launch calls for IICS addressing important health needs and cancer a major burden of disease worldwide.

Other networks[32] and EU funded projects in the Health R&I ecosystem need to be taken into account as potential synergies might exist.

Synergies with EU Funding

The EU's Recovery and Resilience Facility (RRF) offers support to Member States in financing reforms and investments that improve their resilience and their growth potential, mitigate the economic and social impacts from the COVID-19 crisis, including in the area of health, and support the green and digital transition. Research and Innovation contribute to the objectives of the RRF. Access to funding is available at national level in line with the Member States' recovery and resilience plans for a fast and targeted support.

Horizon Europe will promote effective and operational synergies within Partnerships and policies to promote faster dissemination at national and regional level and uptake of research and innovation results. These funding tools will play a significant role in ERA4Health execution since

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[30] Emerging Technologies in Electronic Components and Systems (ECS) – Opportunities Ahead", DECISION Etudes & Conseil, 2020, https://op.europa.eu/en/publication-detail/-/publication/582a3802-d6c3-11ea-adf7-01aa75ed71a1/language-en

[31] https://ec.europa.eu/info/sites/default/files/research_and_innovation/funding/documents/ec_com_heu_randi_missions_29092021.pdf

[32] https://www.era-learn.eu/documents/thematic_analysis_health.pdf

will allow projects to be funded at regional level under the **European Structural and Investment Funds** (ESIF).

European Regional Development Fund for investments in research and innovation, human capital and innovative technologies and new care delivery models. This one promotes balanced development in the different regions of the EU and may feature increased funds dedicated to the take-up of results and the rolling out of novel health technologies and innovative solutions.

InvestEU to attract private investment in research, innovation and digitisation in the area; Since this one stimulates more investment in research and innovation, notably by the private sector, appropriate synergies shall be established, in particular regarding budgetary guarantees and leveraging Venture Capital funds supported by this funding tool.

European Social Fund + for investing in people in terms of education and training and improving accessibility of healthcare systems. ERA4Health will demand the human capital and skills development, as well as social innovation. The ESF can mainstream and scale up new and innovative curricula for education and training programmes developed in R&I projects under this Partnership.

The ERA4Health will actively seek collaboration with other ongoing initiatives and funding bodies, which will be paramount to ensuring maximum synergy and avoiding duplication of effort. Engagement with multiple public and private stakeholders is also foreseen during ERA4Health implementation.
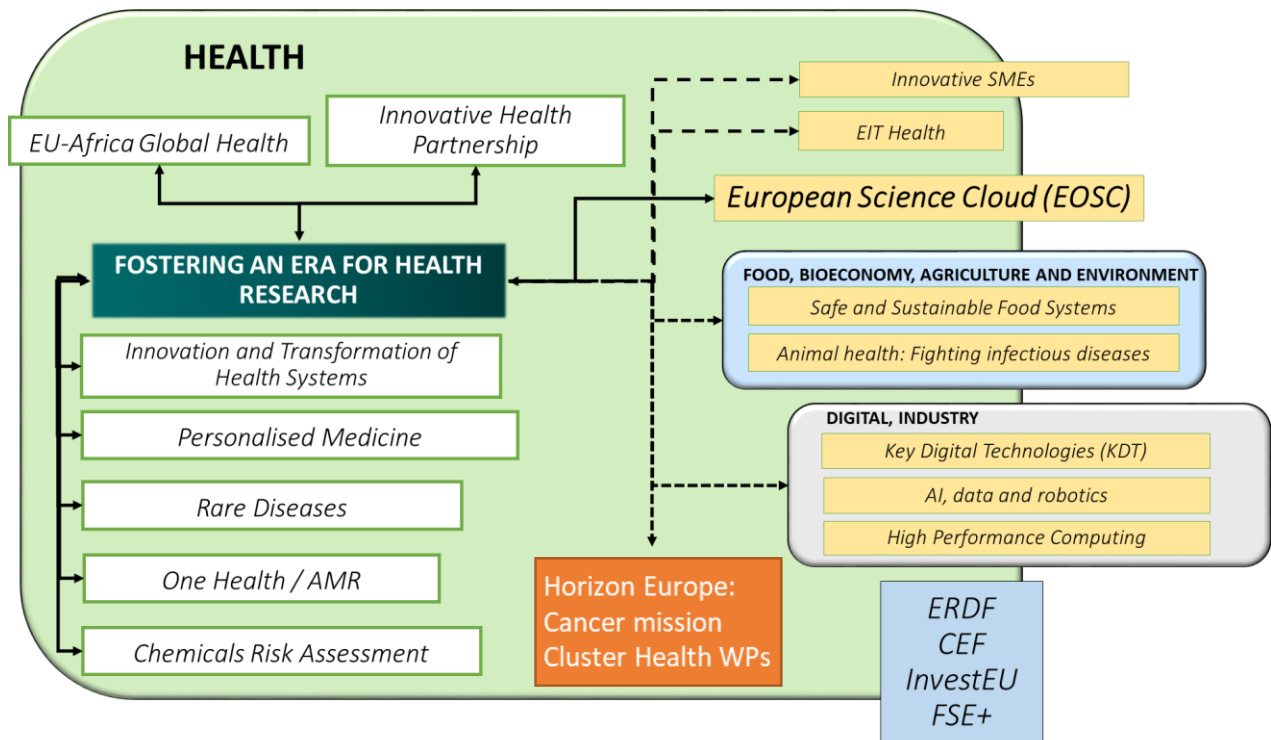
1.2.4. Exit strategy

During the 7 years ERA4Health proposed programme the long-term sustainability will be developed by taking advantage of political opportunities (see 3.1.2). The current political context opens up for new possibilities to discuss the expectations for Europe concerning a joint funding programme as a one-stop shop for researchers.

It is important to ensure a highly efficient communication and dissemination strategy following relevant policy processes to ensure timely input to discussions. A long-term sustainable partnership in Europe should not be reliant on research funds only but requires a wider political endorsement and investments.

During the development phase of the partnership when seeking the political commitment at national level for participation, the long-term sustainability will be discussed and the national interests confirmed. The General Assembly of the partnership will bring together the relevant ministerial representatives and funding organisations be tasked upfront with manoeuvring for sustainability. The necessary research infrastructure required for long-term sustainability will be developed in the partnership as part of the Management Board sustainability strategy.

1.3. Necessity for a European Partnership

The general objective of Horizon Europe is to deliver scientific, technological, economic and societal impact from the Union's and Member States investments in research and innovation. Thus, to strengthen the scientific and technological bases of the Union and foster its competitiveness in all Member States including in its industry. Horizon Europe will thereby deliver on the Union strategic priorities and contribute to the realisation of EU objectives and policies, contribute to tackling global challenges, including the Sustainable Development Goals (SGD 3 on Good Health and Well Being), and to strengthen the European Research Area. The Programme shall thus maximise Union added value by focusing on objectives and activities that cannot be effectively realised by Member States acting alone, but in cooperation.

ERA4Health Partnership at European level is much more effective in achieving the aforementioned objectives than traditional Framework Programme regular calls, because it directly involves the programme research owners and managers and the research performance organisations including health and care systems in defining what their priorities and needs for research and innovation are. It also represents an opportunity to pool funds and other resources around jointly agreed priorities maximising the impact and benefits for Member States and citizens.

At the same time, the whole R&D ecosystem will have direct access to the research and innovation results produced by the partnership, but more importantly, will be able to share their own data and research results, allowing for a knowledge transfer platform that feeds on EU, transnational and national research results, and best practices.

Horizon Europe encourages the collaborative links in Europe to contribute reducing the R&I divide. In this regard, this partnership aims to create a large network in which partners will liaise with representatives of health and research ministries at national level to ensure the R& I impact in different policy areas. The cooperation among MS will facilitate sharing experience, knowledge

and regulatory needs as well as will provide a stimulating environment to foster the excellence-based participations from all Member States, including low R&I performing Member States, in Horizon Europe. As mentioned in 2.1.2, the majority of countries which struggles to invest moneys and staff in such collaboration, despite their wish to do so. This collaboration would mitigate the inequalities by orienting alternative scenario directly linked to further developments.

Directionality: EU action in the area of Health is based on Articles 6(a), 9 and 168 of the Treaty on the Functioning the EU.

Article 168:

1. A high level of human health protection shall be ensured in the definition and implementation of all Union policies and activities.

Union action, which shall complement national policies, shall be directed towards improving public health, preventing physical and mental illness and diseases, and obviating sources of danger to physical and mental health. Such action shall cover the fight against the major health scourges, by promoting research into their causes, their transmission and their prevention, as well as health information and education, and monitoring, early warning of and combating serious cross-border threats to health.

2. The Union shall encourage cooperation between the Member States in the areas referred to in this Article and, if necessary, lend support to their action.

It stems from the EU's commitment to the United Nations SDG. Both national- and EU-level actions aiming at same goals are indispensable to promote health. Indeed, these are driven by forces determined and acting at local and transnational scale to advance and boost health research to:

- facilitate high quality cross-border collaboration within Europe and beyond
- nurture multi-stakeholder research across the innovation cycle and find common goals
- integrate and assess the potential of novel and disruptive technologies
- ensure a comprehensive and aligned, facilitating regulatory framework
- involve citizens and patients
- create value, through health, and a knowledge-based society

Such cooperation implies a transnational, integrated and interdisciplinary approach. Through this Partnership, the efforts of EU and MS/ACs will go in the same direction, towards agreed objectives.

Additionality: Neither single State, nor EU on its own has the capacity to address the health and well-being challenges. As previously mentioned, investments in Biomedical and Health research at EU level belong to Member States. Only 10% belonging to the EU budget could be considered for joint and collaborative research.

Public funding
R&D-all

Public funding
multinational collaborative research

■ Member States
■ European Union
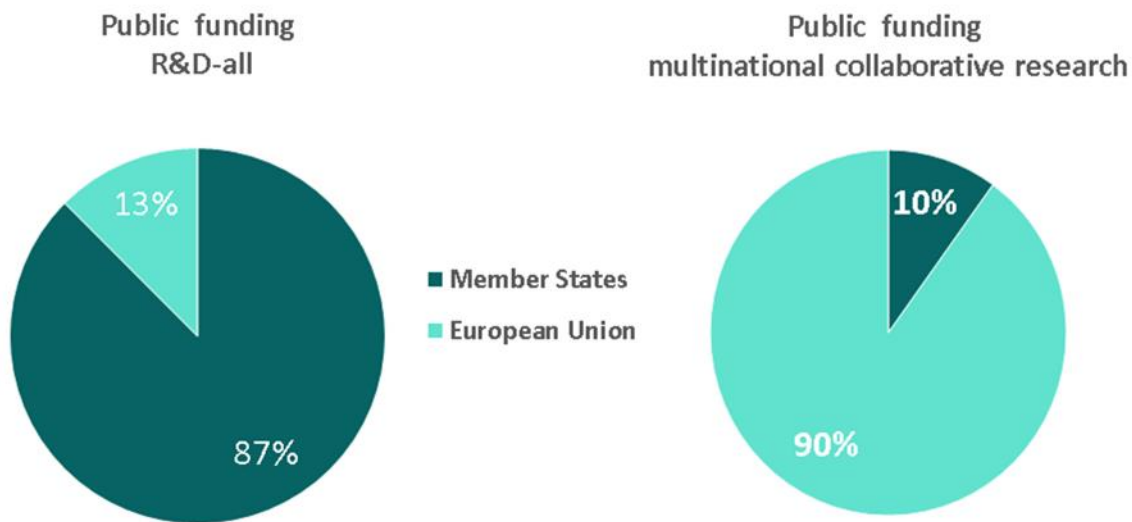
In addition in a post-Brexit European Union, which will reduce by 20% the overall ERA4Health budget, a Partnership could strengthen the EU position in order to attract UK in the ERA orbit rather than spinning-off towards the NIH and US.

