EUROPEAN COOPERATION
IN SCIENCE & TECHNOLOGY

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COST 059/21

**DECISION**

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Subject: Memorandum of Understanding for the implementation of the COST Action “European andrology network– research coordination, education and public awareness” (ANDRONET) CA20119

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The COST Member Countries will find attached the Memorandum of Understanding for the COST Action European andrology network– research coordination, education and public awareness approved by the Committee of Senior Officials through written procedure on 25 May 2021.

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# MEMORANDUM OF UNDERSTANDING

For the implementation of a COST Action designated as

## COST Action CA20119

## EUROPEAN ANDROLOGY NETWORK– RESEARCH COORDINATION, EDUCATION AND PUBLIC AWARENESS (ANDRONET)

The COST Members through the present Memorandum of Understanding (MoU) wish to undertake joint activities of mutual interest and declare their common intention to participate in the COST Action, referred to above and described in the Technical Annex of this MoU.

The Action will be carried out in accordance with the set of COST Implementation Rules approved by the Committee of Senior Officials (CSO), or any document amending or replacing them.

The main aim and objective of the Action is to boost research collaboration, education and public awareness in andrology. This will be achieved by improving research coordination and transfer of knowledge, by supporting training of andrologists and by enhancing public awareness on male health in Europe. This will be achieved through the specific objectives detailed in the Technical Annex.

The present MoU enters into force on the date of the approval of the COST Action by the CSO.

## OVERVIEW

### Summary

ANDRONET aims to boost research collaboration, education and public awareness in andrology, a field of science that deals with male health. Currently there are no European- or world-wide networks through which researchers and clinicians in andrology can interact. The need for such a network is urgent due to the increasing incidence of infertility and testicular cancer, worrying reports of an association of poor reproductive function with poor health, and male predisposition to serious diseases, including Covid-19, leading to shorter life expectancy in men. Male infertility is common, but the patients are currently treated through assisted reproduction technology with primary burden on women. The aetiology of male reproductive problems is heterogeneous and comprises complex interactions between multiple genes and epigenetic factors, with largely unknown impact of environmental factors including infections. This COST Action proposes to increase multidisciplinary research collaboration and data exchange among andrology centres, and transfer of knowledge to European countries with less developed research. The initial consortium includes centres comprising complementary clinical and research expertise at a very high level, but ANDRONET will expand to reach a critical mass necessary for obtaining new knowledge and its possible commercial exploitation across Europe. ANDRONET aims to improve professional education in andrology which is fragmented among several medical branches and will contribute to the recognition of andrology as a medical subspecialty at European level. ANDRONET will strive to properly inform the public with evidence-based knowledge and thereby increase awareness of increasing male health problems and contribute to development of preventive measures.

| **Areas of Expertise Relevant for the Action** | **Keywords** |
|---|---|
| ● Health Sciences: Health services, health care research | ● infertility<br>● male health<br>● spermatogenesis<br>● omics<br>● diagnosis |

### Specific Objectives

To achieve the main objective described in this MoU, the following specific objectives shall be accomplished:

Research Coordination

● To develop a framework for collecting and aggregating existing clinical data on unexplained/ idiopathic male infertility (mainly azoospermia) across Europe, and to define criteria for a standardized central database.

● To promote collaboration and build a network of scientific initiatives in basic and clinical andrology research, with an ultimate aim to uncover the molecular aetiology of diverse disorders using comprehensive and integrated OMICS tools (genomics, epigenetics, RNA, proteomics, exposome, microbiome), as well as complementary in vitro and in vivo models.

● To initiate the integration of the multidimensional and longitudinal data derived from the previous objectives through network analysis and computational modelling, with the potential to identify key genetic determinants, novel molecular pathways, functions and biomarkers.

● To promote exploitation of the new findings to develop novel diagnostic tools and technology among collaboration with small commercial companies and pharmaceutical industry

- To promote the initiation of prospective controlled studies, aimed at the validation of potential novel biomarkers in their utility in clinical management.
- To coordinate studies aiming to gain further insights into the relationships between testicular dysfunction and complex common adult disorders such as metabolic syndrome, cancer and other chronic diseases.
- To disseminate and exploit the outcomes of the project among the professionals through ANDRONET and collaborating andrology centres, and to professionals of 'neighbouring' clinical specialities (gynaecology, endocrinology, urology) as well as to the general public.
- To coordinate the preparation and publication of evidence-based clinical guidelines approved by consensus of internationally recognised experts
- To raise public awareness in male health issues through special events (European Male Health Week) and to prepare multi-lingual educational materials and portals targeting different age groups

Capacity Building

- To connect high-quality scientific communities in the fields of andrology and reproductive biology with the smaller centres from Inclusiveness Target Countries (ITC) and neighbouring countries for better integration of basic and clinical research in Europe.
- To enlarge the existing European network of andrology centres in order to promote the highest level of education in this field, with the wide inclusion of ITC countries.
- To provide networking and leadership opportunities for early career investigators (ECI) in andrology and reproductive biology through their participation in joint activities, training events, meetings and short training missions in partner laboratories.
- To recognize andrology as a multidisciplinary medical subspecialty in Europe, with the ultimate aim of increasing the number of specialized andrologists able to provide the appropriate care for andrological problems.
- To increase collaboration among national and international societies in the field of andrology.
- To reach out to the general community and to include patient organizations, in co-creation strategies to develop awareness tools.
- To establish social network platforms for the general public with focus on various issues related to male health in different age groups (raise social awareness).
- To support the positioning of Europe as a "leading partner" in international andrology-related activities, including input for possible market applications and cooperation with private enterprises.

# TECHNICAL ANNEX

## 1. S&T EXCELLENCE

### 1.1 Soundness of the Challenge

#### 1.1.1 DESCRIPTION OF THE STATE-OF-THE-ART

Andrology is a discipline of health sciences devoted to issues specific to male reproductive and sexual health, in particular endocrine and reproductive disorders of the testis, but also male-specific cancers and male predisposition to some serious diseases. Historically little public health attention has been devoted to andrology in contrast to its counterpart, gynaecology, dealing with the issues related to female reproductive health, for which well-established research and educational programs are available (1). This focus on the female can be explained by various historical societal and medical reasons, despite the fact that **couple infertility in about half of the cases is a result of a problem in the male partner**. The main aim of reproductive medicine has been traditionally on overcoming infertility, one of the most common multifactorial medical problems affecting approximately 20% of couples at reproductive age and having a huge individual and societal impact as well as high associated healthcare costs (2, 3). The role of the male has been largely relegated to merely being a source of spermatozoa, hence current conventional clinical male factor investigations focus on sperm and semen parameters. However, identification of phenotypic sperm abnormalities does not resolve the aetiology of the problem. In only about 15% of the cases causal genetic factors have been discovered (4). Male infertility is clearly multifactorial, and in addition to genetic causes many studies have reported associations, with adverse lifestyle factors, such as smoking, alcohol, obesity; urogenital and/or systemic infections, occupational exposures to toxins, and paternal ageing linked to the changing demographics and delayed parenthood. Therefore, current diagnostic tests used routinely in the clinic identify the cause of just ~40-50% of **male infertility cases. The majority of cases are classified under unknown causes or 'idiopathic'** (5-7).

Despite the lack of knowledge on the aetiology, assisted reproduction technology (ART) and especially intra-cytoplasmic sperm injection (ICSI) are widely and increasingly used to overcome couple infertility. Currently almost 3% of children born in Europe are conceived with help of ART, and this proportion has been growing continuously, reaching a staggering figure of more than 5% of births in some countries (Austria, Czech Republic, Denmark, Slovenia, Spain) (8). However, ART bypasses the problem only temporarily and would propagate male infertility. Under some circumstances, ART combined with testicular sperm extraction can have negative effects on the testis function (9) and may carry specific risks to offspring's health (10). Furthermore, even in cases where couple infertility is mainly due to impaired semen quality, the female partner is subjected to a hormonal stimulation prior to ART and thereby has to carry the major burden of the treatment.