The possibility of joining European funders for multinational clinical trials in this Partnership is an optimal solution for near-future financing of multicountry trials. In this model, proposals would be evaluated by a panel that would review the medical relevance and methodology of the trial protocol. The funding agencies would contribute a funding volume adapted to the cost of the trial. Moreover, the Partnership would allow expansion to countries outside Europe, creating an instrument with global potential.

1.4. Partner composition and target group

The Partnership ERA4Health will be an instrumental platform for joint programming of national and regional research and innovation programmes. Therefore, this Partnership will be open to public funders at both national and regional level from Member States, Associated Countries and third countries. These might be funders that only fund basic research, funders that fund applied/translational research, funders that only fund clinical research and funders that fund all types of research.

ERA4Health partners

R&I Funders that only fund basic research (up to pre-clinical phase)

R&I Funders that fund basic, translational and clinical research

R&I Funders that only fund Clinical Research
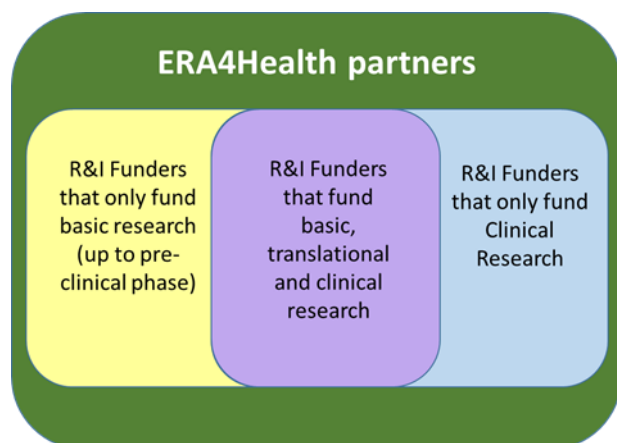
The understanding from the ERA-Net cofund scheme unveiled a complexity of multi factors influencing the commitment and actual spending for partners. A special effort is being made to engage new research funding partners, especially those with relatively small budgets and those that fund Clinical research and Clinical trials. Other Research and/or Biomedical research funders such as philanthropic organisations are also welcome.

The intention for the membership of this Partnership is to consider Europe in a broad manner. Research and Innovation funders in all MMSS and AACC are welcomed as partners. In addition, collaboration with funding organisations placed in third countries is also pursued. The principle of variable geometry allows all partners to participate in the activities that fit in their research portfolio or sector. The entire structure of ERA4Health aims to maximize funding in a flexible and fair way, being inclusive, adaptable to the different commitments and thirdly adoptable by other beneficiaries.

The direct beneficiary (or third party) of ERA4Health joint funding activities will depend on the eligibility of national and regional funding organisations. This Partnership aims to fund the whole Research and Innovation ecosystem including academia (universities, research performance organisations both public and private non for profit), clinical settings and public health organisations, and industry (spin-offs, start-ups, SMEs and the wider European industry).

The Partnership will also engage with other relevant stakeholders such as:

- Other sectorial Ministries, in particular Ministries of Health and Education, either directly for particular activities or through collaboration with other Partnerships mobilizing these Ministries;
- European Commission: DG RTD, DG SANTE, DG CONECT, DG REGIO, The Joint Research Centre (JRC), DG DEVCO, DG TAXUD, DG ECFIN;
- Civil society and end-users (patient/citizen advocacy groups, formal and informal care organisations, health professionals entities, international organisations) – drivers of change by giving input on the needs and priorities of research, as well as employing of the outcomes of the partnership;

2. Planned Implementation

ERA4Health will integrate research and innovation areas covered by previous ERANET co-fund actions, Joint Programming Initiatives (JPIs), as well as investigator-initiated clinical studies (IICSs). It will be composed of two phases.

The Implementation of this Partnership will be carried out in 2 phases:

- Phase 1 will integrate selected European initiatives[33] and implement joint calls focused on nutrition- and lifestyle-related diseases, cardiovascular diseases and nanomedicine. In parallel, it will establish a supporting framework to overcome the challenges in launching international IICSs joint calls. Phase 1 will last for 2 years.

After this period, the Horizon Europe Health Programme Committee will decide whether to extend and intensify the focus on IICSs. This decision will only affect the focus area of the partnership, not its existence over the 7 years.

- On Phase 2, additional multinational calls for IICSs and joint calls for other priority areas will be launched in accordance with the decision of the Health Programme Committee taken at the end of Phase 1 on the focus of the Partnership and the distribution of the budget between IICSs and other areas.

2.1. Activities

"Fostering an ERA for Health" Partnership aims to be a joint funding organisation that pools together public funders of health research in the European Research Area that jointly identify and implement a common funding strategy in priority areas to advance health research and develop innovation. This European Partnership should be implemented through a joint programme of activities ranging from research to coordination and networking activities, including training, demonstration, piloting and dissemination activities, to be structured along the following main building blocks that are structured in different Pillars:

- Joint implementation of the SRIA (Pillar 1);
- Joint annual calls for R&I activities (Pillar 2);
- Framework to overcome challenges in conducting IICSs (Pillar 2);
- Capacity building activities (Pillar 3);

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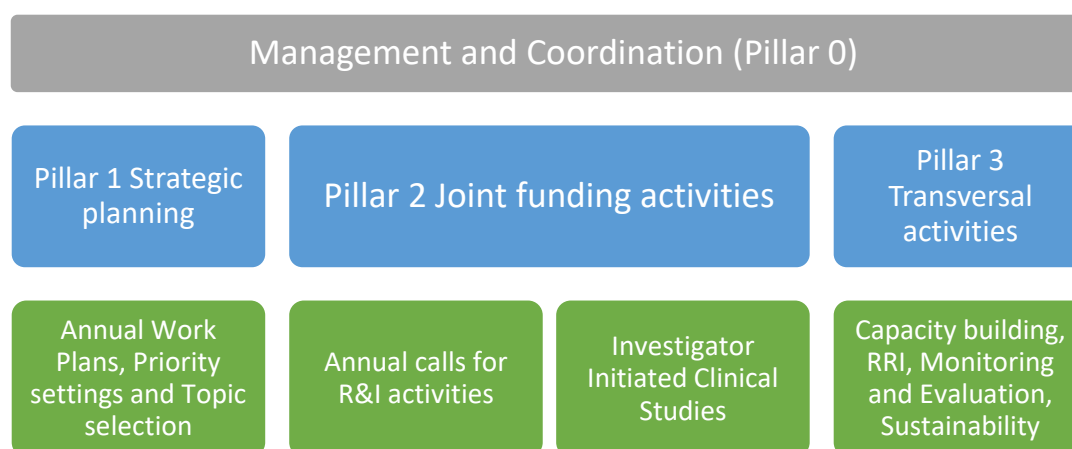
[33] Horizon 2020 ERA-NETs addressing Cardiovascular Diseases (ERA-CVD), Nano Medical Technologies (EuroNanoMed) and the JPI A Healthy Diet for a Healthy Life (Diet related diseases)

2.1.1. Phase 1 (24 months)

ERA4Health partnership will take advantage of the consolidated networks that finish their Grant Agreements with the EU by 2021 and 2022 (ERA-CVD, EuroNanoMed and ERANet cofunds under the framework of JPI HDHL). The inertia of their activities will be the pulling force that moves the wheel towards the consolidation of ERA4Health. These ERA-NETs have been launching yearly calls since many years, some of them since 2009 (such as ENM) so the call procedures and activities are well established. In addition, both the funding organisations involved and the scientific and technological community in the field expect the continuation of their funding activities.

During Phase 1, ERA4Health will respond to the interest from the funding organisations involved in the networks mentioned above by launching parallel Joint Transnational Calls (JTC) under Pillar 2 while developing the consolidated structure of the Partnership.

ERA4Health will benefit from the knowledge accumulated by the existing networks while preparing a common set of improved tools and procedures.

Pillar 0 – Management and coordination

The successful development of a Partnership and its ability to achieve its main objectives will largely depend on:

- (i)   the collaboration between partners and between the different governance bodies;
- (ii)   the efficient link with relevant EC services;
- (iii)   the interaction with a broad range of stakeholders; and
- (iv)   the development of specific links with third parties and bringing in complementary expertise.

In order to ensure that the Partnership delivers on the planned objectives, processes will be needed to allow (i) the organisation of consultations and the collection of relevant advice, (ii) a transparent and efficient decision-making process throughout the duration of the Partnership, in particular regarding the prioritization of activities, and (iii) the proper dissemination of information and engagement of stakeholders.

The governance structure (see 3.3) is instrumental in reaching the objectives of the Partnership. It will largely build on previous experiences that have proven to provide good governance and decision making by all partners, with a strong involvement of Pillar leaders and co-leaders while allowing reinforced advisory processes.

In order to build a coherent and a well running Partnership it will be needed to develop during Phase 1:

- Consortium Agreement and Terms of Reference
- Management Plan with details of the Rules of procedure
- Online tools for effective daily management
- Preparation of the Dissemination, Exploitation and Communication plan that integrate the new Partnership concept and the inherited networks that had their own "corporate image"

The activities for Pillar 0 will continue during Phase 2 by strengthening the communication activities and the strategy to engage new partners and synergize with other stakeholders.

Pillar 1 – Strategic Planning

Fostering an ERA for Health needs a close interaction of the scientific community with policy makers, R&I funding organizations, health and care systems, European programmes and other stakeholders. This partnership holds a strategic position among the biomedical and health research community and relevant funding organizations. It brings together public and private research performance organisations, pre-clinical and clinical research communities. Therefore it is particularly well suited to promote collaboration and the desired interactions at a transnational level, towards a European (and beyond) Research Area in Health Research.

During Phase 1 the following activities shall be performed:

- Adoption of the Strategic Research and Innovation Agenda
- Establishment of the Strategic Advisory Board
- Adoption of the procedure for preparing and approval the annual work plans
- Process for selecting and developing topics for the R&I funding activities

At a **research policy level**, regular advocacy is necessary within the national and regional funding organizations to inform the responsible policy makers about the medical needs and the importance of research into selected priorities areas. Moreover, ERA4Health and European Commission shall work together to coordinate strategic priorities at European level in both Horizon Europe and the activities developed under the Partnership. A **European Strategic Research and Innovation Agenda for Health Research** is under development with the same essence as the strategic programming process for HE. The SRIA is being developed in the spirit of co-creation. Engaging with future partners and external stakeholders is crucial in the preparation of the Agenda (see Annex II). Main components involved are:

- EU Research Priorities as highlighted under Horizon Europe Key Strategic Orientations
- WHO Priority Medicines Report
- UN Sustainable Development Goals
- National and regional priorities
- Existing initiatives and other relevant stakeholders need to be taken into account (IHI, JPIs, International Consortia, etc.)
- All citizens are invited to contribute to the co-design of the SRIA

The different activities launched by ERA4health will be based on ERA4Health SRIA and will be laid in an annual work plan (AWP) elaborated at the year N-1. The activities agreed on the AWP will be selected thanks to the involvement of different stakeholder groups and a final vote by ERA4Health Management Board. This process will be repeated each year.

On the first phase of ERA4Health (years 1 and 2 of the partnership), the ERA4Health AWP will include the selected topics to support health research and develop innovation, in particular research on Cardiovascular Diseases, Nano Medical Technologies and Diet related diseases/Healthy Diets and the different milestones to develop new approaches to overcome potential challenges in conducting multinational clinical research such as establishing appropriate funding mechanisms coupled with a support framework and identifying topics for IICSs addressing important public health needs.

Hence, multinational calls for IICSs will be implemented in the second phase of ERA4Health.

The methodology to identify the topics to support research will be divided in the following steps (see figure below):

1. Consultation of ERA4Health Management Board and EC to identify the research area of their interest for launching joint funding activities
2. Identification of a list of call topics based on the SRIA by ERA4Health Strategic Advisory Board
3. Consultations of scientific communities, other initiatives (partnerships, JPI, missions..) and identification of the expected impacts of the funded research by stakeholders (e.g. patient or consumer associations). The consultation could be organised across the whole SRIA, some identified biomedical disciplines or transversal topics.
4. Submission of a reasonable number of the identified topics to the Policy Board, which is constituted of the Health Programme Committee and the EC. The consultation of this instance will allow alignment of ERA4Health activities with the one of the Health work programme and for some countries to identify national priorities.
5. Suggestions of the Policy Board on the list of topics.
6. Submission of a topic by EC put into a vote by the ERA4Health Management board will be optional if there is an urgent necessity to address it quickly. The EC could give a mandate to ERA4Health to launch a call in a particular topic due to a societal need not covered in other initiatives (e.g. Covid-19).
7. Setting a vote on the SAB/HPC topic list by ERA4Health RFOs and asking a commitment in case they positively vote on a topic.
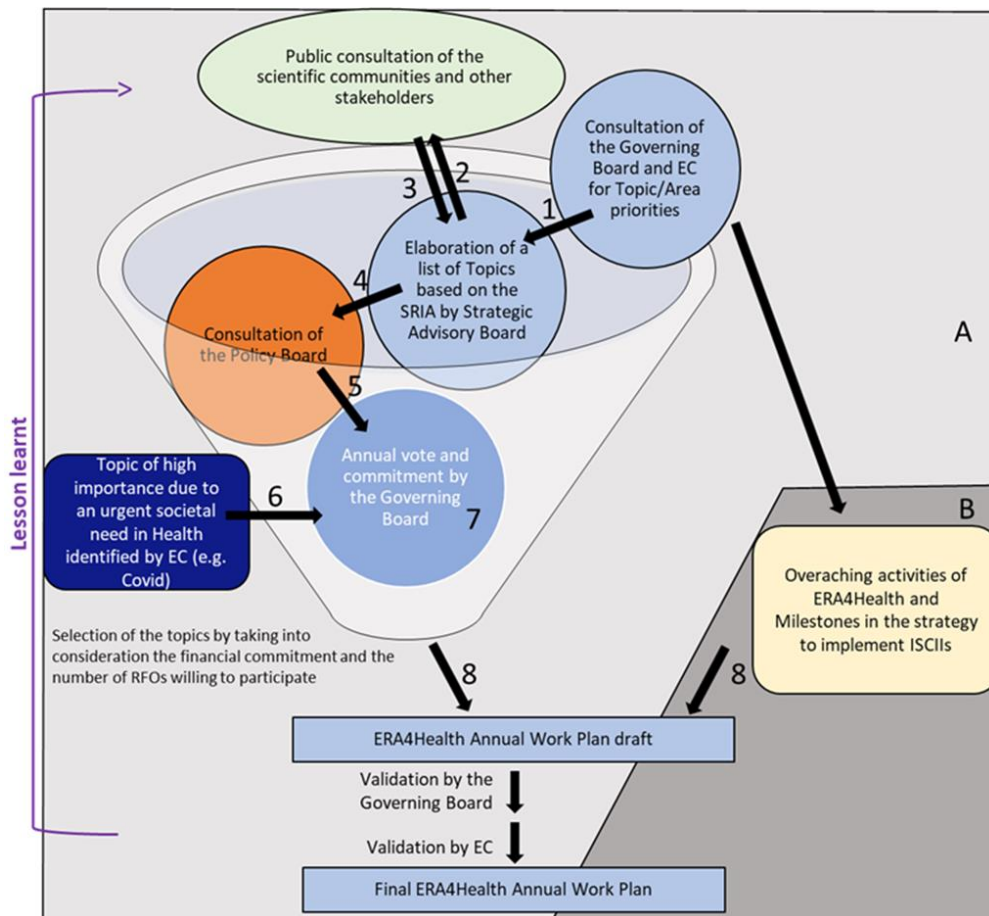
Methodology to elaborate and prioritize the activities of ERA4Health

Launch calls on the decided topics. The decision on the topics will take several parameters into consideration as financial commitments and the number of participating RFOs. Those aspects could also be weighted if a topic has been suggested by another initiative (other partnership, JPI…).

Pillar 2 Joint funding activities

This Pillar is devoted to implement the funding strategy in a standardize way. There are 2 main areas covered by this Pillar: (i) R&I calls for proposals and (ii) Investigator Initiated Clinical Studies.

1. R&I calls for proposals

The following steps will be systematically undertaken for each call:

- establishing a Call Steering Committee (CSC)
- preparation of the call documents and launching of the call
- establishment of review panel and management of the evaluation process; coordination of the funding procedure
- monitoring the joint call and funded projects

The experience of calls launched in previous networks will serve to consolidate the Operational Procedures for Call management and the preparation of the standard call documents:

a) **Internal documents:** existing generic documents will be refined and adapted for specific aspects of each particular call topic and co-funding by the EC in a preparatory phase:
   - Memorandum of Understanding (MoU): This is document delineates the agreement of the partners in the Call Steering Committee to fund a JTC, including the national earmarked budgets.
   - Submission and evaluation procedures: The governance of the call is laid down in a 'Procedures' document annexed to the MoU. It is a compendium of all rules and regulations by the funders for this call i.e., for publication, submission, evaluation, selection, monitoring.

b) **Public Documents for applicants and reviewers**
   - Call text and annexes will be published on the website. The announcement of the call contains the information for the applicants: aim of the call, central rules, guidelines, detailed schedule, national/regional regulations, and earmarked budgets.
   - Proposal templates including the project budget table will be available online. They are intrinsic parts of the electronic online submission tool.
   - Evaluation forms for reviewers are an intrinsic part of the electronic online evaluation tool.
   - Data Management Plan (DMP) will be mandatory for funded projects. A template is provided online.

In addition, web-based tools are needed for processing the call:
- **Partnering tool:** A partnering tool will be used to establish a solid data base for the calls.
- **Electronic online submission and evaluation tool:** a well-established electronic online tool will be used for both, submission and evaluation of the proposals. The tool will be customized for

each call, to allow applicants to securely upload their proposals, and reviewers to access and complete their evaluations online.

Establish the procedures and protocols for the call management. This partnership brings the opportunity to develop a robust assessment for a common methodology of project evaluation that links all aspects (scientific, ethic, RRI, economic...).
The Joint Call Secretariat for each call shall follow similar working methods, documents and procedures. The whole call cycle needs to be monitored, evaluated and follow a continuous improvement cycle.

Finally, it will be also needed to establish the **monitoring and follow-up procedure of funded projects**. Monitoring the output from the research projects shows a measurable impact of ERA4Health. To assess the performance of the funded research projects against these main objectives, answers to a standardized questionnaire by each project coordinator are analysed at the end of the project.

A list of indicators needs to be developed and applied to design the template for periodic and final reports of funded projects. This set of indicators will serve to establish and refine indicators for the ERA4Health funded projects and will need to be adapted to the specificities of the different call topics. The selected indicators will be embedded in the design of the online reporting forms to be used in the follow-up and monitoring activities.

Preparation and implementation of translational JTCs
The planned calls will follow the principle of variable geometry and will be based on priority topics from the SRIA and the Annual Work Plan. Depending on the topic, the scope and the specific needs the JTC could be:

- Standard research and innovation projects (3-year projects)
- Small Collaborative projects
- Call for working groups
- Call for networks
- Any other programme supported by ERA4health partners

Responsibility for management of the JTCs will be shared among several experienced partners who have long standing experience in managing Joint Call Secretariats. In order to guarantee similar standards, SOPs will be revised or further refined for each activity/step. Joint Calls could follow two different schedules depending on the envisaged number of proposals to be received but in any case, call calendars pretend to be the same every year:

- one-stage call (one single submission). Publication of the call in January, the call would be open for at least 2 months and then, proposals are remotely reviewed and discussed during a Peer Review Panel. According to the ranking list is established by the experts, the funding organisations will officially select the project proposals for evaluation.
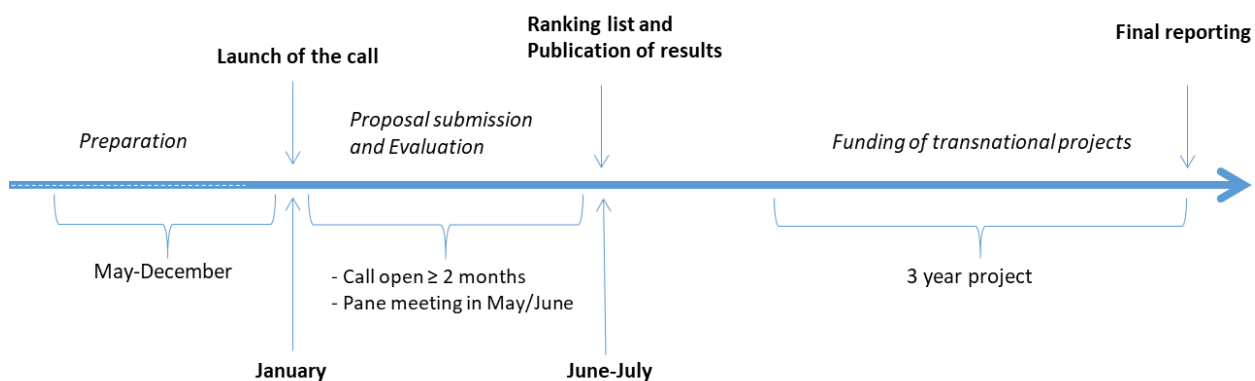
- two-stage call (two submissions: pre-proposal phase and full proposal phase). Publication of the call is planned in November, the call would be open for at least 2 months and then, the pre-proposals are evaluated. After first evaluation step (April/May), consortia are invited to prepare and submit the full proposals that will be evaluated remotely and in a review panel (September). The funding organisations will select then the project proposals for funding according with the evaluation and final ranking list.
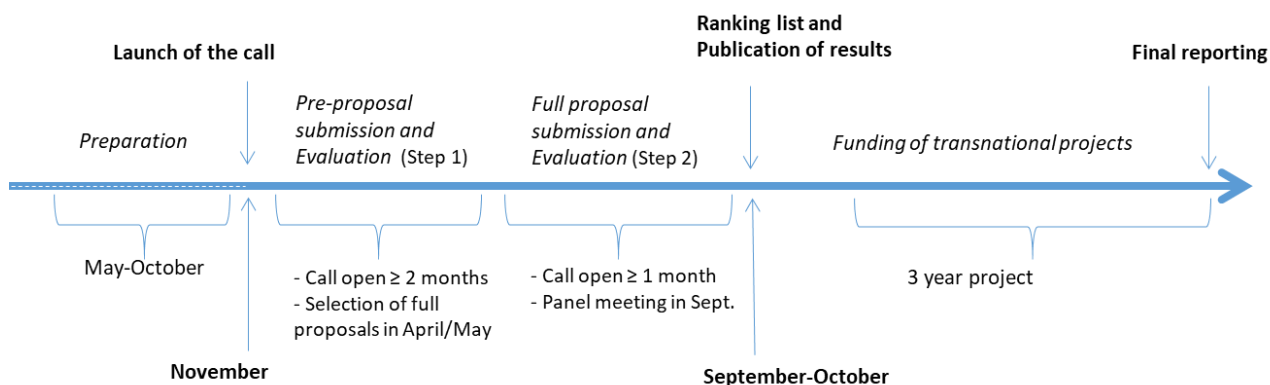
During this Phase at least 2 calls running in parallel will be launched for each year.

2. Investigator Initiated Clinical Studies

According to 536/2014 and 745/2017 Regulations, investigator-initiated clinical studies (IICS) on medicinal products and medical devices require a single sponsor in the European Union, with the possibility of co-sponsorship. The sponsor of IICS is in most cases the employer of the principal investigator (University, Hospital, Research Institute), or other non-profit organisations. The sponsor plays a critical role for the success of the clinical study as it is responsible for the trial management tasks (approval by competent authorities and ethics committees, trial monitoring, adverse event reporting, data management and data sharing, trial master file, archiving, site selection, activation, closure and contracting with investigation sites, financial management, amendments etc). In many countries, clinical trial units (CTUs) were developed to support the universities or hospitals acting as national sponsors, providing expertise in trial design and methodology, data management and biostatistics, and also in trial management tasks (regulatory and ethical approvals, monitoring, vigilance). However, only a few institutions have the capacity and experience to act as sponsors in multinational trials, and for this reason organisations were created to support the sponsors of multinational IICS, acting as a non-profit service provider to IICS

sponsors. This is for instance the main mission of ECRIN, offering federated services based on the coordination of its national partners (consisting of national CTU networks).

Phase 1 of ERA4Health shall serve to develop new approaches that overcome known bottlenecks and challenges to implement **successful** multinational IICS. This will be achieved in close collaboration with ongoing initiatives to support the conduct of multinational non-commercial studies. This would result in stablishing appropriate mechanism(s) to identify topics, pool funding sources, and to launch (joint) calls for EU wide multinational IICSs on various health interventions addressing important public health needs.

Successful and feasible IICS requires both:
- public health relevance, medical soundness and scientific excellence of the proposed IICS
- and the excellence of the trial management, ensuring compliance with the timelines, budget and recruitment target, and delivering high quality data and robust results that can be exploited by the health technology assessment and competent authorities, and transposed into the healthcare strategy.

ERA4Health should be able to provide or make available the necessary tools for Investigators to build robust IICS based on the l**ogistical** and **feasibility** aspects, on the **trial management capacity**, the capacity of the sponsor / co-sponsor and service providers. And in general the following critical success factors:

- compliance with Good Clinical Practice and national / EU regulations
- patient involvement
- compliance with timelines for approval by competent authorities and ethics committees
- trial monitoring strategy
- vigilance reporting
- data capture, data management and data sharing
- GMP manufacturing, placebo, blinding
- country selection strategy
- site and investigator selection strategy, use of objective decision-supporting tools, mitigation measures (closure or activation of sites)
- capacity for contracting with investigation sites, and for contracting with service providers
- provisions for insurance / indemnification
- management of amendments
- cost evaluation and financial management of the study

By the end of Phase 1, all necessary procedures and support should be operational to launch a first multinational call for IICSs on selected health interventions that address important public health needs.

Pillar 3 Transversal Activities

To achieve ERA4Health objectives there are a number of accompanying activities that need to be integrated in the Partnership activities. These are:
- Capacity building activities that will be mainly developed within the funding activities and throughout training workshops for specific issues

- Synergies with other programmes and stakeholders needs to be continuously fed since the activities should be alaign to other programmes and overlaps should be avoided. In addition, new interested funders could join the different funding activities.
- Responsible Research and Innovation is an integral part that covers all aspects of the Partnership activities.
  - Gender
  - Ethics
  - Open Science
- Monitoring and Evaluation Framework in line with European Commission conditions
- Sustainability of the Programme beyond the granted period needs to be analysed in order to take well-argued decisions for the future

2.1.2. Phase 2 (60 months)

During Phase 2, additional multinational calls for IICSs and joint calls for other priority areas will be launched in accordance with the decision of the Health Programme Committee taken at the end of Phase 1 on the focus of the Partnership and the distribution of the budget between IICSs and other areas.

The core activity of the Partnership is pooling resources for funding collaborative research in European priority areas through Joint Transnational Calls. On Phase 2 there will be on place the mechanism established for developing Annual Work Plans, selecting yearly call topics (Pillar 1), operationalize joint calls for IICS and other calls in priority areas (Pillar 2) while running the transversal activities that support the activities of the Partnership (Pillar 3).

In case the decision from the HPC is unsuccessful, ERA4Health will continue its activities and launching joint calls in priority areas addressing important public health needs.

Pillar 1 - From top level objectives to annual priorities

ERA4Health objectives and priorities will be set out in the Strategic Research and Innovation Agenda (SRIA). Annual Work Plans need to be developed according to the procedure described above, which is approved by the Management Board and the EU.

Once topics are selected a Call Drafting Group is created to develop the scope of the call which will be included in the call documents.

The SRIA might need to be updated towards the end of ERA4Health programme.

Pillar 2 – Implementation of Joint Funding Activities

The core activity of ERA4Health is funding transnational research in Biomedical and Health Research and Investigator Initiated Clinical Studies. Annual calls running in parallel are planned to:

- offer new funding and networking opportunities, facilitate international collaboration between research teams through direct support to transnational projects;

- provide a regular, integrated funding opportunity and cover a range of translational approaches (from pre-clinical through clinical and rehabilitation research), and across disciplines;

- provide additional support for the research community to discuss cross-sectional issues e.g. on data harmonization and sharing, RRI, methodological, and scientific exchange, for developing of guidelines, consensus papers etc.

The implementation of calls will follow the documents and standard procedures developed during Phase 1. It is understood that JTC documents will annually be updated according to the specificities of the call and the national preconditions of participating funding organisations.

The electronic online submission tool was also developed during the previous phase and will be adapted for each call.

In case of the IICS, the assessment shall be slightly different in order to ensure that selected studies are properly designed. A two-step evaluation process is proposed with:

1. a first selection round based on the **scientific excellence**, through a central evaluation of the study rationale and protocol as well as the principal investigator (based on the clinical trial template used by DG RTD) including in particular experts on public health / HTA (public health relevance), on methodology (design and scientific excellence), and medical experts (medical soundness). Short-listed projects would then be suggested to seek advice on trial planning, management and consortium engineering, including on partnership with non-profit service providers to the sponsor, or with co-sponsors, to optimise the management capacity of the multinational IICS. The final application dossier will include details on trial management strategy, on the sponsor's capacity and support framework.
2. A second central evaluation step will be conducted by a board of clinical trial operation managers (from non-profit CTUs) and methodology / regulatory experts, including an interview of the PI and sponsor, to select the funded IICS based on the **logistical** and **feasibility** aspects, and on the **trial management capacity**, evaluating in particular the capacity of the sponsor / co-sponsor and service providers.

An important part of this Pillar is the monitoring the call procedures, the progress and the outputs of the calls:
- evaluate the quality of the evaluation and selection procedures of each call;
- monitor and support the projects' progress; and
- analyse the outputs of the funded projects towards the scope of the call.

Monitoring of funded projects

The procedure established during the pilot phase will be implemented during this phase. The main objective is assuring and improve the quality of the funded projects by monitoring their progress.

All funded projects will undergo some reporting requirements. An on-line questionnaire for monitoring annual progress and a final report at the end of the funding period needs to be completed by coordinators of funded consortia. The results of the projects follow-up and assessment shall be presented to the ERA4Health funding partners every year. In addition, the coordinators and/or national/regional group leaders will be asked to present the results of their projects at monitoring meetings.

Pillar 3 – Transversal activities

The transversal activities in Phase 2 will continue as established during Phase 1.

2.2. Resources

Traditionally all ERA-NET partners operated and achieved results together with some clear limitations, no cross border funding and with annual commitment of funds. This partnership wishes to intervene, instead, in several domains aiming to ensure a leader and scalable methodology, providing a documented global simulation result that will evolve gradually by creating new benefits and understanding. Goals achieved will be strong values to validate the innovative planning, attracting incentive for new potential stakeholder to share vision and budget. As a result: competitive investments, empower alternative scenarios, adapt to areas not yet explored.

The planning will meet on one hand the different policies and on the other hand will impact from short to long-term needs. All stakeholders will convey to a work program to accomplish objective and scope of the partnership therefore will contribute to a rapid change moving forward several areas along the years. Embracing a high effective policy that will enable each component to achieve returns.

A major challenge will be the engagement programming structure, this will allow the planning for a variety of stakeholders to join according to the paved plan and the finance conditions favourable to implement suitable activities to reach goals, as following:

- guarantee a methodology, will assess opportunities;
- adoption of key indicators, envisage to monitor developments and will be strategical for staff resources;
- perform a mitigate risk plan for new opportunities, seek compensation of return;
- intensive effort will be devoted to elaborate potential new policies and policy combination;
- The partnership aims to expand progressively the following by the identification of the burden and common risk factor will be functional to better understand the most influencing priorities;
- convey decision on the priority settings will attract investments in several domains and consequently action;
- tailor according to policy options, medium and long-term impact to reinforce the quality level and attractive further funds;
- provide an accurate balance, different health policies around Europe cannot promptly identify emerging signals, to attempt alternative scenarios.