Infertility, reported decreasing sperm counts, regional differences in semen quality and corresponding decline in testosterone levels are temporarily associated with rising incidence of other male reproductive disorders, including cryptorchidism and testicular cancer (11). These associated trends are an outcome of complex and largely unexplored interactions between the individuals' genetic make-up, lifestyle and environment, with growing evidence that some of these interactions begin early in life (11).

Several recent studies presented evidence that reproductive function influences and reflects the function of the whole body and can be a proxy for general male health, showing associations with various other co-morbidities as well as mortality (12-15). These associations need to be corroborated in large multicentre studies. Furthermore, men are more prone than women to many serious diseases, including the recently observed higher mortality from COVID-19 infection, a worrying issue, which needs mechanistic explanation. The so-called X-linked disorders are well known to affect mainly males (e.g. haemophilia A, muscular dystrophy, androgen insensitivity). There are other diseases with more severe clinical course in males, but the underlying causes have not been adequately studied. **There is a clear need for more research in the field of andrology to increase understanding of the aetiology of male-specific health problems**.

Among the reasons for slow progress in the understanding of male reproductive health and its connection to the general health is the **lack of organised connections between the clinics and research**. The research in andrology has relied largely on the efforts of individual laboratories, usually each focusing on a single specific aspect, e.g. genetics, cancer, environmental exposures, and using relatively small cohorts, thus resulting in low statistical power and precluding assessment of the problem from a global perspective. **A more integrated and translational approach is needed to cover all aspects of male fertility and male-specific disorders, and to facilitate interaction between research labs and clinical centres that have large numbers of well-characterised patients and controls**. Such a collaborative approach had recently contributed to improved understanding of genetic aetiology of testicular cancer (16).

Clinical andrology has been a medical discipline largely fragmented among different specialties in different countries. The majority of the andrologists have a specialization in urology, in endocrinology or gynaecology and only a minority of them received appropriately comprehensive andrology education. Few countries officially recognise andrology as a medical sub-specialty, so there is not a great incentive for young trainees to choose this field as a professional career. Education in andrology, meant as a holistic evaluation of male specific health problems, is carried out mainly in the frame of post-graduate courses organized by national andrology societies. At the European level, besides sporadic courses, there are currently only two organizations providing a more structured educational programmes: European Society of Human Reproduction and Embryology (ESHRE; www.eshre.eu ) – with focus on fertility issues, and the European Academy of Andrology (EAA; www.andrologyacademy.net ), which developed a comprehensive curriculum in andrology. However, this curriculum is available only in few EU countries and has no legal value. **Europe-wide recognition of andrology by national and EU-based health boards and institutions is needed**.

To standardize care in clinical andrology, a few manuals have been prepared for some of the aspects related to male infertility, such as the World Health Organization manual on semen analysis (17), or specific reviews on the management of male factor infertility (18). The progress with preparation of standardized guidelines in other aspects of andrology has been slow, and **a coordinated programme is needed to prepare high-quality, evidence-based and focussed guidelines for the professionals**.

The underdeveloped status of andrology is also reflected by poor information and awareness of male health problems among the general community (1). In addition to the worrying trends in reproductive problems highlighted above, it is well known that the mean life expectancy of men versus women is 4-5 years lower in all European countries, and the explanation of this difference remains largely unknown. The gender discrepancy can be attributed not only to genuine biological differences but also to a series of social factors, which require public attention and increased awareness among men. Men in all age groups are at risk of different pathological conditions, some of which are preventable or treatable if diagnosed at an early stage. Access to the relevant information is very variable among European countries: only few have good information available, e.g. in Italy (Amico Andrologo; www.amicoandrologo.it ) and Russia. English-speaking people can find information on the excellent portal on male health developed in Australia (Healthy Male; www.healthymale.org.au ). However, **in most of the European countries, educational materials for the general public are largely missing and filling this gap will be one of the goals of the present COST action**.

### 1.1.1. DESCRIPTION OF THE CHALLENGE (MAIN AIM)

The COST Action ANDRONET will address the needs identified above at three levels: by improving research coordination and transfer of knowledge, by supporting training of andrologists and by enhancing public awareness on male health in Europe.

Research coordination:

Impaired male reproductive function is a multifactorial and highly heterogeneous condition, and may manifest with reduced sperm count/motility, poor sperm morphology or in most extreme cases, with the total absence of spermatozoa in the ejaculate (azoospermia). The focus of ANDRONET research coordination will be on the most severe forms, which account for about 10% of the infertile phenotype and are idiopathic in most cases. In about 50% patients, testicular sperm extraction (TESE) allows the retrieval of spermatozoa and their subsequent use for ICSI. However, TESE fails in a number of cases e.g. arrest of maturation (incl. aberrant meiosis) or complete lack of germ cells, and genetic aetiology has been demonstrated only for some of these phenotypes. The identification of pathogenesis of these phenotypes would be of great value also for some forms of female infertility with problems of meiosis. Importantly, both male and female patients could avoid invasive ART procedures, with consequent health economic benefit for the national health services. ART is expensive and actually not widely available to many couples in EU who require ART. Quantitative and qualitative impairment of spermatogenesis (oligozoospermia or oligo-astheno-teratozoospermia, respectively) remain of unknown aetiology in over 50% of cases, which likely involve genetic/epigenetic and environmental factors. Sample size is a critical issue for identification of clinically relevant genetic factors, since potentially pathogenic mutations must be validated in independent study populations. A required sample size can be reached only in the frame of a network of clinical centres using the same criteria for phenotype description. **Hence, the first challenge of this COST Action is to coordinate and improve the interaction of clinical and research participants across Europe to promote common projects aimed at the genetic dissection of idiopathic azoospermia and oligozoospermia.** The ultimate objective is to develop a panel of genes and possibly epigenetic modifications helpful to stratify patients before attempting TESE or other types of ART management.

The identification of the genetic architecture of male infertility/subfertility is urgently required also in relation to recent epidemiological findings showing higher morbidity and lower life expectancy in men with impaired spermatozoa production versus fertile men, including also an association between azoospermia and cancer susceptibility (12). There is also growing evidence of shared genetic background in some forms of male and female infertility with other phenotypes (18). Apart from a genetic connection, it has been hypothesized that epigenetic factors, changing environment and lifestyle may contribute to the observed association between poor reproductive and general health (9).

Another area of andrology, which recently has gained relevance is the role of the microbiome (19), its alterations and the microbial/viral infections, which can either be sexually transmitted by men (e.g. chlamydia, HPV, Zika) or disproportionally severely affect men (e.g. SARS-Cov-2) (20). It is not clear if COVID-19 can be transmitted with semen and early studies are contradictory. The reasons for higher male mortality from Covid-19 are in urgent need of research input. Preliminary evidence implies a combination of genetic, endocrine and immune factors; the ACE receptor required for the virus entry is encoded by a gene on the X-chromosome, and is highly expressed in the testis, androgen levels have been linked to adverse outcomes, and women can have better immunity and circulatory function, because of oestrogen action and pregnancies (21). Importantly, reproductive outcomes in COVID-19 survivors have not yet been investigated. ANDRONET will coordinate research exchange among centres with required expertise and will launch prospective studies of late effects of COVID-19 in andrology centres in Europe. **Thus, another goal of ANDRONET is to establish a multidisciplinary collaboration addressing the mechanistic background of the unexplored general health-reproductive function connection, with the ultimate aim of implementing preventive measures.**

For all research challenges, the participants of this COST Action will share their specific expertise in clinical andrology, endocrinology, genetics, epigenetics, microbiome and infections, biology of blood-testis barrier and immunology, and environmental medicine.