Financial support provided by the participants to third parties is one of the primary activities of this action in order to be able to achieve its objectives. On the other hand, Horizon Europe contribution will be limited to a maximum of 30% of the total eligible costs of the action with a maximum of EUR 30 million of EU contribution for the first 2 years.

On June 2021 it was launched a dedicated survey[34] for:

1. Identifying research and innovation funders that are willing to participate in ERA4Health as partners. As indicated in section 1.4, these might be funders that only fund basic research,

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[34] https://ec.europa.eu/eusurvey/runner/ERA4HEALTHsurvey

funders that fund applied/translational research, funders that only fund clinical research and funders that fund all types of research.

2. Showing a preliminary overview on the interest in participating, priority areas and indicative budget commitment for Joint Transnational Calls.

3. Getting a preliminary overview on the interest in participating, priority areas and indicative budget commitment for the implementation of **joint calls on IICS**.

The results obtained are only indicative and they should be considered as non-binding. Nevertheless, it shows potential trends on the intention and interest translated in potential funding commitment in different areas.

Thirty-one funding organisations from nineteen countries (16 MMSS, 2 AACC and 1 TC) answered to the survey. However, not all of them were able to provide funding figures. For Phase 1, 23 organizations out of 31 indicated that are willing to support the first 2 calls. The tentative commitment was divided among the research areas that will be covered (Cardiovascular diseases, Nanomedicine and Nutrition and diet related diseases) and the total amount of EUR 83,12 Million. Some of the funding organisations were not able to indicate the priority but they had already some tentative funding commitment.
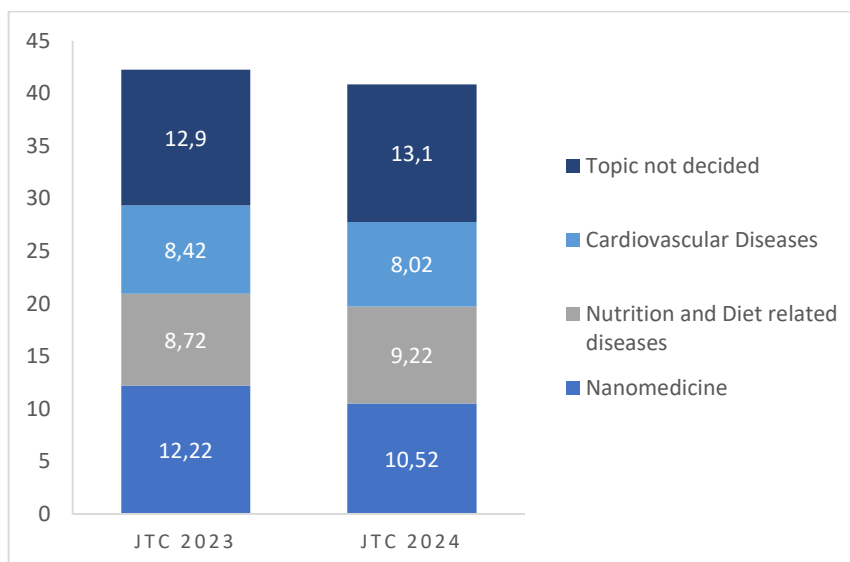
In addition to these figures, there are additional funding organisations that are interested in participating in ERA4health that were not able to complete the survey, thus the budget figures although are only partial suggest that reaching the objective of EUR 100 million for first 2 years is achievable.

The total EU contribution for the overall duration (7 years) is expected to be EUR 110 million[35]. And therefore the total budget of the Partnership is currently estimated to be at least EUR 366,67 Million for research funding including IICS and other implementation costs, described in Section 3.1.

According to the survey results, the potential funding commitment for the 7-year programme that includes potential funding commitment to IICS and other joint calls is EUR 252,45 Million (RE: only

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[35] EUR 30 million in 2022 for phase 1 and a potential EUR 80 million in 2025 for phase 2.

23 answers). Taking into account the implementation phases of ERA4Health, it is planned to revisit the funding commitment and new partners could join between the 2 phases so once the work has started the commitment shall be increased.

Minimum Total Funding Committment € 252,45

- 33% (84,1 M) Clinical studies
- 67% (168,35 M) Non-clinical studies
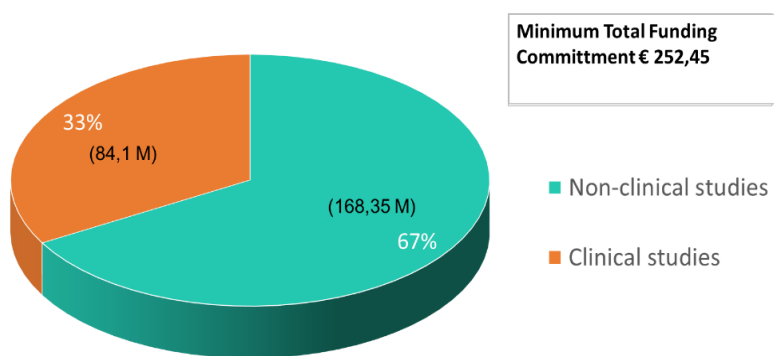
During **Phase 2** a more ambitious activity will take place such as launching of IICS. The efforts devoted during the Phase 1 will exert a pulling force for other Member States and Associated Countries that will join the Partnership, as well as additional funding contributions from those originally participating. It is expected that funding commitments for first call on IICS will be important whereas the following calls might be less attractive. In parallel it is also expected to launch other calls according to the SRIA and annual work plan. The increase on both funding amounts and joint calls launched every year is hard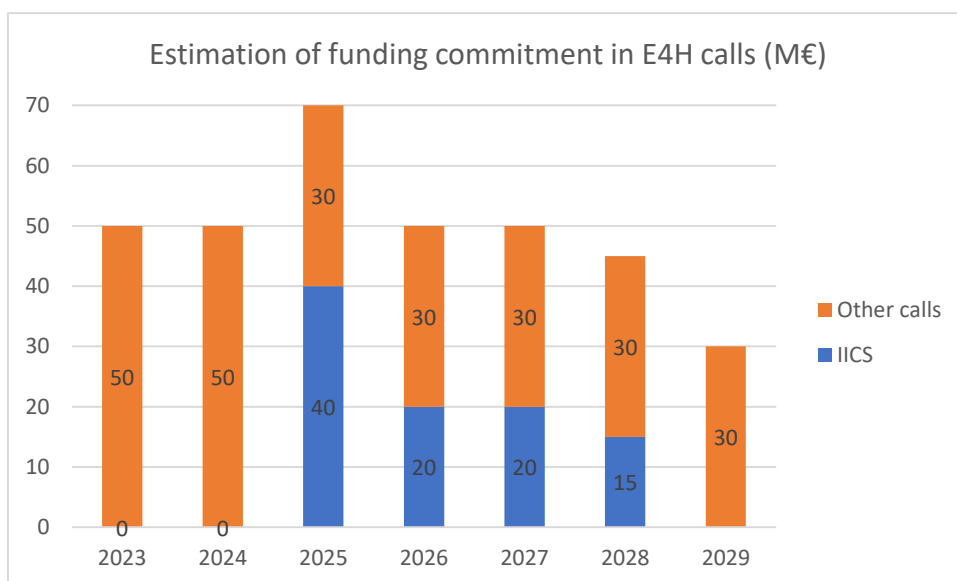 to evaluate, since it will depend on external factors such as the evolving interests and priorities at European and national levels. However, under a realistic scenario, it is forecasted that the minimum funding effort for each year could reach 345 M€. The uncertainties in the follow up of the running projects after the end of the Partnership might result in a low or null interest in launching a call for IICS so according to the figure we preferred to be cautious in the budget estimation.

Estimation of funding commitment in E4H calls (M€)

Year	IICS	Other calls
2023	0	50
2024	0	50
2025	40	30
2026	20	30
2027	20	30
2028	15	30
2029		30

The budget devoted to the implementation of activities shall be up to 3% of total budget. After a preliminary assessment, around 12 M€ have been estimated to be necessary for the completion of the activities planned.

2.3. Governance

The governance of ERA4health address the challenge of integrating previous experiences from different networks and therefore different dynamics created over the years. Nevertheless, although ERA4Health build on previous networks, this Partnership is a completely new instrument

whose governance structure aims to be simple and robust at the same time including both a strategic and an operational level.

The central bodies and main structure to be established are indicated in this Figure. The Terms of Reference document that is under development will describe the detailed functioning of the governance structure, specifying the main tasks and working procedures among the partners as well as the partnership's relation to the European Commission, and other boards and stakeholders. Nevertheless, the central bodies are:

- The **Management Board**, consisting in 1-2 representatives per ERA4Health partner. The MB is the formal decision-making body of the Partnership. It discusses and decides about the strategy and major orientation of the Partnership, priorities and actions to be supported, evolutions in Partnership's membership, contractual issues and allocation of implementation budget among the various activities and among partners. It shall meets at least once a year, preferably twice.
- The **Call Steering Committees** and Clinical Call Steering Committees. The main activity in ERA4Health is the implementation of joint funding activities including IICS and therefore specific Committees will be created for each joint call since ERA4Health follows the principle of variable geometry. The decisions for each call will be taken among the respective CSC. The Call Steering Committee gathers one representative per organisation financially contributing to the given joint call.
- **Executive Committee** drives the operation activities. Composed by the coordination unit and the Pillar Leaders, the Executive Committee will ensure an effective management of the overall activities.

The governance involves key stakeholders, including but not limited to the research and innovation community, patients and citizens, health and care professionals, formal and informal care organisations, innovation owners, policy makers, ethical experts and other Partnerships. These other bodies support ERA4health activities:

- ✓ Call Advisory Boards and Clinical Studies Board. Since the scope of ERA4Health is very broad thematically speaking it will be needed specific or thematic boards for each call that helps in developing the aim of the call and could be involved in the evaluation process.
- ✓ Strategic Advisory Board (Patient organizations, Industry, European Associations for aging or pediatric population, Health Technology Assessment representatives, etc). This board should give a broad and strategic vision, especially on public health perspective.
- ✓ Ethical Advisory Board (ethics and regulatory aspects, patient recruitment…)
- ✓ Policy bodies: Health Programme Committee and EC (DG R&I and DG SANTE)
- ✓ Links to other European Partnerships to ensure complementarities and avoiding potential overlaps

2.4. Openness and transparency

Establishment of the Partnership

The Partnership ERA4HEALTH was originally conceived by the EU with the support of Member States. The concept was presented informally to a wide group of European funding organisations that represent 80% of the funding in current Public to public partnerships. This document was initially developed between three countries (France, Italy and Spain) which expressed interest in the partnership and Commission services. Once the framework of the Partnership was established and all parts of the document filled in, all delegates of the Health Shadow Committee were informed and Commission services produced an assessment with satisfactory results.

After this initial work and further discussions, EC modified the scope of the Partnership by including the launching of Investigator Initiated Clinical Studies. On February 2021, the COM organised a meeting with Member States to present the new scope and kick-off the preparation of the Partnership. Funding organisations for health research involved in the ERA-NETs that will be finished by the eventual start of this Partnership (EuroNanoMed, ERA CVD, ERACoSysMed and ERA-HDHL) were also informed. There were more than 60 participants from 17 countries (AT, BE, CH, DE, DK, EE, ES, FR, HR, IE, IT, LU, NL, NO, PL, PT, SK).