<u>Education and training:</u>

During the past 20 years, major advances concerning diagnostic tools and novel treatment options were achieved from basic and clinical research on reproductive medicine. In order to provide the best possible care to patients with andrological problems, highly educated specialists with specific expertise in andrology are needed. However, only a few European countries recognize andrology as a distinct subspecialty (Germany, Hungary, Croatia, Estonia, Latvia). The andrological education remains fragmented between various medical specialties; endocrinology, urology, gynaecology, sexology and dermatology. Education is mainly carried out by societies. For example, there are some courses for andrologists organised by ESHRE and the European Association of Urology (ESU) and its andrological subgroup (ESAU), but with focus on semen analysis/ART treatment and surgical management, respectively. Only one society, the EAA is dedicated to the comprehensive training of andrologists in EAA-certified, high quality centres that comprise all aspects of andrology. EAA-accredited training centres are limited to 11 countries in Europe, which means that many EU countries are still missing high level education in this field. **Hence, the second challenge of this COST Action is to improve professional education in andrology, with the following specific aims: i) to organize a pan-European platform in order to provide high level educational training both in clinical and basic andrology; ii) to promote the establishment of training centres in andrology all over Europe; iii) to prepare educational material and clinical guidelines for professionals, including general practitioners and specialists; iv) to organize educational training events in andrology targeted to obstetrics and gynaecology communities to facilitate joint assessment of couple infertility, and v) to promote the recognition of andrology as a medical subspecialty.**

Public awareness of male health:

Given the suggested relationship between poor reproductive health and poor general health, education of the lay public must deal with "male health" in general. Information about male health issues that targets general community ought to be available through appropriate media and portals. There are only a few examples of dedicated organizations and websites in this area. On the global scale, the leading country is Australia, where the efforts are centralised under the publicly-supported *'Healthy Male'* portal. This portal has a great reach, with 396,000 visits, 1200 resources downloaded, and 126,000 engagements on social media within last year (www.healthymale.org.au/about-us/annual-reports). In addition, awareness of the general public has risen after the establishment of 'Movember' (www.movember.com), a popular charity focused on the male-specific cancers. There are also some initiatives growing in Canada, thanks to the efforts of a group of dedicated researchers. In Europe, there are very few international patient-related support groups, including a well-established 'Fertility *Europe'* (www.fertilityeurope.eu), which addresses both men and women with fertility problems. For more general male health information there are only a handful of local portals (e.g. in Italy, Russia, Belgium) but these websites are not accessible to others because of the language barrier. Pan-European, high quality multilingual portals are lacking. **Hence, the third challenge of this COST Action is to raise public awareness on health's role in male fertility and male-specific health problems, with two main aims: i) to fill the gap of the lack of public portals dedicated to men's health in Europe; ii) to organize the translation of the global portal content into local European languages in order to ensure a capillary diffusion of evidence-based knowledge.**

## 1.2 Progress beyond the state-of-the-art

### 1.2.1 APPROACH TO THE CHALLENGE AND PROGRESS BEYOND THE STATE-OF-THE-ART

**Challenge 1: Coordinating the interaction between clinical and research participants to establish a multidisciplinary platform suitable to investigate male infertility and its association with other diseases**

To overcome the slow progress in the understanding of the polygenic and multifactorial aetiology of male infertility and an association between testicular dysfunction and complex common adult diseases, a collaborative, multicentre and multidisciplinary approach is necessary. A substantial advance beyond the existing state-of-the art can only be achieved by joining efforts and exploiting the expertise synergies among the different clinical centres and research laboratories. The partners in the present COST Action are at the forefront of European andrology and basic aspects of human and animal reproductive biology, and jointly provide a complementary synergistic expertise. The basic research laboratories have made important contributions in the identification of congenital (genetic), functional, molecular (epigenetic, RNA, proteomic) and environmental causes of male and female infertility and other reproductive disorders, including testicular and prostate cancer. The clinical teams have world-class knowhow in patient clinical phenotyping, including certified hormone labs, and assessment of lifestyle-related and other non-genetic causes of infertility, including infectious diseases. The participating ANDRONET members belonging to clinical centres will have access to thousands of records of patients with infertility, testicular cancer, infections and various forms of impaired testis function, and corresponding archived samples (DNA, blood, serum, spermatozoa and seminal fluid samples, testis biopsies) which are available for research studies. **This potential for research in terms of sample size and therefore statistical power and complementary expertise of the multidisciplinary teams is unique in the world**. **Coordination and further expansion of the network is needed**, going in two directions: i) connecting world-leading labs with special technological expertise, e.g. in proteomics, epigenetics, animal and in vitro models, epidemiology and environmental issues, with existing specialised world-wide consortia, e.g. in Genetics of Male Infertility Initiative (www.gemini.conradlab.org) or International Male Infertility Genomics Consortium (www.imigc.org), and ii) activating and inclusion of additional clinical groups that have large numbers of patients with precise phenotypic description but limited technical or basic science expertise. If additional samples are needed, e.g. from tissues not included in andrological centres, ANDRONET will collaborate with the existing European research infrastructure for biobanking - BBMRI-ERIC (www.bbmri-eric.eu).

To coordinate research activities, the **ANDRONET network will create a centralised list of existing resources, datasets and andrology-related patient cohorts across Europe**. ANDRONET will leverage funding from other sources to establish centralized databases that would allow detailed aggregation of the available data, and characterization of various subsets of patients and controls. For the clinical databases, ANDRONET will either use an existing platform developed by one of the partners in this proposal, or take advantage of a good commercial platform, e.g. “OpenClinica” (www.openclinica.com). For the database that would integrate clinical and basic data, the network will use high-throughput OMICs methods and standards to integrate multidimensional and longitudinal data collected in the different teams through network analysis and computational modelling. ANDRONET will coordinate its data pooling activities with the existing European Research Infrastructure - ELIXIR (www.elixir-europe.org), which has database mining resources, specialised benchmarking tools, and coordinates the newly EU-funded CONVERGE project on Data Management Planning. Such data integration has a potential to identify novel molecular pathways and clinically useful biomarkers, for either diagnostic utility and/or for making in knowledge-based management decisions on the therapeutic interventions with several outcomes, including spermatozoa quality, hormone levels, achieved pregnancies and live births. The novel findings will be exploited to develop technology attracting ‘start-up’ companies or existing industry. ANDRONET will also collaborate with the European infrastructure for translational research, EATRIS (www.eatris.eu), which is able to facilitate contacts with pharmaceutical industry interested in developing novel diagnostic and therapeutic approaches.

### Challenge 2: Improving professional education in andrology

The challenge of the fragmentation of andrology among several medical disciplines can be overcome by an official recognition of andrology as a dedicated medical subspecialty across Europe. The ANDRONET network aims to learn from the experience of education systems and curricula in the countries that recognise andrology, and to implement a coordinated andrology education and subspecialty recognition in participating countries and at the EU level. This COST Action will attempt to coordinate all the existing exams and certificates by collecting the local initiatives and society-backed initiatives and by implementing one pan-European clinical andrology education and certification system. The Action will perform systematic mapping of all existing dedicated andrology centres and public health care professionals with appropriate expertise in Europe. This information with a working title ‘**Andrology Map of Europe**’ will be available on the COST Action website, guiding doctors and patients with idiopathic infertility and other andrological problems towards appropriate health care providers. In addition, efforts will be made to create new dedicated andrology training centres in countries which do not yet have any structures of this kind, in particular in the ITC, such as Bulgaria, Czech Republic, Lithuania and Romania. The approaches used in this part of the Action will include recurrent and systematic educational courses, webinars and **‘Andrology Schools’** with high quality faculty and programmes, tailored specifically for early career clinicians and trainees. The network will exploit recent developments in online teaching ('virtual' online schools, videos, online meetings, some with simultaneous translation) to ensure that everyone has equal access to best experts and highest quality teaching materials. Educational events will also be inclusive of networks in urology, gynaecology and fertility clinics to promote joint quality assessment and cost-effective management of couples with infertility. Amongst the ANDRONET network there are members which belong to highly experienced andrology centres, which will be able to transmit their expertise in education to less experienced new members. The intrinsic **inclusive** feature of the COST Action will ensure that this objective will be achieved.

**Challenge 3: Raising public awareness on male health issues**

Currently it is not defined how well the general public in Europe is informed about the emerging worrying aspects of male health and infertility issues. We assume that the level of general awareness is at best fragmented, because of the lack of high-quality professionally-driven web portals and rampant proliferation of wrong information on social media. Given that some of the measurable outcomes, such as incidence of male reproductive disorders, continue to rise, the public deserves to be better informed on the worrying trends through evidence-based scientific information. We believe that an international concerted campaign is needed in Europe. The approach of this Action is to use several possible tools, including websites, webinars and social media targeting different age groups. Popular social media, such as Twitter, Instagram, and Facebook have the greatest impact in reaching the public, especially young men, but are not well suited to disseminate complex information. Hence, the network aims to use these platforms to alert the users about new relevant information when it becomes available on the dedicated website(s) and social media platforms. The network will also disseminate interviews and popular-science webinars, which - in addition to the dedicated portal - can be placed on widely searched YouTube platform. Social scientists and psychologists will be approached to help target lay people in an appropriate manner. The material will be specially designed for consumption by the lay public, avoiding scientific and technical terms and including rich graphic illustration-based communication; when possible using co-creation strategies involving professionals and focus groups for a target audience. Here we intend to learn from excellent existing efforts, e.g. the above-mentioned infertility patient support group in Europe and platforms in Italy and Australia. For interested people, there will be access to more specialised materials and literature, including information about the '***Andrology Map of Europe'***, so the patients can find information concerning availability of specialists in their countries and regions. The challenge of multiple languages can be overcome by expert-controlled automatic translations and international exchange of available materials.

As an innovative approach, ANDRONET will organise **annual European 'Male Health Week'**, modelled on successful activities in Australia and Europe, such as 'European Fertility Week' and similar local events practiced in Estonia and Italy. The event will combine a variety of outreach events in public media and special events (info-days, webinars, mobile clinics, free diagnostic tests etc.) to promote andrological check-up among men. These events may be organized in conjunction with other networks/societies to draw attention to distinct topics, e.g. couple infertility, cancer, COVID-19, and other problems.

Tools will be put in place to measure the impact of the actions addressing the three challenges and adjust the actions accordingly (described in section 3. Impact). In addressing these challenges, ANDRONET will unite European researchers and expert clinicians in the field of andrology, with an immediate improvement in what has been so far a highly fragmented and neglected field.

## 1.2.2 OBJECTIVES

The ANDRONET strategy builds on three main pillars: 1) coordination of research efforts in clinical and basic andrology, 2) education and training in andrology, and 3) improvement of public awareness in male infertility and health. These pillars will be addressed in parallel, through the objectives specified below.

### 1.2.2.1 Research Coordination Objectives

- To develop a framework for collecting and aggregating existing clinical data on unexplained/ idiopathic male infertility (mainly azoospermia) across Europe, and to define criteria for a standardized central database.
- To promote collaboration and build a network of scientific initiatives in basic and clinical andrology research, with an ultimate (long-term) aim to uncover the molecular aetiology of diverse disorders

using comprehensive and integrated high-throughput OMICS tools (genomics, epigenetics, RNA, proteomics, exposome, microbiome), as well as complementary in vitro and in vivo models.

- To initiate the integration of the multidimensional and longitudinal data derived from the previous objectives through network analysis and computational modelling, with the potential to identify key genetic determinants, novel molecular pathways, functions and biomarkers.
- To promote exploitation of the new findings to develop novel diagnostic tools and technology among collaboration with small commercial companies and pharmaceutical industry
- To promote the initiation of prospective controlled studies, aimed at the validation of potential novel biomarkers in their utility in clinical management.
- To coordinate studies aiming to gain further insights into the relationships between testicular dysfunction and complex common adult disorders such as metabolic syndrome, cancer and other chronic diseases.
- To disseminate and exploit the outcomes of the project among the professionals through ANDRONET and collaborating andrology centres, and to professionals of ‘neighbouring’ clinical specialities (gynaecology, endocrinology, urology) as well as to the general public.
- To coordinate the preparation and publication of evidence-based clinical guidelines approved by consensus of internationally recognised experts.
- To raise public awareness in male health issues through special events (European Male Health
- Week) and to prepare multi-lingual educational materials and portals targeting different age groups.

#### 1.2.2.2 Capacity-building Objectives

- To connect high-quality scientific communities in the fields of andrology and reproductive biology with the smaller centres from Inclusiveness Target Countries (ITC) and neighbouring countries for better integration of basic and clinical research in Europe.
- To enlarge the existing European network of andrology centres in order to promote the highest level of education in this field, with the wide inclusion of ITC countries.
- To provide networking and leadership opportunities for early career investigators (ECI) in andrology and reproductive biology through their participation in joint activities, training events, meetings and short training missions in partner laboratories.
- To recognize andrology as a multidisciplinary medical subspecialty in Europe, with the ultimate aim of increasing the number of specialized andrologists able to provide the appropriate care for andrological problems.
- To increase collaboration among national and international societies in the field of andrology.
- To reach out to the general community and to include patient organizations, in co-creation strategies to develop awareness tools.
- To establish social network platforms for the general public with focus on various issues related to male health in different age groups (raise social awareness).
- To support the positioning of Europe as a “leading partner” in international andrology-related activities, including input for possible market applications and cooperation with private enterprises.

# 2. NETWORKING EXCELLENCE

## 2.1. Added value of networking in S&T Excellence

### 2.1.1. ADDED VALUE IN RELATION TO EXISTING EFFORTS AT EUROPEAN AND/OR INTERNATIONAL LEVEL

Currently there are no European-wide or worldwide internationally funded networks through which researchers and clinicians in the andrology community can interact, communicate and cooperate. To our knowledge, the only existing program with an overlapping focus on male infertility and male health issues, ReproUnion, is tailored to a regional scale (based in the Danish-Swedish Ôresund region and supported jointly by the EU Interreg V and local funds since 2010 and prolonged until 2021). One of the main aims of the ReproUnion is to establish and comprehensively investigate a large cohort of infertile couples. ANDRONET will facilitate and coordinate interactions between the ReproUnion and other andrology centres with the final aim to establish a pan-European network. Additionally, several participants of the current COST Action proposal have nationally funded research projects, which in part can be leveraged to support the international collaborations.

Other recent but finalized European initiatives covered only very specific aspects of reproductive medicine and biology; the Marie Curie Training Networks on “Reproductive Biology Initial Training Network” (Reprotrain; 2012-2015)” and “GrowSperm (2014-2018)”. As far as COST Actions are concerned, we are aware of a few (now finalized) that had a different focus: animal reproduction (FA0601, FA1201, FA1205), the neuroendocrine control of human reproduction (BM1105), or the differences of sex development (BM1303). The current COST programme includes the ongoing “Sexual Medicine Network” (CA18124), which is focussed on the psychosocial aspects of sexuality in both sexes and transgenders, sexually transmitted diseases, sexual violence, and other aspects of sexuality. There are currently no other EU programmes focusing on andrology as such and on male health from an integrated perspective.

The proposed COST Action ANDRONET thus will cover a presently unfulfilled demand to integrate the research, clinical practice, education and public awareness in andrology from a global perspective, including management of male infertility and associated general health problems. We expect by the end of the first year to involve comprehensively all main European teams and countries to facilitate synergies among all different partial or individual ongoing national efforts.

## 2.2. ADDED VALUE OF NETWORKING IN IMPACT

### 2.2.1. SECURING THE CRITICAL MASS AND EXPERTISE

The initial group of the participants in the ANDRONET network comprises researchers from 25 COST countries (13 ITC and 12 non ITC), 2 NNCs (Russia and Egypt) and 1 IPC (Australia). These participants will attract new members from other European countries, achieving a large diffusion of expertise in andrology all over Europe.