After the meeting it was initiated some preparatory works on voluntary basis in three different working groups:

- Working Group for developing the SRIA (Chaired by M. Wierzbicki from Poland)
- Working Group for establishing the Governance (Chaired by Jolien Wenink from The Netherlands)
- Working Group for analysing Investigator Initiated Clinical Studies (Chaired by Jacques Demotes from ECRIN)

On June 2021, there was a second plenary meeting with 40 participants from 20 countries (AT, BE, DE, CR, DK, EE, FR, HU, IE, IL, IT, LT, LU, NL, NO, PL, PT, SP, SE, UK) to validate the work already done and agree on further steps.

From the very start societal and policy considerations will be captured, in addition to scientific criteria. By engaging with policy makers of different policy domains early on in the development of the Partnership, policy needs will be reflected in the structure, building blocks and Strategic Research and Innovation Agenda of the Partnership. In the same way, at the national level policy makers from different policy domains will be involved through a core group of funding organisations. The final SRIA shall be validated by the mandating authorities/ministries (see Annex II).

A clear and transparent governance will be set-up from the beginning of the Partnership, allowing the participation from a broad range of actors in the Partnership, with no unjustified barriers. The **members** of the partnership will consist of ministries in charge of research, national and regional research funding organisations and other funders. All organisations corresponding to this description will be welcome in the Partnership. So far, over 33 members from at least 22 countries are interested to join this European Partnership, most of them participated in the survey for indicating potential interest and commitment in participate as partner. The partnership will remain open to new members during its whole lifetime, and specific efforts will be developed to ensure a

good geographic coverage within the Partnership with special focus on countries in Europe not (sufficiently) represented.

In addition to the Partnership members, a broad range of **stakeholders** will have the possibility to participate within the Partnership through the Advisory Board. By setting-up the Advisory Board through an open and transparent process, the Partnership will create favourable conditions to engage all relevant sectors from the society and will ensure that a broad range of actors can effectively participate in its activities.

Finally, as part of the EU procedures this document will be published for transparency reasons.

Open access to the Partnership outputs & dissemination policy

The realisation of a European Research Area (ERA) through the principles of Open Innovation[36], Open Science[37] and Open to the World[38] has been a key policy priority for the Commission since May 2016[39]. Open science continues to be recognised as a key enabling element of a revised transformative R&I policy for Europe and a renewed ERA.

Communication and information sharing is a key success factor in achieving the goals of the Partnership. Communication with policy makers, stakeholders, the scientific community and the general public will be two-way, with partners both providing and requesting information.

All information, including Standard Operational Procedures and other documents, will be documented and made available through the Intranet. Results will be made available online and through open access publications. Data generated by the Partnership will be stored in a centralized data platform and made available to citizens. An ethical and legal framework will be developed to enable the use and re-use of data for different purposes and by different users, while respecting data privacy legislation.

Open access to the Partnership results will be promoted at two levels. First, the research projects funded along with the Third Parties and the stakeholders engaged will be asked to actively contribute to result dissemination. In particular in the context of joint calls, the Partnership will strongly encourage open access of data and data sharing along with results dissemination to relevant stakeholders. Here the Partnership will contribute to reinforcing the capacity of the research community for both Open Science and knowledge transfer. The Partnership will for example provide support and advice to the projects it will fund to improve their capacity to engage stakeholders, to produce policy briefs, to develop data management plans, etc.

Second, a devoted strategy will be developed at the level of the Partnership itself to ensure that its mains outputs and impacts are known, widely disseminated, and easily accessible. This will be done through activities part of the transversal Operational Objective 'Communication and outreach'.

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[36] Open Innovation will help Europe to capitalise socially and economically on research and innovation results by bringing more actors and investments into the research and innovation process.
[37] Open Science will help Europe benefit from digitisation and support new ways of doing research and innovation as well as opening up access to research data and results via digital technologies and collaborative tools.
[38] Open to the World will make Europe a leading voice in global debates and tackle societal challenges by engaging more in science diplomacy and global scientific collaboration.
[39] https://ec.europa.eu/digital-single-market/en/news/open-innovation-open-science-open-world-visioneurope

Policy for enlargement of the Partnership and inclusiveness

The consortium remains open to the integration of additional European countries or entities that want to join and contribute with the Partnership resources and objectives. To achieve this, organisations from countries with the intention to join the Partnership have the opportunity to take part in the Management Board meetings as a guest. They will have the chance to introduce themselves and any activities related to the Partnership. In follow up, the Management Board will consider how the country's organisations might be integrated into the work flow and will inform the interested partner regarding possible task allocations within the next Annual Work Plan. If the interested partner and the Management Board come to an agreement, the partner's integration into the Partnership will be voted.

After the start of the Partnership, it will actively strive to widen the Partnership and will continue its efforts to mobilize additional partners. A pro-active policy will be set-up to:
- improve the geographical coverage of the Partnership for countries associated to Horizon Europe: if some countries are not participating in the Partnership, it will actively try to engage with them and to convince them to become members, with a view to improving the joint programming of research between countries;
- ensure that both research programmers and funders and policy makers in the health research field are represented in the Partnership. The participation of these two types of actors is crucial to ensure a link between research and policy/implementation, to better take into account and integrate research and policy making temporalities and to improve the uptake of knowledge to support policies and actions. Pro-active actions will be taken to attract actors which might initially be missing from some countries;
- enlarge the Partnership with non-European countries through a pro-active and step-by-step approach: The Partnership will first engage with these countries through specific activities, such as joint calls. Successful collaboration might consequently lead to full membership, upon decision of the General Assembly.

The Partnership will also make particular efforts to ensure inclusiveness and enhance participation of some countries that are less performing in these types of collaborative networks and thus less inclined to participate (widening). Based on the experience of previous involved ERA-Nets, the Partnership will implement specific activities to increase the participation and success of these countries and their research communities and national stakeholders, including:

- Organisation of staff exchanges to share good practices on the functioning of this co-funded European Partnership and on how to improve the participation and success of small research communities. This will contribute to building capacity of the staff from key organisations from these countries;
- Proactive communication on the functioning of the Partnership and its activities and providing a specific support to these countries for joining the Partnership;
- Communication activities of the Partnership when relevant, e.g. its calls, towards the small research communities. This will be done through, e.g., info days and specific events in the concerned countries, increasing awareness and capacities from the research community on these opportunities;
- Promotion of tools and organisation of networking events to help building connection between research communities (e.g. through Partner Search Tool for calls, etc.).

Development of the Partnership agenda and annual work programme

Topics to be dealt with by the Partnership will be systematically prioritised according to a set of criteria through a participatory process that will include EU and national policy decision makers, stakeholders as well as the scientific community. This could be channelled through the national contact points. The prioritisation process as described will result in concrete questions for more data and research concerning the different building blocks of the Partnership. Scoping documents including targeted research activities will then be developed, which will feed into the annual work plans through an inclusive and transparent process involving all ERA4Health Boards and in close collaboration with the task leads from the different building blocks. This way, the research performed within the Partnership is relevant, strategic, sustainable, and translated and communicated in a comprehensible manner to the appropriate authorities.

Clear and transparent processes will be implemented for developing the Partnership Strategic Research and Innovation Agenda (SRIA) and its annual work programmes (Annex II):

- The Partnership SRIA will be developed based on the inputs from all the Partnership members, as well as dedicated experts. In addition, to ensure that a broad range of views are taken into account, an open consultation will be organised, targeting broad European stakeholders, academic and non-academic organisations in the field of health and medicine research. This transparent process – which will be publicly advertised – will ensure to collect the views from a broad range of actors and end-users. After the public consultation a workshop will be organised with targeted experts to validate the feedback receive form the open consultation. Finally, a high level consultation on the pre-draft of the SRIA will be done.
- As for the annual work programmes, they will be developed based on the inputs from all the Partnership's members and from the Advisory Board, along with close interactions with the services of the European Commission.

During the development of the annual work plans, a specific consultation mechanism will be implemented to identify and select the topics of the calls for research proposals to be implemented each year by the Partnership. Each Partner will initially be invited to suggest possible topics for Joint Calls together with a rationale supporting each topic, taking into account the research needs expressed by academic and non-academic stakeholders. These suggestions will be collected and circulated to all Partners. The European Commission services will also be consulted. The Partners will then be asked to prioritize among these topics, and the priority groups of topics for future calls will be taken into account when developing the annual work plans. For each joint call, the development and implementation of the call, including the elaboration of Scope of the call to be included in the call text, will be made by the Call Steering Committee composed exclusively of partners in a position to co-fund the call with the support from the Call Secretariat. This process has proven particularly successful, as it allows combining an open process (bottom-up approach for the suggestion of topics) while ensuring that the topics prioritized for funding can actually be co-funded by a critical mass of organisations.

Annex I – Analysis of the MMSS participation in existing ERA-Net cofunds

Programme	AT	BE	BG	CY	CZ	DE	DK	EE	ES	FI	FR	HE	HR	HU	IE	IT	LT	LU	LV	MT	NL	PL	PT	RO	SE	SI	SK	UK
Neurodegenerative Co-Fund 2 ('19-'23)	OF MBH	FWOV / FNRS			MEYS	DLR	IFD		ISCIII	AKA	FA / ANR / INSERM			NKFI	HRB	MinSal / MIUR		FNR	VIAA		ZonMW	NSC	FCT / FRCT		VR/RSC	MIZS		UKRI
Neurophisiology Neuron ('16-'21)	FWF	FWOV / FNRS				BMBF / DLR			AEI / ISCIII	AKA	ANR / INSERM					MinSal			VIAA		NWO	NCBR	FCT	UEFISCDI			SAS	UKRI
AMR JPI-EC-AMR ('16-'21)		FWOV / FNRS				BMBF / DLR / JÜLICH	IFD		AEI / ISCIII		ANR					MinSal			VIAA		NWO	NSC	FCT		FORMAS / VR/RSC			UKRI
Cancer Transcan 2 ('15-20')	FWF	FWOV / FNRS				BMBF / DLR		ETAg	ISCIII / FICYT		FA? / ARC / INCa	GRST			OOI	MinSal / ACC / ISS / MIUR			VIAA		ZonMW	NCBR / DCS	FCT			MIZS	SAS	
Cardiovascular ERA-CVD ('16-'21)	FWF	FWOV / FNRS				BMBF / DLR		ETAg	ISCIII		ANR					MinSal			VIAA		ZonMW / DHF	NCBR	FCT / MS	ANCSI		MIZS	SAS	
System Biology EraCoSysmed ('15-'20)	FWF	FWOV / FNRS				BMBF / JÜLICH			ISCIII		ANR				SFI	MinSal		FNR			ZonMW					MIZS	SAS	
Biomedical Technologies Nanomedicine ('16-'21)		FWOV	BNSF		TACR	BMBF / VDI		ETAg	ISCIII / AEI / CDTI		ANR	GSRT			SFI	MinSal / MIUR	RCL		VIAA		STW	NCBR	FCT	ANCSI / UEFISCDI			SAS	