With the endorsement of the COST Action network, representatives of each sub-discipline will reach out to new countries to secure research collaborations at the highest possible level. The exchange of samples and pooling of the existing resources across Europe will secure the necessary statistical power for future studies, especially in the field of genetics, epigenetics and screening for lifestyle/ environmental factors that inversely affect male reproduction.

This will address our objectives of promoting research studies to improve understanding of the aetiology of male subfertility/infertility, testicular cancer and other male-specific health disorders, and will place Europe in a leadership position in this field.

ANDRONET participants will organize training schools to secure high-level training and expertise in new emerging centres. The format of these training schools organized by ANDRONET will be partly based on the existing and successful infrastructure developed by the EAA, but will be expanded to include new emerging topics and novel formats of communication including also online teaching. Increasing the number of centres across Europe will secure the critical mass needed for recognition of andrology as a subspecialty at the European level and to ensure specialized andrology care in all European countries.

ANDRONET already groups andrology experts proficient in at least 20 different languages. Expanding into as many countries as possible will secure reaching out to general public in different European cultures and in the Middle East. Developing educational materials in many languages/formats and tailoring them to different cultures is needed to efficiently raise public awareness of male health issues.

### 2.2.2. INVOLVEMENT OF STAKEHOLDERS

This proposal aims to involve several additional stakeholders within the EU, the COST partner countries as well as from other countries, to maximize its impact.

The stakeholders will include **international andrology-focussed societies** inside Europe (EAA, ESHRE, ESAU) and international societies outside Europe that operate within the broad field of andrology: the American Society of Andrology (ASA) and the Andrology Australia (Healthy Male). There is already an ongoing collaboration between EAA and ASA, which share the same official scientific journal Andrology, co-edited by representatives of the two societies. Some of the ANDRONET participants are members of several above-named societies thus facilitating the initiation of inter-continental exchange of ideas.

In addition, some participants in this Action are also active members of **local /national societies,** e.g. the German Andrology Society (DGA), Italian Society of Andrology and Sexual Medicine (SIAMS), Hungarian Andrology Society, Polish Society of Andrology (PTA), Baltic Society of Andrology. Their involvement will be focused on dissemination of knowledge, clinical guidelines, information about meetings and calls for short-term projects. Additional national and regional societies will be involved with the growing ANDRONET network.

The **Network of Young Researchers in Andrology** (NYRA, www.nyra-youngresearch.eu) is another important stakeholder which will be involved in the research exchange and training of early career investigators. NYRA is currently based in Europe but has numerous members from other continents. Their rotating international board is composed of top young scientists interested in male reproductive biology and medicine.

ANDRONET will make sure to use the resources responsibly by using the **existing European Research Infrastructures** as much as possible, e.g. the successful pan-European research programmes supporting databases (ELIXIR) and tissue-banking (BBMRI).

This Action strives to improve the general awareness of male health issues. To that end, the network will engage existing **patient associations**, including Fertility Europe, and other local patient support groups in Europe. Of relevance the proposal already includes a representation of Advocacy/Membership NGOs. The general public will be targeted via dedicated websites and social media. We intend to attract the attention and lobby the European Commission and national governments to support financially the established platforms, in analogy to the Healthy Male platform in Australia which enjoys support of the Department of Health of the Australian Government.

The Action participants also include active members of the recently created **Male Reproductive Health Initiative**, an unstructured 'grass-roots' international group, without specific funding support, that has recently obtained sponsorship from the leading andrology/reproductive medicine societies around the world, including EAA and ASA (1). This Action aims to follow the suggestions recently elaborated by the World Health Organisation (WHO) in the form of a document "Strategy on the health and well-being of men in the WHO European Region" (EUR/RC68/12). In accordance with the proposed strategy, the ANDRONET members will liaise with various stakeholders in national and international health agencies to persuade them to support male health issues as an urgent general health crisis in need of action.

### 2.2.3. MUTUAL BENEFITS OF THE INVOLVEMENT OF SECONDARY PROPOSERS FROM NEAR NEIGHBOUR OR INTERNATIONAL PARTNER COUNTRIES OR INTERNATIONAL ORGANISATIONS

ANDRONET members from two near neighbour countries -Egypt and Russia- will be involved in this COST Action. The members in these countries are active in international urology and andrology societies. These participants have long-standing clinical expertise in andrology and large numbers of patients hence, they will provide clinical materials for our research objectives. The analysis of subjects with different ethnic backgrounds is especially relevant for genetic studies and for the understanding of gene-environment interaction. On the other hand, they will benefit from the scientific exchange with basic and translational research participants with a consequent improvement of their own research skills. Besides research networking, the members belonging to these centres also have specific features that are relevant for the two additional challenges addressed by this COST Action: education and public awareness.

**Egypt** is one of the very few countries where andrology is recognized as an independent specialization. Exchange on educational experience with our colleagues from Egypt will be of relevance to the establishment of a European curriculum, recognized by the EU authorities (UEMS and governments).

The **Russian** secondary proposer in this COST Action has expertise in educational programs in diagnosis and treatment of male reproductive diseases addressed to general practitioners with the widespread use of telemedicine technologies, which may be of interest for other ANDRONET countries. The Russian Centre was involved in a public campaign of the Russian Ministry of Health "You are stronger!", which aimed to educate public in a responsible attitude to reproductive health (www.takzdorovo.ru/deti/reproductive_health). The Russian colleagues will share their expertise with other ANDRONET members.

ANDRONET has secured participation of researchers from **Australia**, belonging to one of the world-leading multidisciplinary andrology groups. This group has founded Andrology Australia, recently re-named 'Healthy Male' and has an extensive experience in promoting awareness in male health among professionals and lay public. They have created a web-based platform of a very high scientific standard (www.healthymale.org.au). ANDRONET will definitely benefit from contacts with the Australian colleagues with regard to our planned efforts to create similar platforms promoting awareness of male health issues among Europeans.

# 3. IMPACT

## 3.1. IMPACT TO SCIENCE, SOCIETY AND COMPETITIVENESS, AND POTENTIAL FOR INNOVATION/BREAK-THROUGHS

### 3.1.1. SCIENTIFIC, TECHNOLOGICAL, AND/OR SOCIOECONOMIC IMPACTS (INCLUDING POTENTIAL INNOVATIONS AND/OR BREAKTHROUGHS)

The joining of efforts of many independent (and sometimes competing) teams across Europe will allow for the collation of the existing resources and available data, thus raising the statistical power of future collaborative research studies on human male and female infertility. Of relevance, the complementation of synergies and the expertise of labs performing research from the clinical, epidemiological, molecular, functional, omics (genomics, epigenomics, transcriptomics, proteomics, and metabolomics) and environmental (exposome) perspectives will provide a background for the study of male reproductive health from a global and integrative perspective.

The projects enabled and underpinned by this COST Action will potentially lead to the identification of novel biomarkers and pathways that are deregulated in male infertile patients, with better understanding of the key mechanisms involved in normal function and dysfunction, including possible targets for non-hormonal male contraception. Significant findings will be exploited to develop novel technologies, diagnostic tools and possibly new treatment approaches which can attract investment from pharmaceutical industry. The impact of such a large-scale collaborative action and future long-term follow–up studies will be major, including **better diagnosis of the infertile patients, improved clinical decision making and novel treatments of relevance for males and females**.

In addition to infertility, this integrated project will collect data on the associated male health problems, including testicular cancer and genital malformations. Moreover, there is increasing evidence that many of these problems begin early in life through environmental exposures. The ANDRONET network will use its resources to **promote research on the health problems associated with impaired testicular function**, such as cardiovascular and metabolic dysfunction, and higher incidence of cancer. In the long run prevention and appropriate treatment of reproductive dysfunction should result in substantial improvements in general male health.