Country column key: Austria (AT), Belgium (BE), Bulgaria (BG), Cyprus (CY), Czechia (CZ), Germany (DE), Denmark (DK), Estonia (EE), Spain (ES), Finland (FI), France (FR), Greece (HE), Croatia (HR), Hungary (HU), Ireland (IE), Italy (IT), Lithuania (LT), Luxembourg (LU), Latvia (LV), Malt (MT), Netherlands (NL), Poland (PL), Portugal (PT), Romania (RO), Sweden (SE), Slovenia (SI), Slovakia (SK), UK (UK)

Legend:
- FO participating 1 /7 Programmes
- FO participating 2 /7 Programmes
- FO participating 3-4 /7 Programmes
- FO participating 5-6-7 Programmes

Acronym	Name of funding organisation
ACC	Alliance Against Cancer
AEI	Agencia Estatal de Investigación
AKA	SUOMEN AKATEMIA
ANCSI	Autoritatea Naţională pentru Cercetare Ştiinţifică şi Inovare
ANR	Agence Nationale de la Recherche
ARC	French Foundation for Cancer Research
BMBF	Bundesministerium für Bildung und Forschung
BNSF	Bulgarian National Science Fund
DCS	Dutch Cancer Society
DHF	Dutch Heart Foundation
DLR	Deutches Zentrum Fuer Luft - Und Raumfahrt EV
ETAg	Estonian Research Council
FA	FONDATION ALZHEIMER
FCT	Fundação para a Ciência e a Tecnologia
FICYT	Fundación para el Fomento en Asturias de la Investigación Científica Aplicada y la Tecnología
FNR	National Research Fund
FNRS	Fonds de la Recherche Scientifique
FORMAS	Swedish Research Council for Environment, Agricultural Sciences and Spatial Planning
FRCT	FUNDO REGIONAL PARA A CIENCIA E TECNOLOGIA
FWF	Austrian Science Fund
FWOV	FONDS VOOR WETENSCHAPPELIJK ONDERZOEK-VLAANDEREN
GSRT	General Secretariat for Research and Technology
HRB	The Health Research Board
IFD	INNOVATIONSFONDEN
INCa	National Cancer Institute
INSEMR	INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE
ISCIII	Instituto de salud Carlos III
ISS	National Institute of Health
JÜLICH	Forschungszentrum Jülich GmbH
MEYS	MINISTRY OF EDUCATION YOUTH AND SPORTS
MinSal	MINISTERO DELLA SALUTE
MIUR	Ministero dell'Istruzione, dell'Università e della Ricerca
MIZS	Ministry of Education, Science and Sport
MS	Ministry of Health Portugal
NCBR	National Centre for Research and Development
NKFI	NEMZETI KUTATASI FEJLESZTESI ES INNOVACIOS HIVATAL
NSC	The National Science Centre
NWO	The Netherlands Organisation for Scientific Research
OF MBH	OSTERREICHISCHE FORSCHUNGSFORDERUNGSGESELLSCHAFT MBH
OOI	National Institute of Oncology
RCL	Research Council of Lithuania
SAS	Slovak Academy of Science
SFI	Science Foundation Ireland
STW	The Dutch Research Technology Foundation
TACR	Technology Agency of the Czech Republic
UEFISCDI	Exec. Agency for Higher Education, Research, Development & Innovation Funding
UKRI	United Kingdom Research and Innovation
VDI	VDI Technologiezentrum GmbH
VIAA	State Education Development Agency
VR/RSC	VETENSKAPSRADET - SWEDISH RESEARCH COUNCIL
ZonMw	Netherlands Organization for Health Research and Development

Annex II – Process for developing the Strategic Research and Innovation Agenda of the European Partnership 'ERA4Health'

ERA4Health content development will be based on HE legislation and the SRIA to set out European Health Research Priorities that will serve as basis for the specific *Annual Research Priorities and Joint Transnational Calls*. These would form part of the *Annual Work Plan*, which will be approved by the Management Board. The annual priorities are going to be based on the need for collaboration in complex areas of biomedical research and innovation and in agreement with all the involved organizations.

The final objective in developing this SRIA is to establish the substantive scope of potential areas of research and innovation to be addressed by ERA4Health. With this in mind, it is necessary to:
- ✓ identify Research and Innovation (R&I) priorities and expectations of individual Member States,
- ✓ ensure alignment and synergies between EU, national/regional priorities and R&I funding programmes,
- ✓ collect additional input from the concerned research and innovation communities (e.g. Scientific and Stakeholder Advisory Board from existing ERA-Nets and JPIs) regarding the R&I priorities,
- ✓ identify and enshrine in the SRIA the expectations of society/patients as well as investigators who contribute to the envisaged ERA-Net like research and innovation activities as well as bottlenecks and measures for the implementation of the IICS,
- ✓ give response to unmet public health needs that are not and cannot be covered by commercially viable clinical trials, or that the current implementation of IICS in these areas is insufficient to meet the needs of society.

The creation of an effective and implementable SRIA will a collective work made by:
- a **Working Group (WG) dedicated to the SRIA**, who will identify priorities and general and specific action objectives, including mapping of the already existing Strategic Research (and Innovation) Agendas in the concerned research fields (with a particular focus on the strategic documents of ERA-CVD, EuroNanoMed, ERA-HDHL, HDHL-INTIMIC) as well as identification of the research and innovation gaps and needs that should be covered by this Partnership for specific research areas as well as overarching research questions to provide a good basis for the flexible topic selection for the annual work plans
- WG on IICSs will identify bottlenecks, which hinder multinational clinical trials and propose measures to overcome them and successfully implement them in a specific joint call for IICSs
- WG on governance will work on the mechanism to prioritize the joint and IICS calls to be launched applying a flexible approach, taking into account the possibility of adapting to changing conditions, including cyclical changes in the SRIA

Together, the 3 WGs will identify the resources at national, regional and European level necessary for effective use of the partnership opportunity.

The SRIA will be the basis of the annual work plans of ERA4Health. The SRIA needs to be finalized and published before the Partnership Proposal and first Annual work plan will be submitted to the EC in response to the call topic HORIZON-HLTH-2022-DISEASE-03-01 by April 2022.

Proposed methodology - Who should WG "SRIA" reach out to?

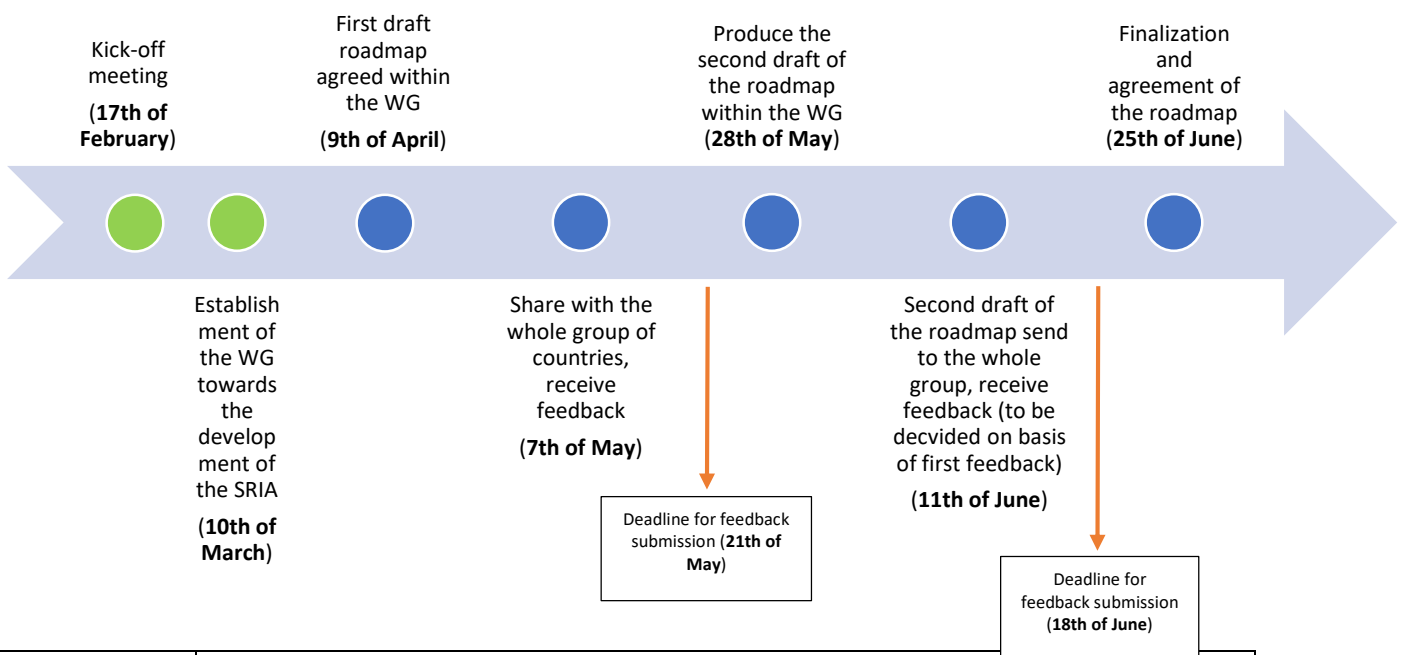At first glance, it would seem that reaching out to:
1. **Policy makers and national decision-making bodies and funding agencies/organizations/ ministries, Member States, associated countries and relevant regions** should be considered in the early development process of a SRIA and in the communication and outreach activities of a partnership to ensure that relevant stakeholders from all countries are made aware of the

opportunities from an early stage of strategy development and have a possibility to jointly define the priorities in this research field. By reaching out to policy makers and national decision-making bodies, a SRIA can inform national and regional policymakers and actively contribute to a better alignment of policy making processes and increase synergies. The local and pan-European regulatory bodies should be also considered for feedback on observed support required for IICS.

The action for this will be sending the first draft among the countries (i.e. the countries representative from the kick-off meeting hosted by the European Commission in February 2021) for their review followed by a survey inquiring first ideas about their national (and regional) research priorities and/or research programmes that they would like to align within this partnership followed by a public consultation with the rest of stakeholders:

2. **Research and innovation communities of the partnership**, including in particular: key opinion leaders, entities able to provide support for the development of the IICS area (local regulatory agencies and the EMA), selected groups or partnerships with a history of conducting international clinical trials (non-commercial). It also seems important to reach out to the corporate sector to identify their capabilities and opportunities for participation in cross-border IICS. Contact the advisory boards or key advisors and experts that are involved in relevant current ERA-Nets/JPIs (e.g. ERA-CVD, EuroNanoMed, ERA-HDHL, HDHL-INTIMIC, JPI HDHL).

Roadmap towards SRIA proposal and further SRIA processing

When?	Milestone
February – May 2020	**Partnership CoDesign** The ERA4Health Partnership concept has been initially developed by a small number of potential partners, in close collaboration and support from the European Commission. The purpose of this task is to create a framework document collecting information through the common template provided by EU for the preparation of European Partnerships. It includes the main elements of the proposed ERA4Health Partnership: a) General information; 2) Context, objectives and expected impacts; 3) Planned implementation. This will act as a basis to receive the inputs from possible members Result: *Partnership Concept Paper Draft*
February 2021	**Kick off Meeting/Implementation of the working group (WG) SRIA**

	The ERA4Health concept was introduced to interested partners and it was decided to implement designated WGs to work on aspects of the proposal (Governance, annual work plans and priorities; SRIA development; IICS)
May 2021	**Roadmap for SRIA development** A roadmap document towards the development of the SRIA has been drafted and agreed within the SRIA WG to be shared with the other WGs and interested funders. It includes information on the ambition, general and specific objectives and methodological approach that needs to be developed. Results: *Roadmap towards the SRIA 1.0*
Mid June 2021	**Enlarging Member States support and Invitation to contribute** A 2nd plenary meeting to present the results from the survey as well as the suggested approaches from the different WG will be held to collect additional input and to obtain new WG members and suggestions for external writers to help with the SRIA writing process.
Mid July 2021	**Roadmap & methodology to develop the SRIA finalized and agreed** A document with the methodological approach including relevant milestones has been developed by the WG SRIA Result: *Roadmap & Methodology to develop ERA4Health SRIA*

Methodology for the development of the ERA4Health SRIA

When?	Milestone
May – June 2021	**Survey to interested partners** A survey has been sent out to interested partners to (1) identify research and innovation funders that are willing to participate in ERA4Health as partners, (2) to get a preliminary overview on the interest in participating, priority areas and indicative budget commitments for joint transnational calls, (3) to get a preliminary overview on the interest in participating, priority areas and indicative budget commitments for joint calls on IICS.
June 2021	**Preparation of the SRIA skeleton** A draft structure of the aspects that need to be covered by the SRIA has been developed by the SRIA WG. Result: *ERA4Health SRIA Draft Structure*
July – August 2021	**Mapping exercise** To successfully reach the ambitious goals of ERA4Health, all relevant areas of health research need to be addressed. Scientific advances continue to be made across the globe and need to

	be taken into account to reach balance between Research and Innovation and to ensure that funds are used in the most efficient way.
	The SRIA will be created on the foundations of European, National and regional research priorities and existing initiatives such as:
	- EU Research Priorities as highlighted under Horizon Europe Key Strategic Orientations *(Martine)*,
	- EU4Health Programme priorities,
	- WHO Priority Medicines Report,
	- UN Sustainable Development Goals *(Martine)*,
	- SRIAs of existing initiatives (JPIs and ERA-Nets like ERA-CVD, EuroNanoMed, ERA-HDHL, HDHL-INTIMIC);
	- Strategic documents of other relevant stakeholders (IHI, EITs, International Consortia, SGPP etc.) and
	- National and Regional specific research programmes, priorities and interests *(will be included during national consultations)*.
	The aims and objectives of the existing initiatives and research strategies will be systematically collected and evaluated to develop complementary research objectives.
Mid-August (internal draft, structure + bullet points) Beginning of Sep: Set date for Nov-workshop Mid-September first draft with input from external experts	**SRIA Draft 1.0**
	A first draft of the SRIA will be developed along a backbone structure based on the survey and mapping results in collaboration with the WG on IICS. The SRIA will be drafted on the foundations of European, national and regional priorities as well as the contributions of existing initiatives (IHI, JPIs, International Consortia, existing SRIAs of ERA-net cofunds, etc.). Interviews with the leaders of existing initiatives would contribute to align ERA4Health strategy with Horizon Europe landscape/environment.
	The document will be prepared by the WG SRIA supported by external writers with the consultation of the responsible EC representatives.
	Result: *first draft of SRIA*
Consultation will be opened first week of October (open for 3 weeks) Survey will be closed end October	**National and stakeholders consultations**
	The public consultation process will gather comments and suggestions from the scientific community, patient associations, interested citizens and other interested stakeholder organisations to identify opportunities for further improvement, potential gaps, suggested collaborations, etc.
	Purposes:
	1. Identification of key gaps and needs in the concerned research fields with priorities over time and recommendations about IICS to inform long-term vision and themes of the SRIA from a broad range of stakeholders, experts and interested members of the public.
	2. Public feedback on the first SRIA draft. A large group of stakeholders is invited to comment on the SRIA while clearly defining the inputs requested in the survey/questionnaire including about the priorisation of the research domains/topics. Oftentimes, targeted dissemination of the public consultation to relevant audiences and targeted invitations can facilitate the quality and relevance of inputs.
	Target group (including but not limited to JPI HDHL, ERA-CVD, EuroNanoMed): Research community, higher education institutions, key stakeholders, policymakers, ministry officials, research funding organizations, industry/professional associations (pharmaceutical,

	diagnostic, biotech and ICT industry), EU/international NGOs, patient organizations, associations, as well as the interested public (citizens). **Method:** The first draft of the SRIA will be published as a pdf-document. An online consultation will be implemented inviting a broad range of stakeholders to give input on specific aspects of the SRIA. Therefore, two different questionnaires will be developed, one for the scientific community, one for citizens and the general public. All the potential members of the ERA4Health Partnership (ministries, funding organizations etc.) will identify the most relevant stakeholders in their country/region. In addition, specific citizen and patient associations will be targeted and asked to share the survey in their network.
End of October 2021	**SRIA Draft 2.0** The outcomes of the consultation activity will be processed and included in the first draft document to develop it into a more comprehensive second SRIA draft. The responsible EC representatives will be consulted during the preparation of the second draft. Result: *second draft of SRIA*
1st half of November (date will be set Mid-September)	**Expert and stakeholder workshop** Organization of a workshop to integrate the input from the public consultation and validate it with experts. **Purpose:** Collating information on SRIA and vision structure and priorities, identification of joint activities to achieve objectives, validation of the input from the general consultation. **Target group:** Key stakeholder, research community, policymakers, enterprises, industry associations, EU/international NGOs, thematic patient organizations and civic / local initiatives **Method:** Physical or virtual. Participation will be on invitation. Invitees could have a wide knowledge on Health Research and Innovation or more specific expertise on one of the sections of the SRIA (research domains but also on the overarching activities (RRI and Impact KPI). They should be gender and geographically balanced as much as possible. The Workshop agenda will be composed of an alternation of plenary sessions, breakout groups and restitution sessions. Group sessions would debate on general concepts to more detailed content of the SRIA. A group will be constituted from the sections/part of the SRIA.
Second half of November 2021	**SRIA Draft 3.0** The 2.0 version will be revised by incorporating the results from the expert and stakeholder workshop including the consultation of the responsible EC representatives. Result: *pre-final SRIA draft*
December 2021	**High level consultation** **Purpose:** Validation of the pre-final SRIA draft by the different participating countries/regions and considering the relevant national/regional health research priorities. **Target group:** Funders and policy makers (national and regional level) **Method:** all the potential members of the ERA4Health Partnership (funding organizations) will validate the document in collaboration with their corresponding national/regional policy makers.
End of December 2021 (Final deadline)	**Final draft SRIA** The final draft SRIA document has been accepted by all partners and is submitted to Commission services for validation. Once validated by EC it will be published. Result: *final ERA4Health draft SRIA* The ERA4Health SRIA will be only approved and adopted by the Management Board once the Partnership is eventually launched.

Annex III All partners in ERA-CVD, EuroNanoMed 3, ERA-HDHL and ERACoSysMed

ACRONYM	COUNTRY	NAME OF PARTNER
AEI	Spain	Agencia Española de Investigación
ANCSI	Romania	Autoritatea Naţională pentru Cercetare Ştiinţifică şi Inovare
ANR	France	Agence Nationale de la Recherche
ASRT*	Egypt	Egyptian Academy of Scientific Research and Technology
BBSRC	United Kingdom	BIOTECHNOLOGY AND BIOLOGICAL SCIENCES RESEARCH COUNCIL
BLE	Germany	Bundesanstalt für Landwirtschaft und Ernährung
BMBF	Germany	Bundesministerium für Bildung und Forschung
BMEL	Germany	Bundesministerium für Ernährung, Landwirtschaft und Verbraucherschutz
BMWFW	Austria	BUNDESMINISTERIUM FÜR WISSENSCHAFT, FORSCHUNG UND WIRTSCHAFT
BNSF	Bulgaria	Bulgarian National Science Fund
CDTI	Spain	Centro para el Desarrollo Tecnológico Industrial
CIHR	Canada	Canadian Institutes of Health Research
CSO-MOH	Israel	Chief Scientist Office of the Ministry of Health
DAFM	Ireland	DEPARTMENT OF AGRICULTURE, FOOD AND THE MARINE
DHF	Netherlands	Dutch Heart Foundation
DLR	Germany	Deutches Zentrum Fuer Luft - Und Raumfahrt EV
ETAg	Estonia	Estonian Research Council
FCT	Portugal	Fundação para a Ciência e a Tecnologia
FNR	Luxembourg	National Research Fund (Fonds National de la Recherche)
FRS-FNRS	Belgium	Fonds de la Recherche Scientifique
FRSQ	Canada	Fonds de la recherche en santé du Québec
FWF	Austria	Austrian Science Fund
FWO	Belgium	Research Foundation Flanders
GSRT	Greece	General Secretariat for Research and Technology
HRB	Ireland	Health Research Board
IFD	Denmark	INNOVATIONSFONDEN
ISCIII	Spain	Instituto de Salud Carlos III
ISS	Italy	National Institute of Health - Istituto Superiore di Sanità
IWT	Belgium	Agentschap voor Innovatie door Wetenschap en Technologie
IZM	Latvia	Ministry of Education and Science
JÜLICH	Germany	Forschungszentrum Jülich GmbH
MEYS	Czech Republic	Ministry of Education, Youth and Sports
MiPAAF	Italy	MINISTERO DELLE POLITICHE AGRICOLE ALIMENTARI E FORESTALI
MIUR	Italy	Ministero dell'Istruzione, dell'Università e della Ricerca
MIZS	Slovenia	Ministry of Education, Science and Sport
MoH - IT	Italy	Italian Ministry of Health
MoST	Taiwan	Ministry of Science and Technology
MS	Portugal	Ministry of Health Portugal
NCBR	Poland	National Centre for Research and Development
NHA	Norway	Norwegian Health Association
RCL	Lithuania	Research Council of Lithuania
RCN	Norway	The Research Council of Norway
SAS	Slovakia	Slovak Academy of Science
SFI	Ireland	Science Foundation Ireland
SPW - DGO6	Belgium	SERVICE PUBLIC DE WALLONIE
STW/NWO	Netherlands	The Dutch Research Technology Foundation
TACR	Czech Republic	Technology Agency of the Czech Republic
TÜBITAK	Turkey	Scientific and Technological Research Council
UEFISCDI	Romania	Exec. Agency for Higher Education, Research, Development and Innovation Funding
VDI	Germany	VDI Technologiezentrum GmbH (VDI), Germany
VIAA	Latvia	State Education Development Agency
ZonMw	Netherlands	Netherlands Organization for Health Research and Development

*Not a partner (GA signatory). Only participating in joint transnational calls as funder