ANDRONET will strive to produce high quality **scientific publications in Open Access journals with peer-review**, with a minimum planned deliverable of at least 12 articles. The articles will report the collaborative results obtained as a consequence of the Action, as well as other Key Performance Indicators (KPIs) described below in the deliverables section. It is also expected that the collaborative efforts will potentially result in identification of novel clinically useful biomarkers, which will be susceptible to intellectual property (IP) protection through patents, and representing the basis for further exploitation by small/medium size commercial companies (SMEs) and the creation of spinoffs.

ANDRONET will also have indirect positive economic **impact on healthcare services expenses** related to treatment of infertility, which is a very common and widespread problem across Europe. Improving patient stratification according to the proper diagnosis should lead to **more cost-effective treatment strategies** in comparison to already established practices, e.g. pre-TESE prediction based on genetic testing. ANDRONET will also possibly indirectly contribute to prevent the late effects of hypogonadism.

One of the most important expected **societal impacts** of this COST Action will be the integration of the existing fragmented efforts in andrology and raising the status of andrology in Europe. During the first year of this Action, all existing andrology teams and centres in Europe will be approached and integrated. ANDRONET will connect their scientific groups, opening-up new scientific collaborations, and enabling networking and **opportunities for early career investigators**. Furthermore, the Action will promote andrology education among medical professionals across Europe and ITC countries, work towards Europe-wide recognition of andrology as a medical specialty, and increase collaboration with international societies. All these impacts will be measured using as KPIs the number of new andrology training centres created in ITC countries, training schools in andrology-related topics in the context of the Action, and number of published clinical guidelines.

Finally, ANDRONET expects to raise the **public awareness of the male health problems** through the creation/co-creation of social network platforms addressed to the general public. As KPIs of this activity, ANDRONET will measure the number of information leaflets and articles for patients and the lay public, disseminated radio/TV programmes, the number of educational webpages created in the different countries in the local languages. The activity of the social media platforms will also be monitored and measured. Better awareness and knowledge of an association between poor reproductive function and general health will undoubtedly contribute long-term to the earlier recognition of the need for specialised care and faster identification and diagnosis of male health problems.

## 3.2 MEASURES TO MAXIMISE IMPACT

### 3.1.2. KNOWLEDGE CREATION, TRANSFER OF KNOWLEDGE AND CAREER DEVELOPMENT

**Knowledge creation and transfer:**

The creation and expansion of a Europe-wide network of andrology centres, distinguished by large numbers of patients, highest quality of clinical care and research excellence can only be achieved by a cross-cutting activity such as ANDRONET. Facilitating exchanges and collaboration between these groups and **transfer of knowledge to groups with less developed research** will undoubtedly impact on the development of andrology as a high-level discipline in those countries where it has not yet received appropriate attention. Even though many of the ANDRONET members belong to centres which treat similar patients, some have unique clinical and research expertise, e.g. expertise in molecular genetics and epigenetics, developmental endocrine physiology, infections and reproductive immunology, testicular cancer, assisted reproduction techniques and environmental aspects. Several partners submitting the present application are also contributing the largest cohorts of patients and complementary medical research and clinical expertise. New partners invited to participate in the Action during the 1st year will contribute additional clinical samples and expertise. We expect that the exchange of the existing biological materials, and **collection of available data** will have significant impact on knowledge creation in the area of male infertility and other disorders. With regard to the clinical knowledge, the participation of national and international societies, such as EAA will assure quick implementation of novel management modalities in international guidelines, and in clinical centres across Europe. To that end, **ANDRONET will coordinate a close exchange of expertise through a dedicated**

**database and frequent meetings,** including an Annual Action Workshop, the organization of which preferably will be rotating among the ITC countries, even if the online mode is required.

**Career development:**

The Action will establish a working group (WG) on education, with a specific aim of facilitating the career development of young investigators and clinicians. Educational courses and dedicated training schools/campus with programmes focussing on different aspects of andrology (e.g. genetics, pathology and histology, laboratory analysis, endocrinology of reproduction, among others) will be organised at least 2 times a year (if face-to-face meetings are possible) or much more frequently online. These courses are expected to continue in the future, once the structures of the network are established and integration with andrology societies are completed. Credits will be given to participants, which can be used to fulfil the requested educational credits needed to accede to the clinical andrologist exam. With regard to basic scientists, this Action will reach out to the members of NYRA, which groups mainly young scientists interested in reproductive biology. Short research missions (1-3 months) will be organised to allow young scientists interested in learning specialised methodologies (e.g. genomics, epigenetics, and emerging biomarkers) of the collaborating centres.

### 3.2.2 PLAN FOR DISSEMINATION AND/OR EXPLOITATION AND DIALOGUE WITH THE GENERAL PUBLIC OR POLICY

The Action will create a **Working Group on Public Awareness, with main aim of broad dissemination**. In addition other working groups will use several parallel modes of dissemination taking into account specific aspects of the three main pillars:

Research:

Research results obtained through collaborations fostered by this COST Action will be disseminated through presentations at scientific workshops, meetings and scientific publications. In addition to meetings, teleconferences and webinars will be organised to quickly disseminate urgent issues and preliminary results. Collaborative studies will be presented at meetings or published upon mutual agreement between the participating centres. Publication policy will adhere to principles of good scientific and publication practice. Positive and negative results will be published, and only international journals with established reputation will be targeted, **with priority on Open Access journals**. The publications will also include authoritative review articles for translational projects helping to facilitate implementation of the basic research results into clinical practice. Highlights of the scientific results will be publicised on the Action website, and on websites of participating centres and collaborating international societies in order to share with the public. Dissemination impact will be measured through various publication/activity metrics tools. The exploitable findings will be identified at as early a stage of the development as possible. This will ensure that they are identified in time and if possible, can be commercialized and create value. Regarding confidentiality issues, early identification of exploitable results is needed to allow further discussion with all participants. It is envisaged that the communication activities will not compromise the protection of Intellectual Property.

Education:

ANDRONET will organise a calendar of recurrent **educational events** for early-stage scientists and clinicians training in andrology and related medical specialties. Educational materials prepared for these courses and training schools will be made available at the Action website and associated international societies' websites, and later translated by participants from other countries into several languages for further dissemination via local andrology societies.

The Action will also dedicate efforts to disseminate **state-of-the-art educational clinical guidelines** in andrology-related topics. In order to adhere to sharing best practices, these guidelines will be prepared by experts in the field from several centres across Europe and the text will be extensively peer-reviewed by the ANDRONET members belonging to established andrology centres. The approved guidelines will be published in the international journal Andrology. The main results and recommendations will be made available in the adjusted executive version for governmental health authorities, patient advocate groups, and disseminated to professionals via websites and social media.

A separate dissemination strategy will be targeting health authorities in the countries where andrology is not recognised as a medical subspecialty. This will be done by sending **reports** from meetings, workshops, educational courses and attendance figures from clinical andrologist examinations, as well as direct **meetings and lobbying** by the Action leaders and members of the boards of the collaborating international societies.

Public awareness on male health issues:

The Action will take advantage of existing websites dedicated to the general public as already mentioned, i.e. Fertility Europe, Amico Andrologo, or Male Health, to create a **Europe-wide dedicated website**, which will disseminate knowledge and advice on male health-related issues targeting both, general practitioners and lay public. The information will be translated into multiple languages under the expert supervision of Action members to ensure the fidelity of translation. In addition to websites, the key information and advice will be spread via social media, including Facebook, Instagram, YouTube and Twitter, especially targeting the youngest members of the general public. The websites and **social media** portals will have an interactive service. Efforts will be made to target different age groups and their main interests by specially tailored educational material, whenever possible using focus groups and psychologists to better define strategies:

**Young men and adolescents** – the focus will be on male contraception, sexually-transmitted infectious diseases, puberty and fertility problems, testicular germ cell cancer (most common malignancy among young men), history of cryptorchidism and testicular dysgenesis syndrome, impact of drugs, tobacco and cannabis smoking and anabolic drugs on male health,

**Middle aged men** – with focus on infertility issues, impact of unhealthy lifestyle and obesity on fertility and sexual function, importance of exercise and healthy diet, screening for prostate and testicular cancer,

**Older men** – with focus on prostate cancer and lower urinary tract symptoms, late-onset hypogonadism, impact of aging and accumulating mutations in spermatozoa on health of the children, etc.

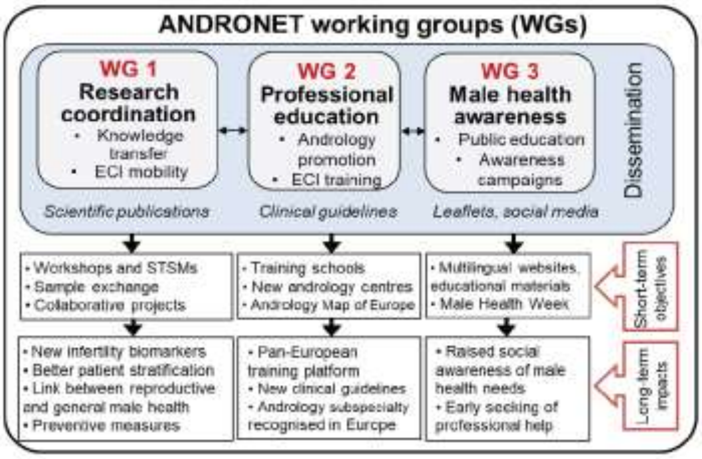
**Women** – they will be targeted especially concerning couple infertility and paediatric disorders, which they should be aware of as mothers (e.g. hypospadias, cryptorchidism, delayed puberty etc.).

# 4. IMPLEMENTATION

## 4.1. COHERENCE AND EFFECTIVENESS OF THE WORK PLAN

### 4.1.1. DESCRIPTION OF WORKING GROUPS, TASKS AND ACTIVITIES

**The Management Committee** (MC) will be responsible for the coordination of the Action, financial management, reporting and monitoring progress in line with the Memorandum of Understanding (MoU) and specific managerial functions such as creation/dissemination of knowledge, website development and management, and the IP policy. During the kick-off meeting with the required representatives from COST countries, the MC will be established and will address the election of representatives to key leadership roles, Action Chair (AC) and the Action Vice Chair (AVC) of the network, Grant Holder, each of the Working Group Leaders (WGLs) and WG Vice Leaders (WGVL), who will jointly form the Core Group (CG). At the first MC meeting additional committees will be established: The Training Committee (TC), Dissemination and Website Committee (DWC), Coordination Committee (CC) and Ethics Committee. The MC will be responsible for gender balance in all committees and activities. Consequently, the issue will remain a standing item on the MC agenda, and gender will be considered when inviting new members and allocating places in TC and short-term scientific missions (STSMs). The CG will meet face-to-face annually and virtually when necessary and will be responsible for direct and daily business of the Action.



The committees will submit annual reports to the MC to monitor and ensure progress in line with the Action objectives. Adjustments will be made if necessary. Working Groups will report directly to the MC.

The interconnection between WGs and their main objectives are summarised in the graph. Subgroups, in accordance with the focus of research will also be created. Note that specific aims of the WGs planned to be achieved within the Action period are listed as “short-term objectives”, while possible “long-term impacts” listed at the bottom of the graph can only be achieved after obtaining additional funding from national and international grant providers.

**Working Group 1: Research coordination**

| | |
|---|---|
| Objectives | 1. To establish a central list of resources and to coordinate the research data<br>2. To monitor and coordinate the exchange of samples between labs<br>3. To organize Short term scientific missions (STSM) for the exchange of early career investigators (ECI) between labs (short term projects) with complementary skills<br>4. To organize the research workshops<br>5. To promote the implementation of research collaborations teams and coordinate contacts with commercial enterprises. |
| Tasks | 1. Collecting information on the available samples and patients, informed consents, encoding of personal data, introducing and updating the information in order to enable collaborations and data mining from the COST action teams.<br>2. Coordination and monitoring of the exchange of samples between labs.<br>3. Prioritisation, approval and monitoring of the ECI exchange.<br>4. Coordination of the speakers and the logistics for the research workshops.<br>5. Monitoring research collaborations initiated as a consequence of the Action |
| Milestones | 1. Availability of a functional and password-protected database of existing resources available online (end of the 1st year)<br>2. Research samples exchanged for joint projects among teams (end of the 2nd year).<br>3. At least one STSM involving a young researcher per lab during the first 2 years.<br>4. Two training workshops (or webinar series) organised by the end of the first year.<br>5. At least one collaborative research project initiated among COST action members by the end of the first year. |

**Working Group 2: Professional education**

| | |
|---|---|
| Objectives | 1. To coordinate the efforts toward recognition of andrology as a subspecialty in the frame of a multidisciplinary joint committee of UEMS<br>2. To help developing new andrology training centres in Europe, with focus on ITCs<br>3. To organize andrology campus/schools to train clinicians in andrology<br>4. To prepare clinical guidelines for professionals |

| | |
|---|---|
| Tasks | 1. Promotion of the recognition of andrology as a subspecialty through meetings and working in liaison with the related scientific European, international and respective national societies, speciality committees and UEMS representatives.<br>2. Coordination of the involvement of the ITC Action participants, training visits to existing established centres and coaching them towards implementation of new andrology training centres.<br>3. Coordination of the speakers and the logistics and venues for training schools.<br>4. Identification of key aspects of andrology in need of updating guidelines, selection of authors, drafting and publication. |
| Milestones | 1. By the end of the 1st year, preparation of the '*Andrology Map of Europe'* and proposal for a multidisciplinary joint committee in andrology in the frame of the UEMS; by the end of the 2nd year establishment of the committee, and by the end of the 3rd year preparation of the European curriculum in andrology.<br>2. A least 3 new andrology training centres established in ITC countries by the 3rd year.<br>3. Two training campus/schools organized by the 2nd year.<br>4. One clinical guideline for professionals prepared each year. |

**Working Group 3: Male health awareness**

| | |
|---|---|
| Objectives | 1. Preparation of information leaflets and articles for patients and the lay public.<br>2. Setting-up internet-based portals with information on male health issues<br>3. Creating the annual European 'Male Health' week.<br>4. Creating the COST Action webpage<br>5. Disseminating scientific/d educational information to professionals, patients and the lay public. |
| Tasks | 1. Identification of the key aspects in need of increased social awareness, drafting, translating and preparation of the contents, dissemination, including assessment of what is currently available.<br>2. Creation of webpages and social media channels, and materials with information on male health issues.<br>3. Coordination of the trainers/speakers, mobile clinics, and the logistics and venues for Male Health week events.<br>4. Designing and drafting the contents of the COST Action webpage and contracting appropriate support technical service for hosting and implementing its functionality.<br>5. Coordinated dissemination of the information through the social media platforms, COST Action dedicated webpage, mailings to interested individuals, though printed material, and through concerted radio and TV programs. |
| Milestones | 1. COST Action webpage available by the end of the 6th month<br>2. To have the first set of materials ready for dissemination by the end of the 1st year<br>3. To have at least one new functional web page with information on male health issues by the end of the 1st year<br>4. Implementation of the first set of disseminations to professionals, patients and the lay public by the end of 1st year. |

### 4.1.2. DESCRIPTION OF DELIVERABLES AND TIMEFRAME

**Deliverables:**

**Working Group 1**: **Research coordination**

- D1.1. Functional central directory of laboratory/country-specific databases (M6)
- D1.2. Reports on the samples between labs exchanged for research purposes at M12, updated yearly (M12, M24, M36, M48)
- D1.3. Report of the young researchers exchanged through short training stays at M12, updated yearly (M12, M24, M36, M48)
- D1.4. Reports of the training workshops organized by the action at M12, updated yearly (M12, M24, M36, M48)
- D1.5. Report on the initiated research projects and scientific publications at M12, updated yearly

(M12, M24, M36, M48)

**Working Group 2**: **Professional education**

- D2.1. Report on the actions taken toward recognition of andrology as a subspecialty at M12, updated yearly (M12, M24, M36, M48)
- D2.2. List of the new andrology training centres created in ITC countries (M24, M48)
- D2.3. Report on the training schools organized in andrology-related topics in the context of the action at M12, updated yearly (M12, M24, M36, M48)
- D2.4. Report on the published clinical guidelines at M24, updated yearly (M24, M36, M48)

**Working Group 3**: **Male health awareness**

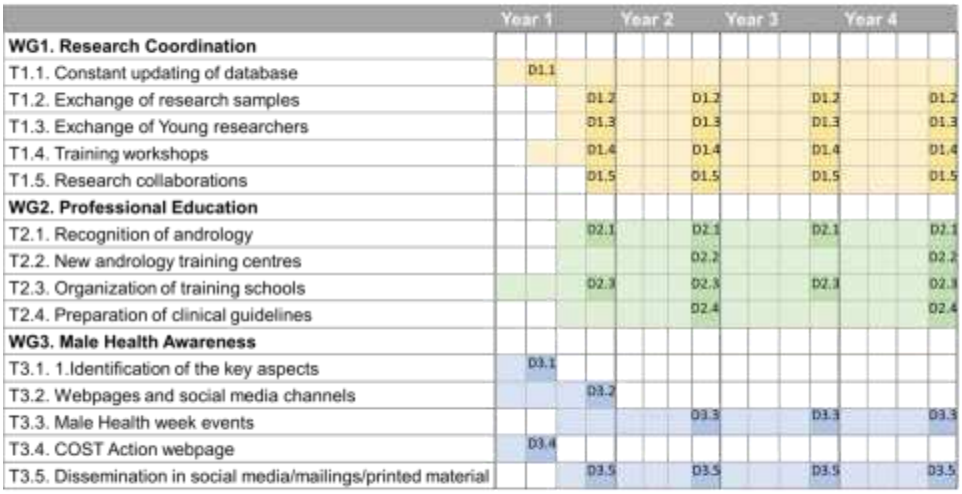
- D3.1. Summary of the key aspects in need of increased social awareness (M12)
- D3.2. At least one web page and social media channels with information on male health issues (M12) D3.3. Male Health Week events report at M24, updated yearly (M24, M36, M48)
- D3.4. ANDRONET Webpage available and functional throughout the action and beyond (M6)
- D3.5. Dissemination Report at M12, updated yearly (M12, M24, M36, M48) including: 1) The availability of the different dedicated action social media platforms (Twitter, Instagram, Facebook, YouTube), 2) The leaflets and articles disseminated for patients and the lay public in the different media and descriptive analysis of the social media analytics, 3) Printed material published by the action (copies of the research articles), 4) The concerted radio and TV programmes by professionals.

### 4.1.3. RISK ANALYSIS AND CONTINGENCY PLANS

The MC will monitor and manage risks. Identified potential risks will be commented at all meetings for joint discussion and implementation of potential mitigation strategies, as summarised in the table below:

| **Risk** | **Mitigation plans** | **Contingency plans** |
|---|---|---|
| Disruption of face-to- face meetings by COVID-19 pandemic. | The meetings and workshops will be adapted to an online format, for which now there is good experience. | The face-to-face events will be planned for the 3rd and 4th years hoping that the situation will be under control. |
| Members do not complete SRs, publications etc. on time | It will be ensured that templates are clear. Dates will be agreed in advance and a reminders used. Difficulties will be circulated early. | If delays occur the MC will directly discuss the relevance of compliance and will jointly agree on new realistic timeframe. |
| Low interaction between participants and WGs | The MC and WG leaders will discuss activities in order to act early and ensure effective communication. | The MC and WG leaders will the necessary meetings and communication means to raise the interaction. |
| Resistance in the EU or other countries to recognize andrology as subspecialty | This risk will be constantly monitored by the WG 2 which will report to the MC in case of resistance detected. | The MC will potentiate dissemination to the lay public and professionals and increase pressure on national societies, politicians/government regulatory offices. |
| Not achieving critical mass and gender balance | The critical mass and gender balance will be constantly monitored by the Chair and Vice-Chair, who will involve all participants. | In case imbalance the Chair and VC will report on this issue at the MC meeting and, if necessary, will discuss, decide and implement corrective measures. |
| Research outcomes not achieved as expected | The research outcomes will be monitored by WG 1 who will report to the CG at each MC meeting. | In case of potential delays, the MC will adopt measures for correction. |
| Not enough funding to deliver some labour intensive tasks | The MC and WG leaders will monitor available funds and adapt in advance the potential difficulties. | Realistic planning in advance will optimize the delivery of the tasks |

## 4.1.4. GANTT DIAGRAM



| | Year 1 | | | | Year 2 | | | | Year 3 | | | | Year 4 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **WG1. Research Coordination** | | | | | | | | | | | | | | | | |
| T1.1. Constant updating of database | ▨ | D1.1 | ▨ | ▨ | ▨ | ▨ | ▨ | ▨ | ▨ | ▨ | ▨ | ▨ | ▨ | ▨ | ▨ | ▨ |
| T1.2. Exchange of research samples | | | ▨ | D1.2 | ▨ | ▨ | ▨ | D1.2 | ▨ | ▨ | ▨ | D1.2 | ▨ | ▨ | ▨ | D1.2 |
| T1.3. Exchange of Young researchers | | | ▨ | D1.3 | ▨ | ▨ | ▨ | D1.3 | ▨ | ▨ | ▨ | D1.3 | ▨ | ▨ | ▨ | D1.3 |
| T1.4. Training workshops | | ▨ | ▨ | D1.4 | ▨ | ▨ | ▨ | D1.4 | ▨ | ▨ | ▨ | D1.4 | ▨ | ▨ | ▨ | D1.4 |
| T1.5. Research collaborations | | | | D1.5 | ▨ | ▨ | ▨ | D1.5 | ▨ | ▨ | ▨ | D1.5 | ▨ | ▨ | ▨ | D1.5 |
| **WG2. Professional Education** | | | | | | | | | | | | | | | | |
| T2.1. Recognition of andrology | | | ▨ | D2.1 | ▨ | ▨ | ▨ | D2.1 | ▨ | ▨ | ▨ | D2.1 | ▨ | ▨ | ▨ | D2.1 |
| T2.2. New andrology training centres | | | ▨ | ▨ | ▨ | ▨ | ▨ | D2.2 | ▨ | ▨ | ▨ | ▨ | ▨ | ▨ | ▨ | D2.2 |
| T2.3. Organization of training schools | ▨ | ▨ | ▨ | D2.3 | ▨ | ▨ | ▨ | D2.3 | ▨ | ▨ | ▨ | D2.3 | ▨ | ▨ | ▨ | D2.3 |
| T2.4. Preparation of clinical guidelines | | | ▨ | ▨ | ▨ | ▨ | ▨ | D2.4 | ▨ | ▨ | ▨ | ▨ | ▨ | ▨ | ▨ | D2.4 |
| **WG3. Male Health Awareness** | | | | | | | | | | | | | | | | |
| T3.1. 1.Identification of the key aspects | ▨ | D3.1 | | | | | | | | | | | | | | |
| T3.2. Webpages and social media channels | ▨ | ▨ | ▨ | D3.2 | | | | | | | | | | | | |
| T3.3. Male Health week events | | | ▨ | ▨ | ▨ | ▨ | ▨ | D3.3 | ▨ | ▨ | ▨ | D3.3 | ▨ | ▨ | ▨ | D3.3 |
| T3.4. COST Action webpage | ▨ | D3.4 | | | | | | | | | | | | | | |
| T3.5. Dissemination in social media/mailings/printed material | | | ▨ | D3.5 | ▨ | ▨ | ▨ | D3.5 | ▨ | ▨ | ▨ | D3.5 | ▨ | ▨ | ▨ | D3.5 |

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